whereby only partial hematopoietic engraftment was achieved. In case of thalassemia, some patients with mixt chimerism can live without transfusion dependency, some progress to full chimerism or greft rejection can occur. That is why chimerism follow up after HSCT in respect to prognosis is so important. Methods In this study 41 thalassemia major patients who underwent peripheral blood stem cell transplantation from matched sibling donor in Akdeniz University School of Medicine Pediatric Hematology and Oncology department were revealed in respect to their chimerism. Conditioning regimens were as follows: BU 16 mg/kg + CY 200 mg/kg for Class I and II patients, BU 14 mg/kg + CY 160 mg/kg for Class III patients. Chimerism evaluation was done in posttransplant first, third, sixth months and at the end of one year. For patients who has same sex with donor variable number tandem repeat was used to evaluate DNA polymorphism while fluorescent in situ hybridization was used for patients who had sex difference with donor. In periodic follow up, patients having more than 10 % donor cell was accepted as having mixt chimerism (MC). Results MC was established in 13 patients (31%). Three patients with MK were given 1.5x108 CD3 + cells as donor lyphocyte infusion. One patients with 20 % donor cells at the the end of year (P4) progressed to aplasia and he died on posttransplat 18th month because of infection. Other patients with MC are still alive without transfusion need. Conclusion Preliminary results of our ongoing study showed that, MC following peripheral blood stem cell transplantation in thalassemia major patients is common finding and it seems sufficient to achieve a stable hemoglobine level.

Abstract: 674 Poster: 581

THE STUDY OF MULTIPOTENCY OF UCB AFTER TWO TIME FREEZING AND THAWING

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Background: The Umbilical Cord Blood (UCB) is the interesting source of stem cells and the its storage procedure is very important for its future recovery. Aims: In this study, the ability of expansion and differentiation of cord blood stem cells after two time freezing and thawing were evaluated. Methods: The UCB was collected after obtaining consent. On average, 60 ml of UCB was collected by gravity into blood bag. Hetastarch was used for red blood cell depletion and total nucleated cells with plasma were freezed with DMSO and Dextran 40 as cryoprotectant in controlled rate freezer and stored frozen in cryovial in liquid nitrogen. After 5 days, the cells were thawed and cultured in expansion media containing stemline Medium supplemented with hematopoietic stem cell expanding stimulatory Factors. After 8 days after expansion, cells were freezed again with the same protocol and thawed after 5 day in IMDM supplemented with cytokines that promote Denderitic Cells (DC) differentiation. The flow cytometry analysis was accomplished for determining DC phenotype. Results: In duration of expansion, total cell count showed a two folds increase in.The viability assay indicated a neglectable differences between two times freezing and thawing. The flow cytometry studies showed that the cells after two times freezing and thawing yet had been maintained their differentiation ability. Sum-mary/Conclusion: In conclusion, multipotency of UCB can maintain even after two times freezing and thawing. These result showed that an efficient protocol for freezing and thawing could be very critical for cell recovery, expansion and differentiation.

Abstract: 675 Poster: 582

AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN CHILDREN WITH NON-HODG-KIN`S LYMPHOMA: A REPORT FROM KOREAN SOCIETY OF PEDIATRIC HEMATOLOGY-ONCOLOGY (KSPHO)

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BACKGROUND. In children, the prognosis of Non-Hodgkin Lymphoma (NHL) cases refractory to treatment or relapsed has been reported to be very poor, and recently, for such pediatric patients, high dose chemotherapy followed by stem cell transplantation has been performed actively. However, presently, the treatment principle and effectiveness have not been established yet. AIM. We examined the result of autologous peripheral blood stem cell transplantation (auto-PBSCT) in

pediatric NHL patients. METHODS. A questionnaire was distributed to the department of pediatric hematology-oncology at university hospitals nationwide and subsequently it was examined by a retrospective method. 34 times of transplantations performed from 1997 to August 2004, at total 11 institutes, and on 33 NHL patients were examined. RESULTS. In regard to the patients, Burkitt lymphoma was 5 cases (15.2 %), lymphoblastic lymphoma was 18 cases (54.5 %), large cell lymphoma was 7 cases (21.2%), and other lymphoma type was 3 cases (9.1 %). Among 34 times of transplantation, patients showing complete response were 22 cases that was 64.7 % of total, the 2year disease free survival (DFS) was 68.1 ¡3/4 9.0 %, and the median follow-up period after transplantation was 2.4 years (range, 0.1 - 7.6 years). All patients are devided to two groups as high risk group and relapse group. High risk group is defined as patient with stage III or IV disease at diagnosis, so underwent auto-PBSCT as a consolidation therapy. NHL patient with relapsed or refractory disease during chemotherapy, who received auto-PBSCT as salvage therapy is assigned to relapse group. The 2-year DFS of high risk group was 83.6 ¡3/4 1.1 %, which was higher than the relapse group 55.9 ¡3/4 12.9 % (P = 0.12). In the cases of the relpase group, in comparison of lymphblastic and non-lymphoblastic lymphoma, their 2-year DFS was 41.0 ¡3/4 16.5 % and 80.0 ¡3/4 17.9 %, respectively, and the survival of non-lymphoblastic lymphoma was high (P = 0.19). After auto-PBSCT, the median engraftment period was 13 days (range, 6 -42 days) in neutrophils, and 19.5 days (range, 7 - 440 days) in platelets. Complications related to transplantation were infection was in 10 cases (30.3 %) that were most prevalent, mucositis was 3 cases (9.1 %), and veno-occlusive disease of liver was 1 case (3.0 %). CONCLUSION. Auto-PBSCT is considered to be able to be applied to pediatric NHL patients safely, and particularly, for the cases of high stage disease at diagnosis (high risk group), it could replace conventional chemotherapy. In addition, relapse group, a high survival rate was observed in the cases with non-lymphoblastic lymphoma, hence, auto-PBSCT is believed to be able to replace conventional salvage chemotherapy, nevertheless, in lymphoblastic lymphoma cases, a low survival rate in auto-PBSCT was detected and hence, to raise the survival rate, it is believed to require the development of other therapeutic modalities.

Abstract: 676 Poster: 583

PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN FANCONI APLASTIC ANEMIA: REPORT OF NINE CASES

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Allogeneic hematopoietic stem cell transplantation (SCT) from healthy donors is the only treatment modality for the correction of hematological abnormalities in Fan-coni aplastic anemia (FAA) patients. We have performed SCT by using two different non total body irradiation conditioning regimens. While anti-thymocyte globulin (ATG, 10-30mg/kg/day, 3 days), cyclophosphamide (5mg/kg/ day, 4 days) and thoraco-abdominal radiation (total 5Gy) were used for six patients (regimen A), fludarabine (120-150mg/m2 totally), cyclophosphamide (10mg/kg/day, 4 days), ATG (30mg/kg/day, 3 days) were given to three patients (regimen B). Five of the patients received regimen A and 4 regimen B. Donors were HLA-matched sibling in 4, HLA-matched parent in 2, partly HLA-matched parent in 2 and HLA-matched unrelated donor in one. All patients and donors were screened by diepoxybutane (DEB) test. Six of the patients were DEB positive. All donors were DEB negative. Median age of the patients was 10 years. All patients received antimicrobial, antifungal prophylaxis and intravenous immunoglobulin (IVIG, 500 mg/kg weekly) from day -7 to day +180. Cyclosporin A (CsA) was used for graft-versus-host disease (GVHD) prophylaxis in eight patients and CsA plus mycophenolate mofetil in one matched unrelated patient. Neutrophil and platelet engraftment occurred in all patients on day 10 (median) and day 21 (median), respectively. Grade II-IV acute GVHD occurred in two patients. Conditioning-related toxicity was milder in regimen B than that in regimen A. Six patients are alive with sustained engraftment and are transfusion independent with a follow-up of 1-48 months. Three patients succumbed from complications of grade IV acute GVHD, post-transplant acute myeloid leukemia and fungal pulmonary infection in regimen A group. All of the regimen B group patients were alive with normal hematological parameters. Totally, six patients are alive with sustained engraftment and are transfusion independent with follow-up of 1-48 months. We conclude that fludarabine based conditioning regimen is safe and associated with

low organ toxicity in FAA patients SCT using sibling, related and unrelated donors.

Abstract: 677 Poster: 584

UNALTERED GLOBAL FIBRINOLYTIC CAPACITY IN ASSOCIATION WITH PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction:Hemostatic alterations due to vascular endothelial damage have been detected during the complicated course of the hematopoietic stem cell transplantation (HSCT). Fibrinolytic response to the ongoing hemostatic cascade activation in HSCT still remains to be elucidated. Material and methods: Global fibrinolytic capacity (GFC) is a unique novel method, which is reflected by the amount of generated D-dimer when the fibrinolysis of a freeze-dried fibrin clot is stopped by introducing aprotinin. GFC is sensitive to all the factors involved in the process of fibrinolysis. The aim of this study is to serially assess GFC at the critical points (days -1, +7, +14, +21 following transplantation) during the course of pediatric HSCT. Twenty-one pediatric patients [4 girls, 17 boys; aged 1-16 years (mean, 7.3 ± 4.9 years)], in whom allogeneic stem cell transplantation (SCT) had been performed (5 acute leukemia, 4 aplastic anemia, 3 chronic leukemia, 3 thalassemia, 3 Griscelli syndrome, and 3 miscellaneous), comprised the study group. Results: In this study, global fibrinolytic response, as reflected by GFC, has been unchanged as an inappropriate response to ongoing hemostatic activation, as indicated by D-dimer, and microvascular damage of HSCT. GFC remained stable despite the development of thrombocytopenia associated with HSCT procedure before the platelet engraftment. Our results indicate that global fibrinolytic response was not evident as a compensatory response to the enigmatic prethrombotic state of the HSCT.

Abstract: 678 Poster: 585

INITIAL WHITE BLOOD CELL KINETICS CORRELATES WITH THE DATE OF ENGRAFTMENT AND TRANSPLANT-RELATED EVENTS IN PEDIATRIC HEMATOPOIETIC TRANSPLANTATION PATIENTS

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Backround: High-dose chemotherapy regimens used in hematopoietic stem cell transplantation (HSCT) patients induce several-fold and sudden drop in white blood cell (WBC) count. Individual response to similar chemotherapy regimens may vary among different patients. In the present study the effect of WBC kinetics on engraftment date and transplant-related events were investigated. Patients and methods: Fifty-eight children who underwent HSCT for malignant and non-malignant diseases were included in this study. Day -9, day 0 WBC count, the ratio of day -9 to day 0 WBC count (WBC ratio), WBC nadir value, and the day in which WBC nadir was achieved were recorded as indicators of WBC kinetics. The effect of those paramaters on the date of engraftment, the probability of developing acute graft versus host disease (aGVHD), grade III-IVmucositis, sinisoidal obstruction syndrome (SOS), total number of febrile days, and overall mortality were investigated. Results: There was a statistically significant positive correlation between the WBC ratio and the date of engraftment in malignant patients ($p<0.001$) which was independent from variables including the degree of HLA match, intensity of the conditioning regimen, G-CSF use, blood group incompatibility and the presence of risk factors for engraftment failure. There was no significant difference in the date of engraftment among malignant patients either with advanced disease or not. In addition, the risk of developing aGVHD in patients with malignant disease positively correlated with the WBC ratio ($p<0.05$) and negatively correlated with the date of WBC nadir ($p<0.05$) independent from above variables. The evaluation of non-malignant patients showed a negative correlation between day 0 WBC count and the total number of febrile days ($p<0.05$); positive correlation between WBC ratio and the total number of febrile days ($p<0.05$), between the total number of febrile days and aGVHD ($p<0.05$), and grade III-IV mucositis and

SOS (p<0.001) all independent from above variables. No significant correlation with mortality was found. Conclusion: The results of this preliminary study suggests that WBC kinetics may influence the date of engraftment and incidence of aGVHD in children undergoing HSCT for malignant diseases. Since the correlation did not seem to be effected by the intensity of the conditioning regimen and other variables, this finding may suggest a critical role for the individual sensitivity to the conditioning regi-men in determining the character of transplant-related events in patients with malignant diseases. In addition, the significant correlation of WBC-related values with the number of febrile days, and the febrile days with aGVHD in non-malignant diseases suggests that the initial response to the conditioning regimen in pediatric HSCT patients should require further attention perhaps to be used as a sensitive marker to determine the probability of transplant-related critical events.

Abstract: 679 Poster: 586

MANNOSE-BINDING LECTIN POLYMORPHISMS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS

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Introduction: Mannose binding lectin (MBL) is an important mediator of innate immune response and has been suggested to contribute to the anti-micro-bial effect in hematopoietic stem cell transplantation (HSCT) patients in whom adaptive immunity is severely depressed. Its anti-microbial effect is principally attributed to activation of complement independently of spesific antibody. MBL levels are highly variable, and largely determined by common polymorphism in the gene encoding MBL (MBL2). We investigated associations between MBL gene polymorphism and the risk of major infection and other transplant related events in children undergoing HSCT. Materials and Methods: Fifthy-four children who underwent HSCT for immunological, hematological and metabolic diseases and their respective donors were included in the study. Exon 1 of MBL gene was amplified by polymerase chain reaction and codon 54 plymorphism (Gly›Asp) analysis was made by RFLP. Results: The incidence of coding mutation was %22 (12/54) in recipients and %32 (17/54) in their donors. Although a positive correlation between the presence of coding mutation in the recipients and the overall mortalite rate was detected this correlation was not statistically significant [%33.3 (4/12) in recipients with coding mutation; %19 (8/42) in those without]. The presence of coding mutations either in the recipients or the donor did not effect the incidence of documented infection, duration of fever, CMV reactivation, transplant related mortality, or neutrophil engraftment time. In addition there was no significant correlation betweeen the incidence of other transplant-related complications including graft-versus host disease, sinusoidal obstruction syndrome (veno-occlusive disease), mucositis (grade III-IV) and the presence of coding mutation in recipients and donors seperately. Blood culture positivity tended to be higher in both recipients and donors with coding mutations; however, this was also not statistically significant. In conclusion, the results of the present study did not show a significant effect of MBL polymorphism on transplant-related events in pediatric HSCT patients

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Abstract: 680 Poster: 587

EXTRAMEDULLAR RELAPSE OF ACUTE MYELOBLASTIC LEUKEMIA FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION: A CASE REPORT

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Background: Extramedullary relapses of acute myelogenous leukemia (AML) after allogeneic transplantation occurs usually in central nervous system (CNS). Here we present a patient who presented with extramedullary relapse outside CNS. Report of the case: A 42 year old female underwent allogeneic transplantion from her sibling in December 2003 during her 1st remission after 3 cycles of chemotherapy. The course was uneventful for 15 months until she presented with swelling and pain in both eyes. She had exophthalmus and oral lesions on physical examination. Magnetic resonance imaging showed bilateral

retro-orbital masses. The biopsy of oral lesions showed no pathology including leukemic infiltration, but biopsy from the right retro-orbital mass disclosed granulocytic sarcoma. Peripheral smear was normal and bone marrow aspiration was free of leukemic infiltration and she was completely chimeric by FISH method. Exophthalmus regressed and her complaints alleviated to a great extend after she received palliative ophthalmic radiotherapy for 15 days. However, lumps in her breasts and a right inguinal lymph node appeared soon after. Fine needle aspiration biopsies from both locations were consistent with leukemic infiltration. Remission induction therapy with daunomycine plus cytarabine was started. Conclusion: Extramedullary relapses outside CNS can occur. Retro-orbital relases may pose a diagnostic challenge because of difficulty in obtaining biopsy from this location.

Abstract: 681 Poster: 588

PERITRANSPLANT USE OF ULTRAVIOLET-B IRRADIATION (UVB) THERAPY IS DETRIMENTAL TO ALLOGENEIC STEM CELL TRANSPLANTATION OUTCOME:

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Graft versus Host Disease (GvHD), GvHD is the major contributor to the morbidity and mortality of allogeneic hematopoietic stem cell transplantation (Allo SCT). Whole body Ultraviolet-B phototherapy has been used for the treatment of GVHD of skin and has systemic immunosuppressive effects. In addition, extracorporeal photopheresis (ECP) has been used for treatment and prevention of GVHD. We hypothesized that whole body UVB therapy may have immunosuppressive effects similar to ECP and improve donor engraftment and reduce the incidence and severity of GVHD in patients receiving HLA-identical sibling or matched unrelated donor allografts. The aim of this study was to test the feasibility of using UVB phototherapy initiated prior to grafting and continued during early engraftment and to determine its impact on transplant complications and outcome.Patients Eight patients median age 55.5 (range 32-65) years with hematological malignancies who were . 55 years of age or had received prior autologous or allogeneic transplantation with myeloablative conditioning or had comorbid conditions that precluded their eligibility for myeloablative transplantation were included in this study.Conditioning regimen was fludarabine 30 mg/m2 iv for 5 days (days8 to -4); cyclophosphamide 1 g/m2/day iv for 2 days (days -3 to -2); equine anti-thymocyte globulin (ATG) 30 mg/kg/day for 2 days (days -2 to -1).GVHD prophylaxis included cyclosporine A (CSA), methylprednisolone and escalating doses of UVB to skin tolerance 3 times a week between T-10 and T+28. Starting UVB dose was based on skin type and escalated to tolerance.Results The conditioning regimen and the UVB therapy were well tolerated. Two patients received all 14 prescribed UVB (cummulative dose of 2000, 3260 mJ /cm2 respectiveley) and, six patients received 8-13 treatments with cummulative dose range of 528-3465 mJ /cm2. Neutrophil (>500ml) and platelet recovery (>20,000/ml) occurred at a median of 13 (12-17) and 6.5 days (1-35) respectively. One patient had secondary engraftment failure and another had mixed chimerism at day 100. Seven of eight patients developed severe acute GVHD, Grade III (n=5) and IV (n=2). Six had skin, 5 had GI and 1 had liver involvement. Four patients died from sepsis (n=2), acute GVHD (n=1), or chronic GVHD (n=1). Four patients are alive (130-287 days), 2 without GVHD or relapse. Conclusions Addition of peritransplant UVB therapy, using the standard minimally erythemogenic protocol is detrimental to outcome of reduced conditioning allogeneic stem cell transplantation. UVB might have altered skin and systemic cytokine and immune cell composition in the host and increased the incidence of GVHD and the treatment related mortality. Although other phototherapeutic modalities may be effective against GVHD, UVB therapy should be avoided during early phases of allogeneic transplantation.

Abstract: 682 Poster: 589

BORDERLINE PULMONARY HYPERTENSION IN PATIENTS WITH MALIGNANT INFANTILE OSTEOPETROSIS

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tion Unit, ² Hacettepe University Medical School, Childrens Hospital, Cardiology Division, Ankara, TURKEY

Introduction: Severe pulmonary hypertension (PH) during the course of hematopoietic stem cell transplantation (HSCT) has recently been described in 20-30% of patients with malignant infantile osteopetrosis (MIOP) and has been associated with poor outcome. The pre-trans-plant evaluation of those patients by echocardiogram has failed to identify pulmonary hypertension before initiation of the conditioning regimen. Patients and results: We hypothesized that a pretransplant sub-clinical PH may progress to a severe defect during the period of fluid overload as part of the conditioning regimen. Three children with MIOP underwent detailed pre-transplant cardiac evaluation by echocardiogram through assessment of tricuspid regurgitation. Two patients were diagnosed as borderline PH, one of whom underwent cardiac catheterization. The diagnosis of borderline pulmonary hypertension was confirmed by cardiac catheterization and the patient was followed closely for respiratory symptoms and responded well to morphine sulphate administration at the times of deterioration. Conclusion: Aberrant macrophage repopulation following HSCT or upper airway obstruction has been suggested to contribute to PH in patients with MIOP. In addition a pathophysiologic link between osteoclast function and pulmonary vascular pressure has also been suggested although not proven. In summary, this preliminary case study suggests that borderline PH may be present in patients with MIOP and may worsen during the course of HSCT at the times of fluid overload. Recognition of the subclinical defect pretransplant may be life-saving by early intervention.

Abstract: 683 Poster: 590

CHEDIAK-HIGASHI SYDROME: HEMATOPOIETIC CHIMERISM IS ABLE TO CORRECT GENETIC DEFECT

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Chediak-Higashi sydrome (CHS) is a rare autosomal recessive disorder characterized by oculocutaneous albinism, bleeding tendency, recurrent bacterial infection and is often lethal by the third decade of life. It affects the lysosomes or lysosome like organelles of cells within multiple tissues throughout the body primarily neutrophils. The hallmark of CHS is the presence of singular or characteristic multiple intracellular inclusions in the neutrophils and other cells. Although allogeneic bone marrow transplantation is the only known curative therapy, experience with the peripheral blood stem cell transplantation is very limited. Here we describe a case of a young boy with Chediak-Higashi syndrome, who underwent peripheral blood stem cell transplantation (PBSCT) resulted in only with partial donor chimerism and with only partial donor engraftment he had been well. 5-year-old boy was admitted to our hospital with the complaint of fewer, cough and abdominal distension. He was the first child of consanguineous parents and he was well until the age of two when abdominal distention being apperaed. He has not been experienced any severe infection or bleeding disorder. In physical examination, hypertrichosis, desquamation, hyperpigmentation, vitiligo changes on the skin, loss of teeth, gingival hypertrophy, generalized lymphadenopathy were revealed. Hepatosplenomegaly was remarkable; the spleen extended to the pelvic brim and the liver was approximately 10 cm in diameter in midclavicular line below the costal margin. Laboratory evaluations weres as follows: Hb: 8.4 gr/dL, WBC:1800/mm3, Plt:17000/mm3. Neutrophil chemotaxis was defective. Opthalmological examination in respect to oculer albinism was normal. Trichogram examination of the hair revealed multiple granules. Neutrophils showed many large coalescent granules diagnostic of CHS. The child underwent PBSCT using stem cells from her younger HLA-DR matched sibling brother. Conditioning regimen included BU (16 mg/kg) + CY (200 mg/kg). GVHD did not develope and engrafment was achieved for neutrophil and thrombocyte on posttransplant day 18 and 25, respectively. Characteristic granules were not seen in peripheral smear. Chimerism follow up was done by VNTR (variable number tandem repeat) and it was 59%, 72% and 71 % of donor cells in posttransplant first, third and sixth month, respectively. Hepatosplenomegaly became less remarkable and he has never had any major systemic infection. CHS is a rare disorder with the only curative therapy is being hematopoetic stem cell transplantation. Although the experiences with transplantation in this group of patients are increasingly reported, there are limited cases in which peripheral blood was used as stem cell sources. In addition, the knowledge about the efficacy of the partial donor

hematopoetic engraftment in these patients is still very limited. The child reported here showed that peripheral blood can be used as a stem cell source in CHS and partial donor engraftment seems to be sufficient for achieving successful protection.

Abstract: 684 Poster: 591

DIFFUSE ALVEOLAR HEMORRHAGE DUE TO DONOR LYMPHOCYTE INFUSION IN A CASE OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Diffuse alveolar hemorrhage (DAH) is a life threatening non infectious pulmonary complication seen in about 20% of hematopoetic stem cell transplant (HSCT) recipients. The onset of DAH is usually within the first 30 days after HSCT. Although the etiology of DAH still remains uncertain, lung tissue injury, inflammation and cytokine release are the defined criminal factors in the pathogenesis of DAH. It is usually presented with the signs and symptoms of pneumonia, such as fever, progressive dyspnea, non productive cough, arterial hypoxemia and diffuse pulmonary infiltrates on chest radiograms. A 34 year old man, who received donor lymphocyte infusion (DLI) 2x107/kg CD3 positive cells performed on day 196 of HSCT because of hematologic relapse of acute lymphoblastic leukemia, developed fever, dyspnea, hypoxemia, hypotension and a slight decrease in hemoglobin level 4 days after DLI. The chest radiogram was normal, while computerized tomography revealed diffuse paranchymal consolidation at lower lobes. Agressive transfusion support and ampiric antibiotic and antifungal therapy were given. Diagnostic bronchoscopy was performed on day 7 of DLI since the patient`s clinic status worsened progressively. During bronchoscopy, progressively bloodier return of bronchoalveolar lavage fluid was observed and hemosiderin-laden macrophages were seen on the cytologic examination of the bronchoalveolar fluid. Afterwards, the patient was treated with high dose corticosteroids, a dose of 1 gr/kg/day (3 days), 500 mg/kg/ day (3 days), 250 mg/kg/day (3 days) and 1 mg/kg/day for 2 months. Two days after the onset of the treatment, arterial oxygen saturation became normal and radiological response was obtained on day 15 of steroid therapy. As DLI is away the early complications of HSCT; the presented patient with the occurence of DAH 6 months after HSCT does not seem to be related to conditioning toxicity. As the patient developed DAH 4 days after DLI, infusion of donor lymphocytes seems to be related to DAH and DLI is the basic factor to facilitate DAH in the late post-transplant period in this case. Since DAH is considered to be a secondary inflammatory response, systemic corticosteroid therapy is used for treatment, but the mortality rate is still about 64-100%. We obtained a satisfactory clinical response in this case of DAH by spesific diagnostic approach and treatment schedule which is composed of systemic high dose corticosteroid treatment. Early diagnosis and prompt treatment seem to be responsible from the mild course.

Abstract: 685 Poster: 592

THE EFFECT OF HEMATOPOIETIC PROGENITOR CELLS` TEMPERATURE ON CARDIAC ARRYTHMIAS IN PATIENTS GIVEN PERIPHERAL BLOOD PROGENITOR CELLS

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Background and aim: Infusion of cryopreserved and non-cryopreserved hematopoietic progenitor cells (HPC) is associated with a broad variety of symptoms. In this prospective study, we have investigated infusion-related toxicity regarding temperature of cryopreserved autologous peripheral blood progenitor cells (PBPCs) transplanted in 31 and allogeneic non-cryopreserved PBPCs in 4 patients receiving high dose chemotherapy and stem cells transplantation for hematological malignancies. Material and method: A 24 hours ECG-Holter recording system was used to obtain cardiac arrhythmias. Two milliliters HPC were collected from entrance site of venous access to evaluate the temperature of infused HPC. Results: We have detected arrhythmias in 17 (48.58%) of our patients. Median temperature of the infusat was 21C (18 - 28.2). The temperatures of infused HPCs were not statistically different in group with and without arrhythmias as 22C and 21C, respectively (P> 0.05). There was no statistically significant relation between temperature of HPC and occurrence of cardiac arrhythmias (P> 0.05).

And also, volume, contents (dimethylsulphoxide, red blood cells, platelet, and total nucleated cell) of product, and rate of infusion speed did not have any effect on arrhythmias. Conclusion: As a result of this study, we have concluded that the temperature of HPC does not cause any systemic hypothermia and does not have any relation to arrhythmias detected during infusion.

Abstract: 686 Poster: 593

ALLOGENEIC STEM CELL TRANSPLANTATION IN LEUKEMIA: EXPERIENCE OF A SINGLE CENTER

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Introduction: Allogeneic stem cell transplantation is the best and promising treatment option in a group of selected patients with leukemia. Transplant related complications and relapse are the main problems limiting the success of the procedure, and the outcome is better in the low risk patients. Material and Methods: Between December 1993 and June 2005, 96 patients with leukemia; acute lymphoblastic leukemia (ALL, n:32), acute non-lymphoblastic leukemia (ANLL, n:37) and chronic myeloid leukemia (CML, n:27) underwent allogeneic stem cell transplantation in our bone marrow transplantation unit. 51 (53.1%) of the patients were female, and 45 (46.9%) of them were male (F/M: 1.1). Mean age of the patients was 28.73 (range 15-54). 55 of these patients were in first CR (acute leukemia) or chronic phase (CML) and grouped as low risk, and 41 were beyond first CR or chronic phase, grouped as high risk. Acute and chronic GVHD status, transplantation related mortality (first 100 days posttransplant), long term mortality, the relapse rates and over-all survival were evaluated. Results: The over-all mortality was 17/55 (30.9%) and 29/41 (70.7%) in the low and high risk groups respectively ($p<0.001$). The early (transplant related) mortality was 4/55 (7.2%) in the low risk patients and 11/41 (26.8%) in high risk patients ($p<0.05$). The over-all incidence of acute GVHD was 28/96 (29.2%), with 11/55 (20%) and 17/41 (41.5%) in the low risk and high risk groups respectively ($p<0.05$). Chronic GVHD was diagnosed in 28 of the 82 patients alive beyond 100 days (34.1%) with 15/51 (29.4%) in the low risk group and 13/31 (41.9%) in the high risk group ($p>0.05$). Relapse rate was 25/96 (26%) among all patients. 11 of these 25 patients were in the low risk group while 14 were in the high risk group, with no statistically significant difference ($p>0.05$). The over-all survival was 67.86±52.55 and 15.9±15.86 months in the low and high risk groups respectively, with statistically significant difference ($p<0.001$). Conclusion: Our results indicate that the transplant outcome is better in low risk leukemia patients than high risk patients in terms of acute GVHD, mortality and survival.

Abstract: 687 Poster: 594

CHANGES IN GRAY SCALE AND DOPPLER ULTRASONOGRAPHY FINDINGS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

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Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has gained world wide acceptance as a treatment for various diseases. Hepatic toxicity of conditioning regimen, requirement of total parenteral nutrition (TPN) lead to hemodynamic modifications, coagulation disorders, endothelial and hepatocyte damage after HSCT. A definitive early diagnosis of complications may contribute to reduce transplant related mortality. Ultrasonography (US) can be used to evaluate organ morphology and also can be used to visualize vessels, measure hemodynamic parameters of arterial or venous flow when coupled with Doppler imaging. Several reports have described the results of US in patients with hepatic venoocclusive disease (VOD) but data in children without VOD are scarce. In this study, we aimed to determine the frequency of changes in gray-scale and Doppler US in the children who underwent allo-HSCT in our unit. From November 1999 to May 2005, a total of 42 patients underwent allo-HSCT for hemoglobinopathy(n:20), leukemia(n:13), aplastic anemia(n:7), and familial hemophagocytic lymphohystiositosis(n:2). The median age of patients was 10.5 years(range 1.1 to 17.0 years). Thirty-six patients received busulfan and no pa-

tient received total body irradition as a conditioning regimen. Thirty-eight patients received TPN for median duration of 16 days(range 6 to 29 days). Acute graft versus host disease(aGVHD) and VOD were detected in 8 and 6 patients, respectively. Seven patients(16 %) died, 6 from transplant related complications and 1 from relapse of the disease. Patients underwent gray-scale and Doppler US examinations before HSCT(baseline), after HSCT(median time:21 days) and at the time of the clinical diagnosis of VOD. Five morphological criteria(liver size, liver echogenicity, spleen size, gallbladder wall thickening, ascites) and 6 Doppler criteria (flow demodulation, congestion index, resistive index-RI, pulsatility index-PI, portal and hepatic blood flow) were examined. Non of the gray-scale or Doppler criteria differed at baseline between the patients with or without VOD/GVHD. Compared to the preHSCT examination; liver size, spleen size, gall bladder wall thickening, and intraperitoneal fluid increased after HSCT who received TPN longer than 14 days(n:27 patients) regardless of VOD or GHVD($p<.05$). Among the doppler criteria, portal vein flow and PI were effected after HSCT in the same group($p<.05$). Non of the patients revealed flow reversal in the portal vein. Despite the limited number of patients who developed VOD, there was a correlation between 3 criteria(liver size, ascites, hepatic blood flow) with VOD. Ascites was a highly spesific criterion of VOD thus detected in all patients who developed VOD. In conclusion, gray-scale and Doppler US examinations have a predictive value of VOD but there is similarity in findings between patients with and without VOD. Our study demonstrated that TPN is a significant factor which may change the US findings.

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DOUBLE STEM CELL TRANSPLANTATION IN MANTLE CELL LYMPHOMA

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Background:Mantle cell lymphoma (MCL) represents one of the most treatment refractory lymphomas with a median survival time of three to four years. Most multi-drug regimens (with or without doxorubicin) are associated with low complete response rates. In current clinical practice, high dose chemotherapy (HDCT) with autologous or allogeneic stem cell transplantation (SCT) is the preferred treatment. SCT usually has been administered in first remission or relapse. Case presentation: A 30 years old woman had admitted to another center with complaints of left upper abdominal pain, night sweats 52 months ago. In physical examination lymphadenopathy and splenomegaly was noted and then splenectomy was performed and MCL was diagnosed. When the patient was referred to our hospital, we noted 39 oC of fever, and cervical, abdominal and retroperitoneal lymphadenopathy. Bone marrow aspiration and biopsy examinations were normal. The immunohistochemical study of spleen and lymph node specimens revealed CD5+, CD23-and stage III-B MCL was diagnosed. Conventional chemotherapy with ProM-ACE-CytaBOM was administered for six cycles. After the fourth cycle, physical examination and computerized tomography of thorax, abdomen, and pelvis were normal. After the sixth cycle, stem cell mobilization with 2,4 gr/m2 cyclophosphamide + 2,4 gr/m2 MESNA + 10 mg/kg G-CSF was performed and 6x106/ kg CD34+ cells were collected. Then CNV regimen (60 mg/kg cyclophosphamide + 60 mg/kg MESNA + 45 mg/m2 mitoxantrone + 2,5 gr/m2 etoposide) was administered. Neutrophil and platelet engraftments were observed at the 13th and 17th days, respectively. Neutropenic fever emerged at the fourth day. The etiologic agent could not be isolated and fever was controlled under meropenem 3 g/d, tobramycin 240 mg/d, teicoplanin 400 mg/d and amphotericin B 100 mg/d. G-CSF 10 mg/kg was used through the treatment. Two months later, the disease relapsed with fever and cervical and inguinal lymphadenopathy and hepatomegaly. Biopsy and aspiration of bone marrow were normal. Stem cell mobilization was performed with the same regimen and 4,5 x106/kg CD34+ cells were collected. CNV regimen was re-adminis-tered and autologous SCT was performed. In the fourth day, neutropenic fever occured and etiologic agent was not found. Fever was controlled by 12,8 g/d ticarcillin/ clavulanate + 1 g/d amikacin + 400 mg/d teicoplanin + 100 mg/d amphotericin B. G-CSF10 mg/kg was used through the treatment. Neutrophil and platelet engraftments were observed at the 14th and 16th days, respectively. Three months later the patient`s physical examination, gallium scan and tomography were normal. The patient was examined with three-month intervals and at the last follow-up of 42th month after the second SCT, she is in complete remission. Conclusion: Double autologous SCT may be an effective therapy in post-transplant relapse in MCL.

Abstract: 689 Poster: 596

OTOTOXICITY AND HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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Hearing loss is a well recognized toxicity occuring in malignancies due to ototoxic medications. Ototoxic medications generally causes sensorineural hearing loss by destroying the sensory hair cells in the cochlea. Hearing loss in these patients usually begins in the high frequency range and later lower frequency range develops as ototoxicity progresses. Previous antineoplastic drug exposure, myeloablative conditioning and ototoxic antibiotics such as aminoglycosides during neutropenic fever makes hematopoietic stem cell transplantation (SCT) a risk factor for ototoxicity. Here we report the analysis of audiological evaluations in 22 SCT patients. Prior to following SCT, audiological evaluation with pure tone audiometry was performed. Underlying conditions were classified as 5/22 acute leukemia, 1/22 lymphoma, 15/22 multiple myeloma, 1/22 chronic leukemia. Type of transplantation was autologous for 15 patients, allogeneic for 6 and nonmyeloablative for 1 patient. The median age of the study group was 51 years (range 2071). Conditioning regimen consisted of melphalan (14 patients), BEAM (1 patient), busulfan/cyclophospha-mide (5 patients), TBI/cyclophosphamide (1 patient) and melphalan/TBI/fludarabin (1 patient). All participants in this study recieved aminoglycosides and broad spectrum antibiotics as initial therapy for their neutropenic fever except one multiple myeloma patient with chronic renal failure. Audiometry was reported as the hearing threshold in decibels (dB) hearing level at the tested frequencies. Post-transplantation pure tone audiometry (PTA) got worse with mild degree in only 1 multiple myeloma patient who received melphalan as conditioning regimen and aminoglycoside as neutropenic fever protocol (PTA increased 10 dB from the baseline value). His renal function tests were within normal limits. Interestingly in one patient with multiple myeloma preexisting severe mix type sensorineural hearing loss improved to moderate level after autologous SCT in which peripheral stem cells might have lead to the regeneration of lost inner ear hair cells. In conclusion; we have not found a significant deterioration of hearing following SCT in our study population. The conditioning regimens in our study group seems not to have a spesific autotoxicity although they also received aminoglycosides for neutropenic fever. Aminoglycosides seems to be less important when compared to conditioning chemotherapies in terms of hearing functions. The small number and spectrum of patients in our study limits us to drow a conclusion, In a prospective study of pediatric hematopoietic SCT, evoked otoacoustic emissions (OAE) were found to be more sensitive indicator of hearing loss than pure tone audiometry. Further studies with large sample size and by comparing OAE with PTA are necessary to determine the effect of SCT in terms of hearing function.

Abstract: 690 Poster: 597

BONEMARROWANDABNORMALITIESOFHEMATOPOIETIC MICROENVIRONMENT

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Bone marrow transplantation or BMT transplantation of progenitor blood cells to regenerate blood normal cells in patients with blood disorders Bone marrow has an organized and structured architecture in which close relationships exist between a regulatory microenvironment and primitive hematopoietic cells. In fact, normal hematopoietic cells depends on critical interactions that occur between stem cells and their microenvironment This microenvironment is a complex meshwork composed of growth factor, stromal cells, and extracellular matrix. Marrow injury can occur as a consequence of a variety of diseases. Some disease could be due to a microenvironment that fails to support hematopoiesis. A possibility is that aplasia and leukemia share a common etiology such as drug, chemical, radiation, virus or other environmental hazards. We can say that microenvironmental abnormalities in interactions between stromal cells and hematopoietic progenitors may be important in the pathogenesis and clinical expression of hematopoietic malignancies in humans.

Abstract: 691 Poster: 598

INFECTION IN BONE MARROW TRANSPLANT PATIENTS

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Human Cytomegalovirus infection is still one of the most important causes of morbidity and mortality in Bone Marrow Transplant patients. HCMV viremia is a reliable marker of systemic infection. Polymorphonuclear leukocytes represent the major viral carrier among peripheral blood white cells during acute infection. Since no specific protein or viral DNA is detected in PMNL of normal subject, direct detection of viral protein or viral DNA in circulating PMNL by different techniques may defiantly represent active CMV infection or disease. Conversely, HCMV latency occurs in mononuclear leukocytes. Consequently, high purity of PMNL is the most important factor for accurate interpretation of the test results. The purpose of this study was to develop a simple, rapid and economical method for the isolation of polymorphonuclear leukocytes from whole blood which provides a high yield and excellent purity without lymphocyte and erythrocyte contamination. In a 3 month period, we studied blood samples from bone marrow transplant patients and from normal subjects. The extraction of leukocyte polymorphonu-clear was obtained with a 6%-7% dextran solution in 0.8% saline. After incubation at room temperature with lymphoprep solution, the mixture was centrifuged. Two clear and separate rings of mononuclear and PMN leukocytes were, obtained. To eliminate any red blood cells, PMNL ring was separated and washed three times with cold ammonium chloride. After a short period of incubation at 4oC, mixture was centrifuged and the PMNLs were isolated. The purity and viability of total leukocyte population was counted and the percentage of PMNL obtained was established. The total blood samples studied were divided in two groups, i.e., bone marrow transplant patients and normal subjects. In both cases the PMNs isolated were of high purity and viability. The overall percentage of PMNLs obtained from both groups under study was 98% to 99% when stained with Gimsa or Wright staining method. The viability of isolated PMNLs was also 98% too, which is excellent for numerous immunological or molecular studies. The PMNLs isolated by this method were highly pure and viable in comparison with standard methods used to isolate human PMNLs. Generation a high amount of PMNLs is another advantage of the suggested method. This method to separate PMNLs is recommended for in vitro studies of different subjects.

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ONE CENTER RESULTS OF ALLOGENEIC AND AUTOLOGOUS STEM CELL TRANSPLANTATION

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The number of marrow transplant centers continues to increase throughout the world. In Turkey marrow transplantation is being done since 1978 and there are 27 transplant centers. We assessed 65 patients who underwent stem cell tansplantation between 1998 and 2005 in Osmangazi University Medical Faculty Hematology Department, Eskişehir. The patients were 38 male and 27 female. The diagnosis was multiple myeloma in 15, acute non lymphoblastic leukemia in 15, non-Hodgkin lymphoma in 10, chronic myeloid leukemia in 8, acute lymphoblastic leukemia in 5, Hodgkin lymphoma in 4, myelodisplastic syndrome in 4, primary amyloidosis in 2, agnogenic myeloid metaplasia in 1 and type I cryoglobulinemia in 1. Thirthy seven of patients underwent autologous and 28 underwent allogeneic stem cell transplantation (Table 1). Stem cell source was peripheral blood in 58 and bone marrow in 7 patients. Allogeneic stem cell transplantation was myeloablative in 17 and RIC in 11 patients. Two patients with multiple myeloma, 1 patient with non-Hodgkin lymphoma and 1 patient with acute non lymphoblastic leukemia had also undergone allogeneic stem cell transplantation since the disease relapsed after autologous transplantation. Forty five patients are still alive and 20 patients have died. The number of patients died in the first 100 days was 13 (Table 2). The complications seen in allogeneic stem cell transplantation were veno-occlusive disease in 1, both veno-occlusive disease and graft versus host disease in 9 and only graft versus host disease in 8. Culture positive bacterial infection was seen only in 9 of all patients. These data are quite valuable because they are the results of our own center. But each center should assess their results also comparing with the international data.

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NITRIC OXIDE GENERATION DURING PARENTERAL ADMINISTRATION DIFFERENTIATES ARGATROBAN FROM LEPIRUDIN AND BIVALIRUDIN

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While all direct thrombin inhibitors (DTIs) produce their anticoagulant effect by inhibiting thrombin, there are differences in their mode of action. This study was undertaken to evaluate effects of DTIs on cellular modulation. Primates (Macaca mulatta; n=6/group) were treated with 100-500 μg/kg iv BID of argatroban, lepirudin, and bivalirudin. Blood samples were drawn at 5, 15, 30, 60, 120, 240 and 360 min. Total nitric oxide (NO) levels were measured by the Griess reaction using a chromogenic method (R&D; Minneapolis, MN), and by a chemiluminescent assay performed on the Ionics Instrument 208I (Sievers Instrument; Boulder, CO). Primates treated with argatroban showed a dose- and time-dependent increase in plasma NO levels. Baseline levels ranged from 4-8 μM (mean±SD = 6.1±1.8 μM), whereas 5 min after argatroban NO levels were 6-11 μM (7.2±1.8 μM) for 100 μg/kg, 8-14 μM (11.8±2.6 μM) for 250 μg/kg, and 11-19 μM (15.7±3.1 μM) for 500 μg/kg argatroban. The increase in NO was observed for 30 min. The area under the curve (0-6 hrs) revealed a dose-dependent increase in a non-linear fashion. For lepirudin and bivalirudin, the NO levels did not differ from baseline during the study period. Flow cytometric studies showed comparable inhibition (29-37%) of tissue factor mediated platelet activation 5 min after dosing for all DTIs. However, the % P-selectin expression was lower with argatroban than lepirudin or bivalirudin treatment (17.1±5.2 vs 29.3±7.1; $p < 0.026$). The 5 and 60 min argatroban samples assayed for 6-keto-PGF1 showed 20-30% higher levels (not significant) compared to lepirudin and bivalirudin. Endogenous levels of NO in platelets as measured by using PRP were also higher in the argatroban treated but not the lepirudin and bivalirudin treated animals. These results support the hypothesis that argatroban is distinct from lepirudin and bivalirudin as it produces an increase in NO and prostacyclin which may contribute to its therapeutic efficacy by modulating cellular function. The upregulation of intraplatelet NO may differentiate the therapeutic efficacy of this thrombin inhibitor from others in heparin-induced thrombocytopenia and related syndromes.

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BIOCHEMICAL AND PHARMACOLOGICAL EQUIVALENCE OF GENERIC VERSIONS OF LOW MOLECULAR WEIGHT HEPARINS. A COMPARATIVE STUDY WITH BRANDED PRODUCTS

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Generic versions of such LMWHs as Dalteparin (DALT, Pfizer), Enoxaparin (ENOX, Sanofi-Aventis), and Fraxiparin (FRAX, Glaxo-Smith-Klein) have become available in some Asian and South American countries. Additionally, several generic drug suppliers/developers/scientific groups have requested USFDA review of the apparent generically equivalent versions of ENOX and DALT to approve the introduction of these partially characterized products for unqualified indications using a fast track (ANDA) submission. Similarly, in Europe such an approach to introduce several generic versions of branded product are being considered for regulatory submission and approval by ENEA. Generic versions of these products are claimed to have similar anti-Xa potency, molecular and structural components, and other analytical attributes, however, a detailed pharmacodynamic equivalence for these structurally complex polycomponent drugs is not provided. Moreover at this time, there are no clear guidelines regarding acceptance of generic LMWHs with the exception of specifications in product patents and pharmacopoeial descriptions.

This study compared 6 commercially available generic versions of ENOX and 2 generic versions of DALT with 2 batches of each branded product. Molecular profiling by GPC and structural profiling by NMR were carried out. Oligosaccharide composition was investigated before and after heparinase I digestion. Potency evaluation was performed using the USP assay and an amidolytic anti-Xa assay in relation to the 1st and 2nd LMWH standards. Anticoagulant effects were compared using global clotting assays. Protamine and Platelet Factor 4 (PF-4) neutralization profiles were determined at gravimetric and anti-Xa adjusted concentrations. The molecular profiles of generic ENOX and DALT were comparable with their respective branded verions, and the anti-Xa potency was within the expected range. However, differences were noted in the oligosaccharide components, heparinase digestion profile and protamine and PF-4 neutralization studies. In the NMR analysis, specific signals for the 1,6-anhydrosugar groups at the reducing terminus and the presence of a double bond at the non-reducing end also varied. Marked differences were observed with some of the generic products in the clot-based assays despite potency adjustment using the WHO standard in the anti-Xa method. Differences in molecular profile and biologic activity were also present with the generic versions of DALT, ENOX, and FRAX. These studies suggest that the current regulatory requirements in terms of anti-Xa potency specifications and molecular parameters may be inadequate as acceptance criteria for the generic verions of branded LMWHs. Moreover each of the branded LMWHs are approved for specific indications, and their therapeutic interchange is not recommended. Until acceptable and firm guidelines for developing the generic versions of branded products become available, a generic interchange is not warranted.

Abstract: 695 Poster: 602

PULMONARY THROMBOEMBOLISM AT AUTOPSY IN A TEACHING HOSPITAL IN SAO PAULO, BRAZIL

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Pulmonary thromboembolism (PTE) is a serious cause of mortality in both surgical and non-surgical hospitalized patients. The purpose of our study was to investigate PTE as a cause of death in a Teaching Hospital in Brazil. We reviewed all autopsy reports from patients who died at Central Institute of Clinics Hospital (Hospital das Clínicas) of the University of Sao Paulo, Brazil, from 1994 to 2003 (15.383 autopsies) and classified PTE as fatal (primary cause of death) and non-fatal (present in the autopsy but not considered the primary cause of death). The presence of PTE was observed in 1.169 autopsy reports. Monthly mean number of PTE cases was 9.7 ± 4.1 cases (mean ± SD, range 1-26). This number corresponded to 9.7 ± 4.1% of all autopsies (range 0.7-17.1%). The monthly mean numbers of fatal PTE and non-fatal PTE were, respectively, 5.0 ± 2.3 cases (range 0-13) and 4.7 ± 2.9 cases (range 014). No seasonal pattern of fatal PTE was observed. There was no significant difference in the numbers of fatal and non-fatal PTE among the years studied. Despite the existence of effective thromboprophylaxis, PTE remains one of the major causes of death in hospitalized patients. The numbers of fatal and non-fatal PTE diagnosed at autopsy are similar. Supported by AstraZeneca, Brazil.

Abstract: 696 Poster: 603

TECHNOTHROMBIN(r) TGA A NOVEL THROMBIN GENERATION ASSAY SUITABLE FOR THE NEW ROUTINE COAGULATION ANALYZER CEVERON(r) ALPHA

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We developed a new routine coagulation analyzer, Ceveron(r) alpha, with the aim not only to measure routine clotting parameters, chromogenic substrates and immunological parameters by LIA technology, but also to allow to measure thrombin generation (TGA) utilizing a fluorigenic substrate. Measurement of TGA would allow analyzing clotting defects and patients with thrombophilia in more detail and to possibly separate novel subgroups of patients. Furthermore such an assay would also allow measuring circulating microparticles currently though to be one of the major risk factors for thrombosis in atherosclerotic patients. For this purpose we de-

signed a novel thrombin generation assay, TECHNOTHROMBIN(r) TGA, employing specific phospholipids micelles and incorporated tissue factor into these micelles at different concentrations. This assay was applicable to the routine coagulation analyzer Ceveron(r) alpha allowing direct comparison of clotting and TGA activities measuring TGA in plasma or whole blood. When the maximal slope of thrombin generated per minute or peak thrombin in nM thrombin was used, a correlation with an r value of 0.9969 was obtained for INR values determined with TECHNOTHROMBIN(r) TGA and those determined with routine clotting assays and Thrombotest(r) or Normotest(r) as PT reagent. Furthermore, TGA was significantly increased in patients with deficiencies in ATIII, Protein C or Protein S and patients with Factor VLeiden mutation and decreased in hemophilic patients. Furthermore a correlation between TGA and the number of circulating microparticles was found. From these data we conclude that TECHNOTHROMBIN(r) TGA is a rapid and reliable assay for measuring coagulation parameters in patients under anticoagulant therapy, in patients with hemophilic or thrombophilic disorders and to measure circulating microparticles. Furthermore the routine coagulation analyzer Ceveron(r) alpha can be used also to routinely measure TGA.

Abstract: 697 Poster: 604

IN VIVO CORRELATION BETWEEN SOLUBLE ENDOTHELIAL PROTEIN C RECEPTOR (SEPCR) AND TUMOR NECROSIS FACTOR ALPHA (TNF- A)

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Background: Activation of Protein C has a major importance in the natural anticoagulant pathway. Antiapoptotic, anti-inflammatory and anticoagulant roles of activated protein C (APC) have been reported. The activation process occurs on the endothelial cell surface by thrombin (T)-thrombomodulin (TM) complex and it is enhanced by the endothelial cell protein C receptor (EPCR). When the rate of the reaction has been ceased by an 23 bp insertion located in the third exon of the EPCR gene that alters the function of EPCR, a thrombotic risk occurs. The cleavage of the membrane bound EPCR resulting in a increased level of soluble form of EPCR (sEPCR) also increases the risk of thrombosis. The effect of EPCR on the generation of APC has been shown by in vitro studies (cell culture and animal experiments). Plasma levels of sEPCR have been claimed to be genetically controlled by recently reported haplotypes. In vitro effects of TNF-a on protein C receptor of endothelium has also been reported by using human umbilical endothelial cells (HUVECS). The effect of TNF- a on TM and EPCR expression has been evaluated by measuring APC formation. But there is no study revealing the possible effects of TNF- a on APC formation via EPCR. The inflammatory cytokines, interleukin-1 b, TNF- a and endotoxin have been claimed to reduce TM, EPCR and protein S levels. Aims: Here we present the possible effects of plasma sEPCR and TNF- a levels, also the TNF- a promoter -308 G-A polymorphism and their associations in a group of 104 healthy controls. The mean age of the controls was 28.58±7.8 and the median age was 25. Methods: The plasma levels of the parameters were performed by ELISA. To determine TNF- a -308 G-A polymorphism, PCR/RFLP method was used. For statistical analyses SPSS statistical package version 11 were used. Results: The results can be summarized as follows: 1.The relationship between TNF- a and sEPCR levels: Correlation was significant at the 0.01 level (2-tailed) between TNF- a and sEPCR levels. 2.The relationship between TNF- a -308 G-A polymorphism and sEPCR levels: Among 84 individuals with TNF- a GG genotype, 12 were found to have sEPCR levels higher than 100 ng/ml, and 3 individuals were found in the 20 TNF- a GA group with high levels of sEPCR. These groups were compared with each other for their sEPCR levels. The OR was 1.05 (Cl: 0.27-4.07) and P value was 0.77. Conclusions: Our study is the first study that shows the in vivo effects of TNF- a and sEPCR levels and also with TNF- a gene polymorphism. We also found a correlation between TNF- a and sEPCR levels among healthy controls whereas we are unable to find an association between the TNF- a promoter gene variant and both plasma parameters according to performed risk analysis. We think that this correlation should be analyzed in patients with thrombosis, as it will be a correct approach to determine the influences. (This study is supported by Ankara University Research Fund)

Abstract: 698 Poster: 605

RENAL VENOUS AND ARTERIAL THROMBOSIS IN CHILDREN

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Background-Aims: Renal vein thrombosis (RVT) and renal arterial thrombosis (RAT) are well-recognized clinical entities which are associated with serious morbidity. The present study was designed to evaluate prothrombotic risk factors and long term follow-up results in children with renal vein and/or renal arterial thrombosis. Material-Method and Results: Between January 1998 and June 2005, 415 pediatric patients were admitted to Hacettepe University Faculty of Medicine Pediatric Hematology Unit for evaluation of thrombosis. Of these 415 pediatric patients with thrombosis, 18 (4.0%) had renal vein and/or arterial thrombosis. Nine patients (50%) were girls and nine patients (50%) were boys. Of these 18 children, 14 (77.7%) had RVT, 3 (16.6%) had RAT, and 1 (5.5%) had renal vein and arterial thrombosis. Renal thrombosis was left sided in 15 patients (83.3 %) and right sided in 3 patients (16.6 %) and unilateral in all of the patients. Two patients had associated thrombosis at vena cava inferior (VCI), one had associated thrombosis at bilateral iliac veins and one had widespread thrombosis at VCI, bilateral iliac veins, bilateral femoral veins and right renal artery and vein thrombosis. The follow-up period was 23±21.8 months (range: 1-82 months) for all of the patients. On the follow-up period, renal atrophy was present in 16 out of 18 (88.8%) affected kidneys. Underlying diseases and protrombotic risk factors: Among these 18 patients with renal thrombosis, one patient had end stage renal disease, renal transplantation, and Prothrombin G20210A heterozygous mutation (after transplantation, she had RAT and unilateral nephrectomy was performed); one patient had dilated cardiomyopathy, elevated levels of fibrinogen and D-Dimer; one patient had dilated cardiomyopathy, elevated level of D-Dimer; one patient had elevated levels of factor 8, factor 11, hereditary protein C and protein S deficiency and Factor V Leiden (FVL) heterozygous mutation; one patient had trauma and FVL heterozygous mutation; one patient had operation (appendectomy) and FVL heterozygous mutation; one patient had elevated D-Dimer and FVL heterozygous mutation; one patient had elevated factor 8 level and FVL heterozygous mutation; one patient had congenital heart diseases (atrioventricular septal defect, pulmonary binding operation), central venous line, and hereditary protein C deficiency; one patient had congenital heart diseases (double outlet right ventricle, atrial septal defect, ventricular septal defect), hereditary protein C deficiency, elevated factor 8 levels, and homozygote MTHFR mutation; three patients had FVL heterozygous mutation; two patients had hereditary protein C deficiency; one patient had elevated D-Dimer; only two patients had no prothrombotic risk factors. Among 18 children with renal thrombosis, six patients (33.3%) had 1, five patients (27.7%) had 2, three patients (16.6%) had 3, one patient (5.5%) had 4, and one patient (5.5%) had 5 prothrombotic risk factors and/or underlying diseases. Eight patients (44.4%) had FVL heterozygous mutation. Conclusion: Data from our patients show that a) Males are equally effected with girls b)Left-sided renal thrombosis are more common than right-sided c) The majority of our patients (16/18: 88.8%) have underlying diseases and/or prothrombotic risk factors d) FVL mutation is the most common (44.4%) prothrombotic risk factor in our patients e)Renal thrombosis occured in 10 patients (55.5%) at the neonatal period f) Renal thrombosis still leads to irreversible kidney damage in the majority of cases.

Abstract: 699 Poster: 606

SOLUBLE P-SELECTIN LEVELS IN DIABETES MELLITUS WITH CORONARY ARTERY DISEASE

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Type 2 (non-insulin-dependent) diabetes is associated with a marked increase in the risk of coronary heart disease. Platelets play a significant role in coronary artery disease. Soluble P-selectin is an index of platelets activation. In this study, Soluble P-selectin levels were measured by ELISA in the peripheral blood of 55 diabetic patients with coronary artery disease [21 acute myocardial infarction (AMI), 20 with unstable angina (UA), 14 with stable angina (SU)], 20 patients with diabetes mellitus without coronary artery disease (DM without), and 10 healthy controls.Solu-ble P-selectin level was significantly higher in patients with AMI (M±SD; 239.3±13.0 ng/ml), than those with UA (141.5± 15.2 ng/ml), SU (92.1±7.7 ng/ml), DM without (89.8±7.1 ng/ml), and healthy control (86.1±4.5 ng/ml) (P<0.001). In patients with US, sP-selectin was found to be significantly elevated as compared to the SU, DM without and control group. sP-selectin was not

significantly different in DM without as compared to controls. The sP-selectin levels was correlated to the duration of diabetes mellitus(R= 0.33, P=0.03). Moreover, sP-selectin level was significantly higher in AMI patients with recurrent anginal attack as compared to that in those with single attack(P=0.041). Multivariate analysis revealed that sP-selectin level at presentation had high adverse influence on coronary artery insult compared to LDL cholesterol level, and the degree of hypertension. In Conclusion: Plasma levels of soluble P-selectin were increased in patients with AMI, and UA compared to patients with SA and normal controls. Measurement of soluble P-selectin may be helpful marker of impending coronary artery insult in diabetic patients.

Abstract: 700 Poster: 607

THE ROLE OF THROMBOPHILIA IN HEMODIALYSIS VASCULAR ACCESS THROMBOSIS

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BACKGROUND: Fistula and graft thrombosis are common and costly complications in hemodialysis patients. Recent studies suggest that thrombophilia is associated with access thrombosis in these patients. However, many, large, multicenter studies are needed to confirm these results. AIM: The aim of this study is to assess the association between thrombophilia and vascular access thrombosis in hemodialysis patients. METHODS: In this retrospective study, 78 patients (37 men, mean age 63,2±10,9y and 41 women, mean age 62±12,2y) were studied from the hemodialysis Unit of the University Hospital, Heraklion Greece, between July 2003 and March 2005. The mean time of hemodialysis was 74,8±43,1 months. All patients were tested for antithrombin III, protein S, protein C, activated protein C resistance (APC-R), Lupus anticoagulant, antiphospholipid antibodies (panel), factors VIII and XI, homocysteine and lipoprotein(a). Samples with low APC-R were confirmed for factor V Leiden with PCR technology. Prothrombin gene mutation and methylenetetrahydrofolate reductase genotype will be included in the study. All participants were divided into two groups, those with access thrombosis and those with no access thrombosis and we assessed the prevalence of thrombophilia factors in both groups. RESULTS: Univariate analysis showed that there was a statistically significant association between thrombosis and the existence of one (at least) of the following thrombophilia factors: protein C, protein S antithrombin III Lupus anticoagulant and antiphospholipid antibodies. (x2=4,320, df=1, p=0,038). Crude odds ratio (OR) (unadjusted) revealed a 3 times higher risk for thrombosis on these patients, OR: 3.06 (95% CI: 1,04-8.996). A corresponding analysis which took APC-R into account showed 5-times higher risk for thrombosis: x2 =9,238, df=1, p=0,002, OR: 4,95 (95%CI: 1,69-14,46). Finally, a multiple logistic regression analysis was assessed to estimate adjusted OR. In the final model, sex, age, smoking habits, months of hemodialysis and thrombophilia factors(inc. factor VIII) were initially included. Adjusted OR was: 5.75 (95%CI: 1,14-28.90). In the previous statistic model no statistically significant differences were found after adjusting for Hypertension, Diabetes Mellitus, Coronary Artery Disease, Cerebrovascular Disease, Peripheral Arterial Disease and Malignancy. CONCLUSIONS: This study showed that there is a significant correlation between thrombophilia and access thrombosis in hemodialysis patients.

Abstract: 701 Poster: 608

FOLLOW UP OF ADAMTS13 ENZYME AND ITS RELATIONSHIP WITH CLINICAL EVENTS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Von Willebrand Factor cleaving protease (ADAMTS13) has been studied for thrombotic thrombo-cytopenic purpura; but, there is paucity of data about the relationship between ADAMTS13 and hematopoietic stem cell transplantation. Aim(s): To evaluate the weekly ADAMTS13 activity after the hematopoietic stem cell transplantation and its relationship with clinical outcome and complications. Methods:Thirty patients undergoing allogeneic hematopoietic stem cell transplantation with different conditioning regimens and fifteen healthy controls were

studied. The plasmas were collected from patients before the conditioning regimen, the day of transplantation, and 7th, 14th, 21th, 28th days after transplantation, for once from healthy controls. Patient plasmas were further collected when acute, chronic graft versus host disease (GVHD) developed. The median follow-up period was 15(2-24) months. Activity of the enzyme was studied with Ristocetin co factor based method which was described by Bohm M. Results: Mean age of the patients and healthy controls were 35± 12 and 33 ±10, respectively. The ADAMTS13 activity of healthy controls was found between 76% and 136%. The median enzyme activities of patients did not show significant changes through weeks (87% (39-145), 82% (16-110), 80% (36-134), 86% (47-127), 89% (11-127), 90% (10127), respectively.) None of our patients had enzyme activity lower than 5%. When patients were grouped as those having enzyme activities lower than 75% and between 76%-136% before the transplantation, prior group(n=9)had lower activity than the later on the day of transplantation (n=21) (60±27% vs 86±13%, p=0.023) but the rest of the weeks were similar for both groups. Among the patients complicated with acute GVHD (n= 14), the enzyme activity on the day of acute GVHD (AGVHD) was similar with pretransplantation period (73±32% vs 87±20%, p=0.231); but significantly lower than healthy controls (73±32% vs 97±16%, p=0.02). Besides, by the posttransplantation 28th day, patients with AGVHD had lower enzyme activity than the patients without AGVHD (n=16) (62±36% vs 95±22%, p=0.009). ADAMTS13 activity was lower in samples taken from patients with chronic GVHD compared to baseline level (67±13% vs 91±30%, p=0.15) and to healthy controls (67±13% vs 97±16%, p=0.002). During the febrile neutropenic period, activity was statistically lower than healthy controls 67±25% vs 97±16%, p=0.004). None of the patients had thrombotic microangiopathy, thromboembolism or hepatic venooclusive disease during the follow up period. Summary/Con-clusions: According to our data, ADAMTS13 enzyme activity does not have a pivotal effect in respect to clinical outcome of transplantation.Acute, chronic GVHD and infections cause a slight decrease of the enzyme which may indicate the possible negative effect of cytokines. To our knowledge, this is the first report performed via using ristocetin cofactor based method for allogeneic stem cell transplanted patients.

Abstract: 702 Poster: 609

ROLE OF ACQUIRED RISK FACTORS IN DEVELOPING THROMBOSIS DURING CHILDHOOD

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Thromboembolism is a major cause of morbidity and mortality both in adults and children. Therefore, in this study, we searched for the effects of both genetic and acquired factors causing thrombosis during childhood. This study analyses the data of 57 thrombotic children who were followed up at the pediatric hematology ward in Bursa, Turkey. between January 2000 and December 2004. The diagnosis was confirmed according to both clinical and radiological findings. Genetic factors (FVL G1691A, PT G20210A, MTHFR C677T) were identified. The genetic analyses were done by light cycler real-time PCR. The following kits were used for the procedure; a) Factor V Leiden mutation was detected by a commercial kit using a real time PCR thermocycler (Light Cycler, Roche, Germany). b) PT G20210A mutation was detected by Light Cycler Prothrombin G20210A Mutation Detection Kit., Germany c) MTHFR C677T genotypes were detected by a real-time PCR thermocycler (LightCycler, Germany) following a melting curve analysis as described by Aslanidis and Schmidtz. Protein C, protein S and antithrombin III were also screened in children with thrombosis by coagulometric tests and serum antiphospholipids were analysed by ELISA. The same mutations were investigated in the control group consisted of 250 non-throm-botic children. Acquired factors which were infection, cardiac defects, catheterization, malignancy, surgery, nephrotic syndrome and antiphospholipid syndromes were questioned both in the thrombotic and nonthrombotic settings. The statistics: Odd ratio and chi square tests were used in analyzing the thrombotic effect of the each factor in both groups. Of the children, 17% were infants less than 1 year old. Thromboembolic events mostly occurred in the cerebral vascular system (46%), followed by the deep venous system of the limbs, femoral and iliac veins (30%), portal veins (7%), and intracardiac region (7%). Acquired and inherited risk factors were present in 47.3% and 31.7% of the children, respectively. Infection 38.5% was the most common underlying acquired risk factor. Among the inherited factors, FVL was the most common one. Acquired and inherited risk factors were present simultaneously in 23% of the pa-

tients. However, 25% children had none of these factors. We divided the patients into 4 groups (table1). We compared the results of each group with the control group. Patients carring both genetic and acquired factors had significant risk for thrombosis ($p< 0.002$). Patients with acquired factors had significantly greater risk for developing thrombosis than the others.This study, environmental factors independently increased the risk of thrombosis, where as the genetic factors did not. The presence of both factors were also found significantly more effective in developing thrombosis comparing to the children with no risk factor. This data revealed that environmental factors were very important in causing thrombosis.

Abstract: 703 Poster: 610

PLASMA SEPCR LEVELS AND EPCR 4031INS23 POLYMORPHISM IN TURKISH PEDIATRIC STROKE PATIENTS AND IN HEALTHY CONTROLS:

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Background: To understand the anticoagulant mechanism of heamostasis, the components of the protein C system has been studied for years. The protein C system is triggerred by the binding of thrombin to the thrombomodulin receptor of endothelium. And another receptor of endothelium, the endothelial protein C receptor (EPCR) augments the activation of protein C results in an activated protein C functions as an anticoagulant from now on. A defect in the gene causes the synthesis of a truncated protein or low expression or absence of the protein. Aims: We studied the effect of 23 bp insertion in the exon 3 of the EPCR gene on sEPCR levels and we also evaluated the association between sEPCR levels and pediatric stroke. Methods: A group of controls consisting 104 healthy individuals and a study group consisting 97 pediatric stroke were included. 17 of them were analysed for sEPCR. To detect the 23 bp insertion and the plasma levels of sEPCR, PCR and ELISA methods were performed, respectively. Results: The results of the study was shown in Table 1. We found out that two patients in the study group were carried prothombin 20210 G-A mutation and the insertion at the same time. The frequencies of the FVL and PT 20210 G-A mutations in the pediatric stroke group were 21.6 and 9.2 %, respectively. The mutation analysis showed that 2 patients also carried FVL who has sEPCR levels over 100 ng/ml. The frequency of the 23 bp insertion was found to be very low parallel to the literature (2%). Conclusions: Although the number of the patients is few, the increased levels of sEPCR over 100 ng/ml, it can be included as a possible etiological factor in the development of stroke. Further studies are warranted to study the effects of sEPCR in a large series of patients and the role of haplotypes in the increased plasma levels. (This study is supported by Ankara University Research Fund)

Abstract: 704 Poster: 611

COMPARISON OF TWO D-DIMER ASSAYS FOR THE DIAGNOSIS OF VENOUS THROMBOEMBOLISM:ELISA AND AN IMMUNOFILTRATION ASSAY (NYCOCARD DDIMER)

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Previous studies have suggested the utility of D-Dimer ELISA assays in eliminating a diagnosis of venous thromboembolism (VTE): deep venous thrombosis (DVT) or pulmonary embolism (PE). Our objectives were to evaluate the performance of a rapid and quantitative immunofiltration method: NycoCard D-Dimer (Nycomed). One hundred seventy eight consecutive patients (53 women and 125 men) hospitalised in our institution between April 2004 and October 2004, suspected of presenting a VTE with recent clinical signs, were included in this study. Diagnosis of PE and DVT was based on clinical evaluation, lower limb compression ultrasonography and helicoidal thoracic scanner. Among the 178 patients tested, 12 (6.7 %) were classified as VTE positive (4 DVT and 8 PE). The sensitivity, negative predictive value, specificity and positive predictive value were, for Nycocard D-Dimer 100%,

100%, 40 % and 10%, for ELISA 100%, 100%, 32% and 9%, respectively. Comparison of test results by concentration category revealed a good agreement between ELISA and NycoCard D-Dimer, and the correlation coefficient was r = 0.85. A plasma sample is tested with NycoCard D-Dimer in less than 2 min. Thus, this test combines advantageous analytical properties comparable to the ELISA test, with rapidity and simplicity. These findings suggest that this rapid and simple technique provides a useful diagnostic tool for the clinician with regard to exclusion of VTE.

Abstract: 705 Poster: 612

COMPARATIVE STUDY ON THE ANTICOAGULANT EFFECTS OF LOW MOLECULAR WEIGHT HEPARINS AS MEASURED BY WHOLE BLOOD ACT, ANTI-XA AND A NEWLY DEVELOPED PROTHROMBINASE INDUCED CLOTTING TIME (PICT) ASSAY

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Low Molecular Weight Heparins (LMWHs) are currently developed for anticoagulation in various intravenous indications such as DVT treatment and percutaneous interventions (PCI). Traditionally, these drugs are administered in anti-Xa units. The purpose of this study was to compare the relative levels of anticoagulation produced by different LMWHs in whole blood ACT (Hemochron), an amidolytic anti-Xa method and a plasma-based global anticoagulant assay, the PiCT test (Pentapharm, Basel, Switzerland). Various LMWHs such as dalteparin, enoxaparin, reviparin and a synthetic pentasaccharide were supplemented to freshly drawn native blood samples to simulate patient samples containing 1 U/ml anti-Xa levels. Three generic versions of enoxaparin were also included in this study. In addition to the ACT measurement in whole blood, citrated plasma samples were also tested for APTT, Heptest, PiCT, amidolytic anti-Xa and IIa activities, and protease generation assays. All agents produced assay-based effects on different tests, which were not proportional to the adjusted anti-Xa activity. Correlation of the ACT data resulted in a good relationship with PiCT for the commercially available branded products(r2=0.97). ACT and Heptest (r2=0.51), ACT and anti-Xa (r2<0.3), ACT and anti-IIa (r2= 0.93). The correlation of PiCT and Heptest was (r2=0.73) better than ACT and Heptest. However, the generic versions of enoxaparin did not provide similar results. PiCT and Heptest also gave the good correlation. These results clearly suggest that for the global anticoagulant actions of LMWHs, anti-Xa measurements are of limited value and should not be used to asses the anticoagulant efficacy of LMWHs in PCI and other surgical conditions. These differences may be more obvious in the generic versions of LMWHs, which are apparently produced using pharmacopeial specifications. Thus, it is important to include a clot-based method in the cross referencing and standardization of LMWHs.

Abstract: 706 Poster: 613

IS FAMILIAL MEDITERRANEAN FEVER A THROMBOTIC DISEASE?

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In our study, we aimed to show the effects of procoagulant activity, tissue factors which are released after endothelial damage, and markers of thrombosis and fibrinolysis on the progression and the severity of familial mediterranean fever and also their correlation with acute phase reactants in the appearence and recurrence of the disease. The study group comprised 64 patients with a diagnosis of familial mediterranean fever in attack or attack-free period. We grouped our patients as colchicine using attack-free patients on follow-up (group 1), colchicine using patients in familial mediterranean fever attack (group 2) and newly diagnosed patient during attack period (group 3). We compared these study groups with 24 control subjects. Fourteen normal healthy subjects (group 4), five inpatients with febrile neutropenia (group 5), and 5 inpatients with significant infection (group 6) were studied as controls. These last two groups were our positive control groups. The aim of grouping of these control groups was to observe the effects of the leukocyte and thrombocyte counts both to the acute phase reactants and to the coagulation and anticoagulation factors, p-selectin, tPA and PAI-1 levels. Leukocyte and thrombocyte counts, erythrocyte

sedimentation rate, CRP, fibrinogen, PT, aPTT, factor VIII, vW factor, d-dimer, p-selectin, tPA and PAI-1 were tested in all patients. We showed ongoing inflammation by increased CRP, sedimentation and fibrinogen levels in attacks and attack free period in familial mediterranean fever patients. We detected increased CRP in both attack-free (%70) and attack period (%75). Erythrocyte sedimentation rates were 22, 36 and 54 mm/h in group 1, 2, and 3, respectively. There were positive correlation between fibrinogen and sedimentation in all three familial mediterranean fever groups ($p<0.0$, <0.0 and <0.003 respectively). We confirmed that endothelial damage, caused by the ongoing inflammation, may contribute to the systemic activation of the coagulation. We showed an increase in acute phase reactants and also significant prolongation in PT and aPTT in acute attacks ($p=0.008$ and 0.024 respectively). We found increased levels of tPA during attack periods of colchicine using patients. This increase in tPA levels was statistically significant ($p=0.006$). Also p-selectin levels were statistically significant in all familial mediterranean fever groups ($p=0.03$, 0.02, 0.03 respectively). We showed that PAI1 levels, independent of using colchicine, increased during attack periods. These results made us think that PAI-1 might be used as a marker for the attacks of the familial mediterranean fever (PAI-1 levels; attack free period: 8.96 ng/ml, during attack period: 33.5 ng/dl). Colchicine shows its antiinflammatory effect by preventing leukocyte chemotaxis. In our study, there were significant difference between the erythrocyte sedimentation rates of patients on colcicine therapy and newly diagnosed patients. D-dimer levels were 160, 294 and 454 mg/dl in group 1,2 and 3, respectively. According to these results we thought that colchicine supressed inflammation and this supression decreased fibrinolytic activity by limiting coagulation. When we compare the patients in attack period (group 2+3) and the colchicine using attack-free group (group 1), PAI-1 levels were statistically significant ($p=0.000$). PAI-1 levels were higher in group 3 than in the other two familial mediterranean fever groups (group 1 and 2). We thought that colchicine not only prevents amyloidosis but also decreases thrombotic activity by keeping the plasminogen activity in a low level. Finally these findings made us think that hypercoagulability may have effects on etiopathogenesis and prognosis of familial mediterranean fever.

Abstract: 707 Poster: 614

FREQUENCIES OF COAGULATION FACTOR GENE MUTATIONS AND SMALL NUCLEOTIDE POLYMORPHISMS IN TURKISH ISCHEMIC STROKE PATIENTS

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Background: In recent years altered hemostasis has been reported to occur in ischemic stroke, ishemic heart disease and peripheral vascular disease. Point mutations and single nucleotide polymorphisms in coagulation factors have been intensively studied in terms of their association with stroke. Aims: We aimed to investigate effect of genetic mutations/single nucleotide polymorphisms (SNP) as a risk factor for stroke in Turkish population. Methods: Factor (F) V Leiden; prothrombin (Pt) G20210A; methylenetetrahydrofolatereductase C677T; angiotensin converting enzyme (ACE) insertion/deletion (I/D) polymorphism; endothelial nitric oxide synthase (EcNOS) intron 23 G10T, intron 4 VNTR, and exon 7 G894T polymorphisms; F XIII Val34Leu polymorphism, alpha-fibrinogen (AF) Ala314Thr polymorphism, and F VII R353Q polymorphism were investigated in 162 ischemic stroke patients. Results were compared with the frequencies of these genotypes in normal Turkish population reported previously. Results: Frequencies of ACE D/D, EcNOS exon 7 T/T, AF Ala/Thr, and F XIII Val/Leu genotypes were significantly higher than normal population in Turkish stroke patients. Conclusion: SNPs should be considered as a risk factor for ischemic stroke in Turkish patients. Further studies are needed in Turkish and other ethnic groups to elucidate the effect of this SNPs in stroke.

Abstract: 708 Poster: 615

ANOTHER PIECE IN THE "HYPOFIBRINOLYSIS-AIDS PUZZLE": THROMBIN-ACTIVATABLE FIBRINOLYSIS INHIBITOR (TAFI)

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Background Human immunodeficiency virus (HIV) infection and a wide variety of its complications lead to a significant morbidity and mortality in HIV/AIDS patients. Thrombotic tendency and vascular occlusive events may further complicate the natural course of HIV infection. Although several hemostatic abnormalities such as Von Willebrand Factor, protein C, protein S, platelet activation with P selectin, microendothelial disturbance, antiphospholipid antibodies have been investigated, the exact pathogenetic cause underlying the prothrombotic state of HIV/AIDS is still unknown. Thrombin-Activatable Fibrinolysis Inhibitor (TAFI, car-boxy peptidase B) is a zymogen molecule, which is activated by thrombin to TAFIa (carboxy peptidase U) during the hemostatic process and was recently reported as an independent risk factor of thrombosis, irrespective of antithrombin, prothrombin, protein C and fibrinogen. Aims The aim of this study was to assess the circulating TAFI concentrations in HIV-infected patients. Hence, elucidation of the role of this critical regulatory hemostatic molecule in HIV may help better understand the pathobiology of the enigmatic pre-thrombotic state of the disease. Methods Plasma TAFI activities were assessed in 13 (7 females and 6 males) patients with HIV/AIDS and equal number of age-and sex-matched healthy adults as controls. All of the AIDS patients were followed by the Infectious Diseases team of the Department of Internal Medicine, Hacettepe University Medical School. The controls were selected from individuals admitted over the same period to the check-up outpatient clinic of the same hospital. Plasma TAFI levels were measured using a commercially available ELISA assay (IMUCLONE(r), American Diagnostica Inc.). TAFI concentrations in plasma were compared in patients with HIV/AIDS and controls, using Mann-Whitney U test. Results Cases aged between 24 and 46 years, with a mean (± standart deviation) of 36.2±7.8 years. Heterosexual route was the major reported cause of transmission of HIV (54.0%). Of the patients, 61.5% were Category A at admission, 23.1% were Category B and 15.4% were Category C, according to CDC, revised-93 classification. Eighty-two percent of the cases were receiving anti-retroviral therapy at the time of the study. The mean plasma TAFI level of the cases was 201.15±21.13 with a median of 205 (ranged between 174 and 235). Controls were matched to cases by gender and age group. Accordingly, age distribution of controls were similar to cases: ranged between 26 and 46 years, with a mean of 36.5±7.5 years. Plasma TAFI levels of the controls ranged between 97 and 189, with a median of 145 and the mean was 143.2±28.4. Comparison of plasma TAFI levels of cases and controls was statistically significant ($p<0.001$), with higher levels in cases. Conclusions HIV patients have elevated levels of TAFI, which is another clue to demonstrate the hypofibrinolytic state in this patient population. Further studies are needed to determine interactions of critical hemostatic molecules, including TAFI, and HIV for better understanding the disease biology and improve clinical management of HIV-infected patients at thrombotic risk.

Abstract: 709 Poster: 616

MULTIPLE THROMBOSIS IN CHILDREN: PROTHROMBOTIC RISK FACTORS

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Background-Aims: Various clinical underlying conditions as well as congenital prothrombotic risk factors contribute to the development of pediatric venous thrombosis. The aim of the study was to evaluate the prevalence, underlying disorders, and prothrombotic risk factors of children with multiple thrombosis. Mate-rial-Method and Results: Between January 1998 and June 2005, 415 pediatric patients were admitted to Hacettepe University Faculty of Medicine Pediatric Hematology Unit for evaluation of thrombosis. Of these 415 pediatric patients with thrombosis, 17 (3.8%) had multiple thrombosis. The mean age of the children with multiple thrombosis was 8.67±6.5 years (range: 3 months-18 years) and of these 17 children, six patients (35.3 %) were girls and eleven patients (64.7 %) were boys. Recurrence was observed in 4 of the 17 patients (23.5 %). Thrombus localization: Among these 17 patients with multiple thrombosis, one patient presented with left renal artery and VCI thrombosis; one patient with small and mesenteric arteries thrombosis; one patient with portal-hepatic vein and mesenteric artery thrombosis; one patient with femoral vein and small arteries thrombosis; one patient with VCI, SCV and vena basilica thrombosis; one patient with left atrial and basillary arteries thrombosis; one patient with hepatic and mesenteric veins thrombosis; one patient with SCV, juguler vein, and sagittal sinus thrombosis; one patient with renal, iliac and mesenteric vein thrombosis; one patient with PTE and brachiocephalic vein thrombosis; one patient with PTE and femoral vein thrombosis; one patient with

femoral vein and sinus rectus thrombosis; one patient with femoral vein, VCS and brachiocephalic vein thrombosis; one patient with VCI, SCV, axillary vein thrombosis and PTE; one patient with femoral and iliac veins, PTE, VCI and right atrial thrombosis; one patient with cranial infarct and PTE; and one patient with femoral vein and right atrial thrombosis. Underlying diseases and prothrombotic risk factors: Among these 17 patients with multiple thrombosis, one patient had trauma and FVL heterozygous mutation; one patient had operation for aort coarctation; one patient had infection, elevated D-dimer, hereditary protein S (PS) deficiency, and FVL heterozygous mutation; one patient had APA and FVL heterozygous mutation; one patient had trauma; one patient had elevated levels of lipoprotein-a and D-dimer and Prothrombin G20210A heterozygous mutation; one patient had otoimmune hemolytic anemia and elevated D-Dimer; one patient had atrial septal defect, ventricular septal defect (VSD), pulmonary binding operation, infection, and hereditary protein C (PC) deficiency; one patient had hereditary PS deficiency and FVL heterozygous mutation; one patient had infection, central venous line, elevated levels of fibrinogen, factor 8 and lipoprotein a; one patient had infection, elevated levels of D-Dimer, factor 11, and hyperlipidemia; one patient had elevated levels of factor 8 and FVL heterozygous mutation; one patient had VSD, pulmonary stenosis and FVL heterozygous mutation; one patient had beta thalassemia major, elevated levels of factor 8 and D-Dimer, and hereditary PC deficiency; one patient had infection, elevated levels of factor 8 and FVL heterozygous mutation; one patient had hereditary PC and PS deficiency, elevated levels of factor 8 and factor 2 and FVL heterozygous mutation; one patient had tetralogy of fallot and Behçet disease. Among 17 children with multiple thrombosis, two patients had 1, seven patients had 2, two patients had 3, four patients had 4, and two patients had 5 risk factors. All of the patients had risk factors. Conclusion: As a consequence of the data presented here, it is suggested that carriers of combined prothrombotic risk factors and underlying chronic diseases are more prone to multiple thrombosis.

Abstract: 710 Poster: 617

THROMBOTIC RISK FACTORS IN THE EGYPTIAN POPULATION

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Background: Thrombophilia have been investigated among populations since prothrombotic risk factors have begun to be discovered in 1993. Thrombophilic structure of the Egyptian population has not been reported yet and this study has an approach to investigate two common mutations of the factor V gene (1691 G-A and 4070 A-G), prothrombin gene 20210 G-A mutation, EPCR 23 bp insertion and ACE ins/del polymorphisms in the Egyptian population. The Egyptian population has a mixed genetic background with an ethnic heterogeneity and does not have an African origin. Most of the population has Mediterranean origin or Arabic that migrated from Saudi Arabia and surrounding areas. The prevalence of VTE in the Egypt population has not been estimated locally in Egypt. Aims: The genetic tendency of the risk factors in 188 randomly selected healthy individuals with Egyptian origin from Cairo which includes a mixture of all cultural groups in Egypt have been assessed. Cairo is considered as a referral center with people coming from different regions and discrete all over Egypt. Methods: Factor V 1691 G-A and Prothrombin 20210 G-A mutations were analyzed with Real-Time PCR method using Light Cycler-FVL and Prothrombin 20210 G-A mutations detection kits (Roche Diagnostics GmbH, Roche Molecular Biochemicals, Mannheim, Germany). For the detection of insertion/deletion polymorphisms of ACE gene and EPCR gene and HR2 haplotype of factor V gene was determined according to previously described PCR and RFLP techniques. Results: Both mutations in the factor V gene were found to have a high frequency of 16.5 % for 1691 G-A mutation and 11.2 % for 4070 A-G mutation in the Egyptian population. Prothrombin 20210 G-A mutation and EPCR 23 bp insertion were found to be very low in Egypt. ACE 300 bp ins/del polymorphism was found to be frequent similar to other factor V gene changes. Of the 188 individuals we found twentyone carrying the R2 haplotype and four carrying the R3 haplotype. Conclusions: Our study is the first report presenting the frequency of five thrombosis-related risk factors in healthy Egyptians. The two factor V gene mutations were both found to be very frequent whereas Prothrombin 20210 G-A mutation was found to be rare. The frequency of FactorV Leiden was reported for many populations and there is a marked difference in genetic backgrounds. With this study, we revealed the genetic tendency and the frequency of the Egyptian population for the five risk factors. Further studies are needed in thrombotic

Egyptian patients. (This study is supported by Ankara University Biotechnology Institute)

Abstract: 711 Poster: 618

INCREASED CONCENTRATION OF SOLUBLE CD40 LIGAND IN PREECLAMPSIA

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Preeclampsia is associated with increased platelet activation detected even before the onset of the disease. Platelets are not only involved in haemostasis but they also directly initiate an inflammatory response of the vessel wall. Inappropriate activation of platelets may be involved in pathogenesis in preeclampsia by promoting coagulation and thrombosis, and also as an important mediator of inflammation. Platelets may release inflammatory mediators such as soluble CD40 ligand (sCD40L). We investigated the plasma level of sCD40L during preeclamptic and normal pregnancies to emphasize inflammatory response in preeclampsia. Twenty patients with preeclampsia (mean age ± SD 29.5±1.22; range 22-38) and 20 normal pregnant women (mean age ± SD 25.7±0.82; range 20-33) were included in our study. The concentrations of sCD40L were measured by enzyme immunoassay (EIA). The mean sCD40L levels were 1.08±0.43 ng/ml in patients with preeclampsia and 0.76±0.24 ng/ml in normal pregnant women. A statistically significant difference was found between sCD40L levels of two groups (p=0.01). We believe that in order to clarify whether inflammation may cause inapproprite endothelial cell activation or inapproprite endothelial cell activation may start this inflammatory response, there is a need of future studies involving larger study population.

Abstract: 712 Poster: 619

POTENTIAL ROLE OF ADAMTS13/FXI COMPLEXES IN THE PATHOGENESIS OF END STAGE RENAL DISEASE

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ADAMTS13 alternatively known as von Willebrand Factor (vWF) cleaving protease is a Zinc metalloprotease which cleaves macromolecular M-vWF multimers at the Tyr (1605)-Met (1606) bond located in the AT domain of vWF. Down regulation of ADAMTS13 is known to be associated with thrombotic thrombocytopenic purpura (TTP). ADAMTS13 forms stable complex with factor XI and factor XIa. Measurement of ADAMTS13/FXI complexes in plasma may provide additional information on the pathogenesis of ESRD associated thrombotic complications. ADAMTS13/FXI can be measured using an ELISA based immunoassay. A polyclonal antibody reacts with a peptide in C-terminal region of the ADAMTS13 molecule is quoted on the micro titer plate. ADAMTS13 present in these test samples bind the antibody. After washing the bound ADAMTS13/FXI complexes were quantified. To test the hypothesis that ADAMTS13 levels are altered in ESRD, blood samples from 62 patients with ESRD prior to dialysis session were collected. Control group comprised of 34 normal healthy age match controls. The vWF antigen levels were also measured in both the groups using an ELISA method. The ESRD group exhibited a marked variation in the ADAMTS13/FXI complex levels with a range of 0 to 1100% (mean = 161±315) of the 62 samples. Eleven patients exhibited a greater than 250% where as the 51 patients exhibited less than 100 % complex. The distribution of ADMTS13/FXI complex was bi-modal. In the normals, the ADAMTS13/FXI complex activity ranges from 147-201% with a mean of 169±16. Unlike the ESRD population the normal group exhibited guassian distribution. The vWF antigen levels relatively higher in the ESRD patients (175±30) vs the normal (88±19). These results suggest that ADAMTS13/FXI is dysregulated in ESRD patients. While most of the patients exhibit a marked decrease in ADAMTS13 level, some of these patients exhibit markedly higher levels. Such fluctuation in the ADAMTS13/FXI level may contribute to the potential thrombotic and bleeding complications in ESRD pathogenesis.

Abstract: 713 Poster: 620

THE ANTITHROMBOTIC ROLE OF THE HETEROZYGOTE S-GENE

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BACKGROUND: Malaria has been linked with increased levels of plasma fibrinogen concentration and a consequential risk of Thromboembolic disorders. Also, hypofibrinolytic activity has been reported in this condition. The protective role of the S-gene against malaria has also been explained. AIM: Despite the known evidence of the protective effect of hemoglobin S in malaria prevalence, its role in haemostatic mechanisms during malaria parasitaemia has not been viewed with any serious attention. This accounts for our interest in investigating any possible role of the S-gene in malaria haemostasis and rheology. METHOD: A total of one hundred malaria patients comprising of seventy five (75) heterozygote Hb AS and 25 homozygote Hb SS patients confirmed with malaria diagnosis were investigated together with 50 apparently healthy homozygote Hb AA and without any parasitaemia as controls. Plasma fibrinogen concentrations, (PFC) and Euglobulin lysis time (ELT) were estimated from their blood samples using standard methods. RESULTS: There were statistically significant depletion of fibrinogen in heterozygote Hb AS having malaria with a concomitant decrease in ELT, which translates to hyperactivity of the fibrinolytic system ($P<0.05$) respectively, while there were observed increases in fibrinogen concentration of Hb AA and Hb SS during malaria attack. Though the increase in Hb AA was not significant, an experimental increase was however established while the increase in Hb SS was significant ($P<0.001$). The ELT in Hb SS had a significantly reduced value while AA recorded a significant hypofibrinolytic activity($P<0.05$ respectively). CONCLUSION: Decreased fibrinogen concentration coupled with hyperfibrinolytic activity could be a major antithrombotic role induced by heterozygote S-gene in malaria patients while double inheritance of the gene exhibits enhanced fibrinolytic activity which further indicates an antithrombotic protective mechanism in the presence of increasing plasma fibrinogen concentration.

Abstract: 714 Poster: 621

THE ROLE OF THROMBOPHILIC DISORDERS IN THE ETHIOLOGY OF HEMIPARETIC CEREBRAL PALSY IN CHILDREN AND CRANIAL MAGNETIC RESONANCE FINDINGS

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Background: Cerebral palsy (CP) is defined as a group of non-progressive position and motion disorders resulting from a defect or a lesion in developing brain. Hemiparetic cerebral palsy (HCP) is a CP variant affecting one side of the body. CP and its pathogenetical mechanisms still remain unclear. Aims: In this study, we aimed to investigate the frequency of thrombosis factors and their relationship with radiological findings in children with HCP. Methods: 36 subjects with HCP and 30 healthy children were included in this study. Blood samples were taken from both groups with EDTA and citrate. DNA isolation procedure was performed in blood samples taken with EDTA. Gene series including factor V leiden, methylene tetrahydrofolate reductase and prothrombin 20210A were multiplied in-vitro by using multiplex PCR (polymerase chain reaction) method. Mutations are studied by the way of insitu hybridization. Protein - C, protein - S and antithrombin - III levels were determined in blood samples taken with citrate by using chromogenic method. Cranial magnetic resonance (MRG) findings of 30 HCP patients were evaluated. Results: There was no difference between the HCP and control groups by means of thrombosis factor frequency. The most common monitoring findings in children with HCP has included periventricular leucomalacy (PVL) (80 %), atrophy (70 %), proencephalic cyst (50 %) and infarct (16 %). While there was no relationship between the thrombophilic disorders and PVL, atrophy and proencephalic cyst, it has been found that all of the patients with infarct have had an associated thrombophilic disorder. Conclusions: Our study is among the very rare research attempts that aims to investigate the thrombophilia in children with HCP by using a control group. Although we have found a significant correlation between the infarct and thrombophilia, there was no such relation between the HCP and thrombophilia. This can be caused by very restrictive number of patients. More different results can be obtained by increasing the number of subjects.

Abstract: 715 Poster: 622

LUPUS ANTICOAGULANT AND ACQUIRED PROTEIN C RESISTANCE IN AUTOIMMUNE THYROID DISEASES

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Autoimmune mechanisms are involved in the pathogenesis of many thyroid diseases.The autoimmune thyroid diseases are an immunological disorder in which lymphocytes become sensitized to thyroidal antigens and autoantibodies are formed that react with these antigens.. Autoimmune diseases tend to appear together with the other autoimmune diseases. In this study, we were planned to investigate the lupus anticoagulant (LA) which is an antibody involved in thrombosis process and the acquired active protein C resistance that was developed as a result of existence of autoantibody against active protein C in autoimmune thyroid patients. The study involved 118 patients with autoimmune thyroid disease and 54 healtly control subjects. The coagulation system parameters, thyroid function test, ANA, antidsDNA, anti-TG, anti-TPO and LA were studied. APC resistance was studied in 110 patients and APC resistance was found as positive in six patients (5,5 %). There was no correlation between the existence of thyroid auto-antibodies and APC resistance. On 4 out of 6 patients, factor V Leiden was found positive in heterozygote form and it was identified that all these patients had genetic APC resistance. LA was studied on 118 thyroid patients. LA positivity was detected in 41,5 % for all patients. 5,63 % for the control group, 45,9 % for the patients with positive thyroid autoantibody and 36,8 % for the patients with negative thyroid autoantibody. No statistically significant relation could be identified among LA positivity and type of thyroid disease and the positivity of thyroid autoantibodies. Consequently, the APC resistance of autoimmune thyroid patients was found similar to the normal population while LA positivity was found significantly higher than the control group.

Abstract: 716 Poster: 623

VON WILLEBRAND FACTOR: A RELIABLE INDEX OF BOTH CORONARY AND PERIPHERAL ATHEROSSCLEROSIS

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Introduction: Von Willebrand factor (vWF) is an emerging index of increased risk for the development of atherosclerosis and its clinical sequelae. Hypothesis: In this cross-sectional study we evaluated the hypothesis that von Willebrand factor plasma levels are associated with the extent of atherosclerosis in patients with CAD Methods: One hundred fifty patients, less than 65 years old (mean age: 52.6+/-7.2 years),135 men and 15 women, who were submitted to coronary angiography (indicated because of recently diagnosed or suspected CAD), underwent an additional B-mode ultrasound of their common carotid (CC) and common femoral (CF) arteries bilaterally. Intima-media thickness (IMT) and plaque presence (PP) were recorded and the concomitant detection of at least one plaque in both arterial beds was defined as bifocal PP. Imaging was performed bilaterally but only the maximum values were included in the analysis. An immunoturbidometric assay was used to measure vWF antigen plasma levels. Pearson`s correlation and logistic regression were used for data analysis. Results: vWF correlated with both CC and CF IMT (r=0.217, p=0.04 and r=0.291, p=0.036). The presence of 3-vessel CAD was significantly associated with bifocal PP (exp(B)=5.624, p=0.002). As shown in the table below, vWF was an independent predictor of both 3-vessel CAD and bifocal PP in multivariate logistic regression analysis. Conclusions: Von Willebrand factor, a marker of endothelial activation, may represent a new reliable index of substantial atherosclerotic burden in both coronary and peripheral arterial beds.

Abstract: 717 Poster: 624

THROMBOTIC RISK FACTORS IN HAEMOPHILIACS

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Haemophilic patients not only are born with a defect of coagulation, but also carry their bleeding tendency throughout their entire life. Therefore, it would be expected to bleed continuously. However, life itself proves that this is not the case, though the reason has not yet been explained. In fact, haemophiliacs bleed only under certain and specific circumstances (trauma, surgery, etc) so that it seems for a prophylactic mechanism to have been developed, through the century`s, in which we will try to bring some light. We examined blood samples from 65 patients, 47 normal individuals- 29 men and 18 women with a mean age 37±12 and 58 hemophiliacs with a mean age 42± 11. Methods: 14 coagulation factors and natural anticoagulants were studied as well as the 3 mutations related to thrombophilic tendency (FVLeiden, FIIG20210A, and MTHFR C677T). Subjects were divided into 2 groups, one comprised the non-haemophiliacs (control group) and the other the haemophiliacs. Patients with levels of natural anticoagulants of less than 75%, or levels of coagulation factors of more than 135% were designated as having one or more risk factors for thrombotic events. Methods We used Compact STA (STAGO co) for measurement of natural anticoagulants level, and BCS (Dade-Behring) for measurement of coagulation factors level. Mutations were detected with classic RFLP PCR analysis. Results There were 4 subjects with a single risk factor detected among the control group (2 with FV-Lei-den mutation 1 with partial deficiency of factor XII and 1 with elevated levels of factor VIII). In contrast 50 from the 58 subjects in the haemophiliacs group were found to be carriers of one or more risk factors. More particular, low levels of PC were detected in 6 haemophiliacs, low levels of PS in other 6, low levels of AT in 4, of plasminogen in 2, while 3 haemophiliacs showed a significant increase in FII levels, 7 in FV levels, 6 in FVII levels, 5 in FIX levels, 1 in FXI levels. 13 were found with reduced levels of FXII, 12 with increased levels of vWF:RiCof activity and 20 with increased levels of vWF:Ag. Abnormal aPC resistance was detected in 10 haemophiliacs, and heterozygosity for FV Leiden mutation or prothrombin G20210A polymorphism in 13 haemophiliacs. 16 haemophiliacs were MTHFR TT677 homozygous, and 4 more were both FV Leiden heterozygous and MTHFR 677TT homozygous. Chi square (x2) criterion was applied to determine the statistic difference between the 2 groups and x2 value of 24.05 ($p<0.0002$) is considered to be statistically significant. It is worth noted that only 8 subjects were found to be risk factor free. 14 carried 1 risk factor, 14 carried 2 risk factors, 8 carried 3, 9 carried 4, and 5 carried 5 risk factors. The above results are in line with the observation that haemophilic patients bleed only after trauma or surgical intervention etc. It seems probably that during the million years of human life on earth one or more compensatory mechanisms have developed. These appear to play a significant role in the rate of bleeding episodes in haemophiliacs and may also be able to explain the increasing frequency of thrombotic events in this group of patients.

Abstract: 718 Poster: 625

UPREGULATION OF TISSUE FACTOR, THROMBOMODULIN, AND P-SELECTIN IN END STAGE RENAL DISEASE

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Arterial thrombosis is commonly associated with End Stage Renal Disease (ESRD) leading to acute coronary syndrome, microvascular thrombosis and associated disorders. The generation of tissue factor, activation of platelets and endothelial damage significantly contribute to the pathogenesis of this syndrome. To investigate the relative involvement of these processes, plasma samples from ESRD patients (n=170) were analyzed for soluble tissue factor, P-selectin and thrombomodulin utilizing sandwich-based ELISA methods. Almost 80% of the ESRD patients had soluble tissue factor in their plasma. P-selectin levels were markedly increased (184±45 ng/ml vs 45.1±14.9 ng/ml) exhibiting a 4 fold increase. Similarly, soluble thrombomodulin levels were also increased (11.3±2.4 ng/ml vs 2.1±0.7 ng/ml), exhibiting a 5.3 fold increase. Additional biomarker analysis of plasma samples using protein chip array technique (SELDI) revealed the presence of unique biomarker profile in the 11-12 kDa range in 70% of these patients. This data is highly suggestive of the involvement of the blood vessels, platelets and tissue factor mediated activation of proteases in this syndrome. Additional studies are warranted to characterize the unique biomarker profile with the elevation of the thrombotic mediators of ESRD.

Abstract: 719 Poster: 626

THERAPEUTICAL USE OF FONDAPARINUX IN PATIENTS WITH HIT-II: (OUR EXPERIENCE)

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We present our experience from the use of Fondaparinux as alternative treatment for heparin induced thrombocytopenia (HIT-II), something that simplifies patients` handling, since neither continuous iv infusion nor frequent monitoring is required. Patients and Methods 17 13y). Among 11 years), and 7 females (57,3 patients (pts), 10 males (mean age 52 the 15pts, 4 developed HIT after unfractionated heparin administration during or post surgical thrombectomy, and 13 had received low molecular weight heparin (LMWH): 1 woman with breast cancer suffered pulmonary embolism (PE) while on LMWH, in 3pts oral anticoagulants were substituted by LMWH as for preoperative anticoagulation, 1 woman with atrial fibrillation was on LMWH due to Warfarin induced gastrointestinal bleeding, and 9pts were on LMWH for recurrent lower limb DVTs). Since pseudothrombocytopenia was excluded, HIT was assessed using the aggregation test to detect platelet activation in normal PRP, in the presence of therapeutic concentrations of heparin and pts serum. Diagnosis was confirmed with the HIT-test (Stago). Results 12pts received Refludan with continuous iv infusion, after heparin discontinuation. Satisfactory results were observed as defined by the absence of major side effects and a rise in the platelet count from treatment day 2. Fondaparinux 2.5mg was given 3/daily subcutaneously to 5pts. Platelet count increased from the 2nd day and physical signs improved. Discussion The effectiveness of Refludan is well known. The lack of interaction between Fondaparinux and PF4, as recent studies have proved, as well as the absence of HIT manifestation when Fondaparinux was given as prophylaxis in orthopedic surgery is due to its low MW, minimal chain length and minimum charge per carbohydrate required for induction of the HIT antigen on PF4. Arixtra was chosen because of its advantages that include simple mode of administration and less side effects, as opposed to already used modalities for HIT treatment. Taken into account its clinical effectiveness, the use of Arixtra in HIT seems to be justified.

Abstract: 720 Poster: 627

DNA-MICROARRAY TECHNIQUE FOR THE IDENTIFICATION OF THROMBOPHILIC DIATHESIS. COMPARISON WITH SPOLA TECHNOLOGY AND CLASSIC PCR ANALYSIS

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Introduction: DNA Microarray have the ability to test a large number of samples for a large number of mutations on the same time, something practically impossible with the traditional hybridization methods. The advantage of SPOLA (Solid Phase Oligonucleotide Ligation Assay) is the hybridization of two probes on the PCR product and the use of ligase to stabilize this complex. Furthermore, it simply requires incubation in room temperature as well as minimum laboratory equipment. The aim of this study was to compare the ability of DNA microarray application to recognize genetic predisposition to thrombosis, in relation to SPOLA technology and with the classic RLF-PCR analysis. Material: DNA samples from 37 subjects (24 male with mean age 41.9 and 13 female with mean age 38.8) were studied with micro-array and PCR analysis, Furthermore, in 26 of them (14 men and 12 women) an analysis of their DNA has been made with SPOLA. All of these subjects had a history of either recurrent thrombosis or thrombosis at unusual sites (e.g. retina`s central vein thrombosis). Method: The thrombo-check microarray contains the following mutations and polymorphisms: FV Leiden (FV G1691A), FII G20210A, FV Cambridge (FV G1091C), MTHFR C677T, MTHFR A1298C, CBS 844ins68, Plasminogen Activator Inhibitor (PAI 1 4G/5G). The thrombo-check microarray can distinguish between the normal sequence, as well as heterozygosity and homozygosity for the mutated sequence. To ensure the result is correct specific probes are included on the microarray to control for the RLFPCR reaction, the hybridization reaction and the silver staining procedure. In addition to the correct function of the entire reaction can be checked using an external control DNA. With SPOLA technology we checked the mutations of: FV Leiden, F II, MTHFR C677T, PAI 4G/5G. Results: As long as FVL and FII are concerned, in 35 out of 37 patients (pts) both methods (microarray and PCR) gave similar results. However, the re-

sults of DNA analysis were different for the other two patients. The first one was found to be, using the microarray DNA method, a double heterozygous carrier of both FVL and FII mutations, while RLF-PCR did not relieve such genetic defects. The other patient was found to be, using the RLF-PCR a homozygous carrier for the prothrombin mutation, while microarray also revealed heterozygous mutation of FV Leiden. With SPOLA, a homozygous MTHFR C677T carrier was revealed, for whom the microarrays were not able to determine his carrier status. In addition to this result, two patients that were characterized as heterozygous carriers of the PAI mutation were shown to be normal (homozygous for the wild type allele) with SPOLA, and a homozygous carrier was shown to be heterozygous.

Abstract: 721 Poster: 628

CENTRAL VENOUS CATHETER-RELATED THROMBOSIS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND SCREENING WITH DOPPLER-ULRASOUND

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Backgrounds: Central venous catheters (CVCs) are vital component of care for patients with hematological malignancies. The use of CVCs provides an important means of venous access. CVCs are associated with the long-term risks of thrombosis and CVC-related thrombosis causes significant morbidity in the patients. However, not all of the thrombosis is symptomatic. Aim: To estimate the incidence of CVC-related thrombotic complications in patients with hematological malignancies. Methods: We designed a prospective, observational study in our department. A total 78 CVCs in 42 consecutive patients with hematological malignancies were included in the study (males 28.6%, mean age 37.81 years ± 2.89). Most frequent diagnosis was acute leukemia (87%). Three lumens catheters were inserted in the subclavian vein of all of the patients. A record of all complications and catheters loss and final out come were analyzed. Blood samples for thrombophilia screening tests were taken from all patients before insertion of CVCs. All patients underwent serial Doppler-ultrasound until CVC removal and we evaluated whether clinically manifest thrombosis could be predicted by screening with Doppler-ultrasound. Patients were clinically assessed each day for signs and symptoms of thrombosis. In case of clinically suspected thrombosis, routine diagnostic and therapeutic procedures were done. Results: A total 78 catheters remained in subclavian vein for a median of 43 days (range 4-140). Total CVCs-related thrombosis was observed in 6.4% (5/78) of patients. Of the 5 patients with thrombosis, 3 had subclinical thrombosis by Doppler-ultrasound and no of them developed clinically manifest thrombosis later. Two patients had clinically manifest thrombosis without prior abnormal Doppler-ultrasound. Thrombosis of the catheters lumen (diagnosed upon the inability to aspirate blood with or without inability to flush occluded catheter) occurred in 20.5% (16/78). Catheter loss rate due to complication was 6.4% (5/78; 2 infection, 1 catheter thrombosis, 2 venous thrombosis). Neither total parenteral nutrition (p:0.46) nor difficult insertion of catheters (p:0.37) were related to thrombosis. Four patients had activated protein C-resistance (APC-R) and one of them had internal jugular vein thrombosis. Conclusion: The incidence of clinically overt CVC-related thrombotic complications in patients with hematological malignancies is not negligible. The thrombosis of the lumen of the catheter is the most frequent complication of central vein canulation. However their necessity of catheter removal is negligible. Although symptomatic disease was not developed in our cases of subclinical thrombosis, Dop-pler-ultrasound screening may be useful to identify the patients with subclinical thrombosis that require anti-thrombotic treatment.

Abstract: 722 Poster: 629

A STUDY OF FACTOR VII,TISSUE FACTOR PATHWAY INHIBITOR AND MONCYTE TISSUE FACTOR IN NONINSULIN DEPENDNET DIABETES MELLITUS

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ABSTRACT OBJECTIVE: To study the changes in plasma TF activated FVII and plasma TFPI in typeII diabetes mellitus and compare the results in vascular complicated and non complicated patients. Also their impact on prediction of vascular complications of diabetes and improvement of risk assessment. BACKGROUND: Vascular endo-

thelium, the primary defense against thrombosis, is abnormal in diabetes.The plasma levels of many clotting factors e.g. fibrinogen,FVII. FVIII and FXI are elevated as well in diabetes(Carr,2001).Tissue factor (TF),a high affinity receptor ad cofactor of FVII,is widely expressed in extravascular tissue and can be induced in monocytes and endothelial cells in response to various stimuli.Khechai et al.(1997) found that glycated albumin causes blood monocytes to produce TF mRNA.Tissue factor pathway inhibitor is responsible of inhibiting FVIIa and FXa by trapping them in an inactive complex of TF,VIIa,Xa,and TFPI. Studies showed that TFPI had increased activity in insulin - dependent diabetes with nephropathy. DESIGN/METHODS: The study included fifty type II diabetic patients;24 men and 26 women. They were recruited from the diabetes clinic of Internal Medicine Cairo University hospitals. Twenty healthy controls matched in age,sex and body mass to patients group.All patients and controls were subjected to careful medical history and examination,fasting plasma glucose level,glycosylated haemoglobin,lipid profile. Haemostatic parameters;PT,PTT,FVIIa by coagulation method,Plasma tissue factor activity by chromogenic assay,TFPI and expression of TF on blood monocytes by flowcytometry. RESULTS:The mean TF,meanTF activity,mean TFPI,and mean FVIIa were significantly increased among hyperlidemic diabetics more than normolipidemic diabetics and in normolipidemic diabetics than in control subjects. The mean % of TF +ve monocytes without lipopolysaccharide,tissue factor +ve monocytes with lipopolysaccharide was significantly higher among complicated diabetics than non complicated diabetics. The mean levels of plasma TFactivity. TFPI and mean FVIIa were significantly higher among complicated diabetics than among non complicated diabetics. Although the mean % of tissue factor +ve monocytes withot lipopolysaccharide,tissue factor +ve monocytes with lipopolysaccharide,plasma tissue factor activity,plasma tissue factor pathway inhibitor and activated FVIIa were higher among diabetics with macrovascular complications than among those with microvascular copmplications. There was a high significant correlation between HbA1c and triglycerides and the %of tissue factor +ve monocytes with and without LPS stimulation,plasma tissue factor activity and both FVIIa and tissue factor pathway inhibitor. CONCLUSIONS: The endothelial cells and monocytes are the possible common source of the tissue factor and tissue factor pathway inhibitor and the blood clotting activation obsereved in these patients may be related to elevated TF circulating levels not sufficiently inhibited by elevated TFPI plasma levels present, so anticoagulant therapy by direct inhibition of tissue factor activity may thus be particularly effective in type IIdiabetic patients.

Abstract: 723 Poster: 630

THROMBELASTOGRAPHY PATTERN AND D-DIMER PROFILE IN CHILDREN WITH THALASSEMIA MAJOR IN DR HASAN SADIKIN HOSPITAL BANDUNG INDONESIA

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Thalassemia is acondition in which a reduce rate of synthesis of one or more of the globin chains leads to imbalanced globin-chain synthesis, defective hemoglobin production, and damage to the red blood cells or their precursors due to effect of excessive globin unit produced. The damage of the red blood cells or their precursors will cause stimulation of coagulation activity that leads to hypercoagulability, followed with fibrinolysis process. Hypercoagulability can be detected by Thrombelastography (TEG), whereas one of fibrinolysis activity marker is D-dimer. This study aims to find out the TEG pattern and D-dimer profile in children with Thalassemia major. The subjects in this study were 96 children, 51 girls and 45 boys, who had been diagnosed as Thalassemia major, and admitted to Hematology and Oncology Clinic of Pediatric Department of Dr Hasan Sadikin Hospital Bandung Indonesia. The TEG was performed with syringe method, while D-dimer with latex agglutination method. Data were analysis with interval estimation, 95% confidence intervals, proportion test, and Spearman`s correlation coefficient. From this study we found that 65.6% of the children showed hypercoagulation pattern with TEG, while 34.4% were normal, and 52.1% were D-dimer positive while 47.9% were D-dimer negative. There was no correlation between those two parameters (r=0.13; p=0.206). We can conclude that more than a half children with Thalassemia major showed hypercoagulability, and around half of them with increase activation of fibrinolytic process. We suggest that TEG and D-dimer test should be added to a routine laboratory tests in the management of Thalassemia.

Abstract: 724 Poster: 631

RELATIONSHIP BETWEEN SMALL-FOR-GESTATION-AL AGE BIRTHS AND MATERNAL THROMBOPHILIC MUTATIONS

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Background: Small-for-gestational-age (SGA) describes a neonate whose weight is less than estimated range based on gestational age as established by population studies. Thrombophilic mutations could affect placental circulation and result in a SGA newborn. Aim: Our aim was to investigate whether there was a relationship between mother`s thrombophilic mutations and SGA deliveries. Methods: Sixty-five mothers who gave birth to one or more SGA babies and 104 mothers who gave birth to appropriate-for-gestational age babies included in the study. We investigated following mutations; Factor V (FV) Leiden (G1691A), FV Cambridge (A1090G), FV A1299G, prothrombin G20210A, methylenetetrahydrofolate reductase (MTHFR) C677T, MTHFR A1298C, and MTHFR T1317C. Results: There was no difference between groups considering FV Leiden, FV Cambridge, FV A1299G, and MTHFR T1317C. However, significant difference between groups was found with regards to MTHFR C677T ($p=0.01$) and MTHFR A1298C ($p<0.001$). Conclusion: We suggest mutations in mothers` MTHFR gene can result in SGA deliveries in Turkish population.

Abstract: 725 Poster: 632

CLINICAL AND LABORATORY FINDINGS IN CHILDREN WITH DISSEMINATED INTRAVASCULAR COAGULOPATHY

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Background: Disseminated intravascular coagulaopathy (DIC) is a syndrome characterized by systemic intravascular activation of coagulation resulting in depletion of platelets and coagulation factors. It`s a frequent complication of a variety of disease such as infection, trauma and malignancy. Consumption and exhaustion of coagulation proteins and microvascular thrombosis cause simultaneous bleeding and thrombotic problems. This microvascular thrombosis leads to multiorgan failure and multiple bleeding complicates treatment. Aim: To evaluate clinical and laboratory findings of 40 consecutive children in a single center, diagnosed as DIC according to ISTH criteria and compare vascular endothelial growth factor (VEGF) levels with 40 healthy objects. Results: In the study group median age of patients was 23 months (93-192 months). There were 24 females and 16 males. Congenital heart disease in 7 patients, chronic renal failure in 5 patients, malignancy in 3 patients, metabolic disease in 3 patients and collagen tissue disease in 2 patients were underlying disorders. Twenty four patients had infection, whom 17 of them were documented. Acute lower respiratory disease in 15 (68,2), urinary tract disease in 3 (7,5 %) and acute gastroenteritis in 3 (7,5 %) were predisposing factors in patients. Mean acute CRP level was 6,0±6,2 mg/dl. At the time of diagnosis median WBC count was 7050 /mm3 (600-154000), platelet count was 70.000 /mm3 (3000-624000) and hemoglobin level was 9,5 gr/dl (5,8-16,3). Low level of protein C and S levels were detected in 13 (32.5%) and 9(22.5%) patients respectively. Platelet count was below 50000/mm3 in 14 (35%), in 50000100000 range in 16 (40%) and over 100000/mm3 in 10 (25%) patients. Fibrinogen levels were decreased only in six of patients. Majority of patients (37 (92.5%)) had prolonged prothrombin time. D-dimer levels over 2 μg/ml in were detected in 36 (90%) patients. There were no significant difference in VEGF levels between study group(mean 320,25±327,33pq/ml)and healthy controls (514,51± 679,19) ($p=0.603$). Major bleeding episodes were detected in 15 (37,5%) patients. All patients received fresh frozen plasma. Antithrombin III and active Factor VIIa treatment were given to three and five patients respectively. Two patients had plasmapheresis. Twenty three patients required ventilatory support. After being diagnosed as DIC, 23 patients were exitus on mean two days. This study has been supported by Turkish Society of Hematology.

Abstract: 726 Poster: 633

ABNORMALITIES IN THE COAGULATION SYSTEM AND FOLATE METABOLISM IN PATIENTS WITH MIGRAINE WITH AND WITHOUT AURA

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Background: Migraine has been considered a risk factor for ischaemic stroke or cerebrovascular disease because of the increased platelet activation detected. Coagulation abnormalities, antiphospholipid antibodies and other prothrombotic genetic risk factors have been suggested to be synergistic with the genetic risk factors for thrombosis. The association between migraine and ischaemic stroke still remains unclear. Most of the studies have shown that factor V Leiden is not a common and a significant risk factor in the pathogenesis of migraine. But there are also studies implying the opposite. One study has shown that prothrombin cleavage products are increased in patients with migraine with aura between attacks. Recently, it has been determined that folate metabolism, increased homocysteine levels and related genetic risk factors could be involved in migraine pathogenesis. C677T variant of MTHFR gene has been studied and like other prothrombotic factors, the findings are conflicting. DHFR gene deletion has not been studied until now in patients with migraine and DHFR is a key regulatory enzyme related with folate biosynthesis. Aims: We planned to study four mutations related both with prothrombotic factors and folate metabolism. Our study group included 24 patients with migraine with aura (MA group) and 173 patients with migraine without aura (MO group) with a mean age of 37.4±11.2. Materials and methods: After withdrawn of the blood from migraine patients with an informed consent, DNA was isolated by classical phenol-chloroform method. For FVL, PT 20210 G-A and C677T variant of MTHFR gene, real-time PCR was performed. To detect the deletion in the DHFR gene PCR was performed. Results: The results are shown in Table 1.Conclusions: At least one thrombosis related polymorphism has been detected in patients with migraine with aura. Patients who did not carry any genetic risk factor were belong the migraine group without aura. Our results revealed a high prevalence of the risk factors in migraineurs. While prothrombin alteration brought up to a statistically important 7 fold risk, homocysteine related polymorphisms decreased the risk, but the decrease was not found to be important statistically. By a statistical program evaluating all polymorphisms together, there can be an increased risk related with thrombosis in migraneurs. (This study is supported by Ankara University Biotechnology Institute)

Abstract: 727 Poster: 634

EVALUATION OF THE FIBRINOLYTIC SYSTEM BY USING GLOBAL FIBRINOLYTICCAPACITY AFTER HEAVY EXERCISE AND TRAUMA:

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ABSTRACT Objectives: The aim of this study was to investigate the early and late effects of heavy exercise and trauma on fibrinolytic system in wrestlers by using global fibrinolytic capacity (GFC). Methods: A total of 20 men wrestlers aged between 11-21 years, making medium to heavy exercise and exposed to minor trauma, were enrolled in this study. Blood samples were taken immediately before and after exercise and 24 hours after completion of exercise. Fort he investigation of blood coagulation prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, D-dimer, anti thrombin III (AT III), protein-C (PC), protein S (PS) and a new test that showing the fibrinolytic activity named GFC were measured. Results: Just after the exercise aPTT became shorter ($p<0.05$), but 24 hours after the exercise it returned to previous values. PT lengthened a bit just after the exercise ($p<0.05$) but it also returned to previous values after 24 hours. Protein-C level reduces just after the exercise ($p<0.05$) however 24 hours later than the exercise it returned previous value. 24 hours after the exercise fibrinogen was significantly low ($p<0.05$), whereas the ATIII was significantly high ($p<0.05$). No change in Protein-S and D-dimer values was designated. GFC increased nearly significant just after the exercise ($p=0.06$). However 24 hours later than the exercise it significantly decreased both

after and before the exercise level ($p<0.05$). Conclusions: The increase in the levels of GFC shows that the fibirnolytic system is activated after exercise but 24 hours later its activity is declined significantly via the decrease in GFC ($p<0,05$). These results suggest that the fibrinolytic capacity of sporstmen who train hard decreases in the late term and it may not be sufficient during the thrombotic period. We think that the fibrinolytic activity should not only be monitored just after exercise but also should be monitored later.

Abstract: 728 Poster: 635

CLINICAL EVALUATION OF PEDIATRIC THROMBOTIC EPISODES IN A SINGLE CENTER

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Aim: In this retrospective study we aim to evaluate clinical and laboratory findings of pediatric thrombotic episodes occured between years 98-05 in a single center. Results: In the present study between 1998-2005 years, 415 children with a history of trombosis episode were retrospectively evaluated. Out of which 261 (%62,9) were male children and 154 (%37,1) were female. Median age of patients were 72,0 (10-252) month. Age distribution was as follows: 0-3 month 31 (%7,5), 4-12 month 30 (%7,2), 13-36 month 87 (%21), 37-72 month 66 (%15,9), 73-144 month 108 (%26) and over 144 month were 93 (%22,4) children. Family history was present in 21 (%5,1) of the patients. 39 (% 9,4) of the patients had congenital heart disease. Majority of episodes were acute 381 (%91,8), and the rest 5 (%1.2) were subacute and only 29 (%7) episodes were classified as chronic. Mostly cerebral thrombosis 173 (%41,7) were seen and deep vein thrombosis 54 (%13), portal thrombosis 48 (%11,6) and cardiac thrombosis 40 (%9,6) were other frequent thrombosis types seen in the patients. In 174 (%41,9) patients thrombosis were arterial origin. Venous originated thrombosis were seen in 176 (%42,4), intracardiac thrombosis were seen in 39 (%9,4), thrombosis in sinuses were in 21 (%5,1), hemorrhagic thrombosis were in 5 (%1,2) patients. Infection at the time of thrombosis episode were detected in 106 (% 25,5) of patients. 24 (% 5,8) patients had a history of trauma. 388 patients had FV leiden mutation report, and 66 (%17) were heterozygot, 11 (% 2,8) were homozygot and other 311(% 80,2) were normal. 18 of 383 (%4,3) patients were heterozygot, and 365 (%95,3) were normal for screened prothrombin A2020 mutation. MTHFR data were available only in 38 patients, of whom 16 (42,1) were heterozygot, 4 (%10,5) were homozygot, and rest 17 (%44,7) were normal. Homocystein levels screened in 125 of patients and eleveated levels were in 16 (% 12,8). Other laboratory results evaluated were high lipoprotein A levels in 22 of 90 (% 24,4), high cholesterol levels in 12 of 88 (%13,6), high triglyceride level in 16 of 85 (%18,8), low fibrinogen level 10 of 149 (%6,7) patients. Factor VIII levels were eleveated in 72 of 138 (%52,2) while decreased in 13 (%9,4) and normal in 53 (%38,4)patients. 11 (%6) patients had very low protein C levels (0-20 mg/dl), and further 80 (43,5) had low protein levels (21-69 mg/dl), while 93 patients (%50,5) having normal or high values. Protein S levels screened, was within 0-20 mg/dl range in 8 (%4,5), within 21-59 mg/dl in 67 (%38,1), within 60-130 mg/dl in 91 (%51,7) and higher in 10 (%2,4). 21 patients were having malignant disease, 13 were having vasculitis and/or collagen vascular disease, hepatic and renal disease were present in 9 and 8 patients respectively. Hematological disease mostly sickle cell and thalassemia were seen in 12 patients. Five patients were Down Syndrome and 3 other patients were having Behçet disease.

Abstract: 729 Poster: 636

ANTIPHOSPHOLIPID ANTIBODIES IN CHILDREN WITH THROMBOSIS

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Background-Aims: The antiphospholipid syndrome is a thrombophillic disorder characterized by the presence of antiphospholipid antibodies (APA). It often occurs in patients with systemic lupus erythematosus (SLE) and may be associated with recurrent abortions, thrombocytopenia, and occasionally catastrophic thrombotic events. The aim of the study was to evaluate the prevalence, clinical associations, and outcome of children with APA and thrombosis. Material-Method and Results: The presence of APA was investigated in

120 children who were applied to Hacettepe University Faculty of Medicine, Pediatric Hematology Unit for evaluation of thrombosis between January 1998 and June 2005. The frequency of APA among 120 children with thrombosis was 11,6 % (14/120). The mean age of the children with APA and thrombosis was 10,14±4,86 years (range: 2,5-18 years) and of these 14 children,11 (78,6 %) were female and 3 (21,4 %) were male. Recurrence was observed in one of the 14 patients (7.1%) with a mean follow up period of 33.1±21.8 months (range: 5-60 months). In four patients (28.5%), the presence of APA was associated with SLE. Thrombus localization: Among these 14 patients with APA and thrombosis, one patient presented with multible thrombosis (PTE and cranial infarct), one patient with right atrial thrombosis, one patient with sino-venous thrombosis, two patients with arteriel thrombosis (one had pulmonary artery thrombosis and the other had small arteriel thrombosis), one patient with portal vein thrombosis, three patients with deep venous thrombosis (one had VCI thrombosis and the others had femoral vein thrombosis), and five patients with cranial infarct. Underlying diseases and protrombotic risk factors for thrombosis: Among these 14 patients with APA and thrombosis, one patient had congenital heart disease (mitral and aortic insufficiency), and FVL heterozygous mutation; one patient had congenital heart disease (PDA, aort coarctation, congenital mitral valve abnormalities), pulmoner binding operation, infective endocarditis, and elevated fibrinogen level; one patient had congenital heart diseases (tricuspid and pulmoner insufficiency) and infective endocarditis; one patient had SLE, renal transplantation, and hyperlipidemia; one patient had SLE, hereditary protein S deficiency, elevated levels of fibrinogen and D-dimer; one patient had SLE, Wolf-Parkinson-White syndrome, elevated levels of factor 8, and FVL heterozygous mutation; one patient had SLE, and FVL heterozygous mutation; one patient had lymphoma and central venous line; one patient had hereditary protein C and S deficiency and FVL heterozygous mutation, and one patient had elevated levels of factor 2, factor 5, factor 8 levels and FVL heterozygous mutation. Among 14 children with APA and thrombosis, four patients (28.5%) had 2, two patients (14.2%) had 3, four patients (28.5%) had 4 additional risk factors except circulating APA. Four patients had no additional risk factors. Conclusion: Thrombosis, venous or arterial are the most common clinical findings in patients with circulating APA. It should be kept in mind that APA may be responsible for the pathogenesis of the thrombosis and should be tested for all of the children with thrombosis.

Abstract: 730 Poster: 637

THE FREQUENCY OF FACTOR V LEIDEN, PROTHROMBIN G20210A, AND MTHFR GENE MUTATION IN PREGNANT WOMEN WITH PREECLAMPSIA AND ECLAMPSIA

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Background: Preeclampsia and eclampsia are the most significant reasons of mortality and morbidity in pregnant women.Currently it is mentioned that many complications leading to maternal morbidity and mortality are due to thrombosis, hemostasis disorders and plasental vascular anomalies. Aims: Our aim is to investigate the frequency of factor V Leiden (FVL), prothrombin G20210A, and MTHFR gene mutation in preeclamptic and eclamptic patients. Methods: One hundred patients with preeclampsia and eclampsia and 74 women with healthy pregnancy were evaluated for those factors.The study was carried out on a basis of case-control. Stu-dent-t test and Chi-square method were used for stastistics. Results: Heterozygous FVL was found in the 6% of patients group and in 4% of control group (p=0.570). Homozygous FVL was not found in the two group. Heterozygous PT G20210A gene mutation was found in 4% of patients group and 1% of control group (p=0.291). Homozygous PT G20210A gene mutation was not found in the two group. Heterozygous MTHFR mutation was found in 46% of patients group and 40% of control group (p=0.185). Homozygous MTHFR mutation was found in 16% of patients and 12% of control group (p=0.565). Statistically difference was not found between all patients group and controls. Summary/Conclusion: The role of hereditary thrombotic risk factors in preeclampsia and eclampsia is stil controversial. In our study, we didn`t find any correlation between FVL, PT G20210A, and MTHFR and preeclampsia/eclampsia.

Abstract: 731 Poster: 638

THE ASSOCIATION OF CEREBRAL VASCULAR THROMBOSIS WITH ANTIPHOSPHOLIPID ANTIBODIES

IN PATIENTS WITH THROMBOPHILIA

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Background: The preavlence of cerebral vascular thrombosis and its association with antiphospholipid antibodies (aPLs) in Chinese patients with thrombophilia remain unclear. Methods: From 1995 to 2002, consecutive patients referred to the coagulation laboratory for thrombophilia screening (Taiwan Thrombophilia Study) were assessed. The clinical diagnosis of thrombophilia was based on our previous studies that excluded patients whose onset of thromboembolism was associated with surgery, pregnancy, immobilization, liver disease, renal disease, myeloproliferative disorders and usage of oral contraceptives. Only thrombophilic patients with objectively comfirmed venous thromboembolism or recurrent habitual abortion related to antiphospholipid syndrome were recruited for the evaluation of occurrence of cerebral vascular thrombosis related to aPLs(anticardiolipin antibodies or lupus anticoagulants). Factor V Leiden mutation and prothrombin G20210A mutation were screened in all recruited patients in addition to thrombophilia profile. Results: 270 Chinese patients were studied and all DNA samples were negative for factor V Leiden mutation and prothrombin G20210A mutation. Of them, 226 patients (group A, age range 18-81 years) with deep vein thrombosis and/or pulmonary embolism were negative for aPLs and 44 patients (group B, age range 19-75 years) with vascular thrombosis and/or habitual abortion were positive for aPLs on 2 or more occasions at least 6 weeks apart. A total prevalence of crebral vascular thrombosis (arteries or veins) in 270 patients was 12.2% (n=33). The sub-group prevalence of crebral vascular thrombosis was further evaluated. In group A, cerebral thrombosis was confirmed in 22 patients (9.7%), i.e., arteiral stroke (n=1; onset age, 50 years), cerebral sinus thrombosis (n=20) and both (n=2). The onset age ranged from 19 to 75 years. In group B, cerebral arterial stroke was confirmed in 11 patients (25.0%) and none of them had cerebral sinus thrombosis. The onset age of arterial stroke ranged from 2075 years (<=25 years, one; 26-35 years, three; 36-45 years, three; >45 years, four). The prevalence of cerebral vascular thrombosis in group A was significantly higher than those seen in group B ($p<0.001$ by Chi-Sqaure test). Conclusions: Cerebral vascular thrombosis was commonly seen in Chinese thrombophilic patients. Two most prevalent genetic mutation seen in Caucasians, i.e, factor V Leiden mutation and prothrombin G20210A mutation were absent in our subjects. The prevalence of cerebral vascular thrombosis significantly increased when having aPLs and early stroke (<=45 years) seemed strongly associated with thrombophilic patients with aPLs.

Abstract: 732 Poster: 639

TREATMENT OUTCOME OF PLASMAPHERESIS IN THROMBOTIC THROMBOCYTOPENIC PURPURA: THE EXPERIENCE OF SINGLE CENTRE

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Background: Thrombotic thrombocytopenic purpura (TTP) is a life threating, coombs negative microangiopathic hemolytic anemia which is characterized by thrombocytopenia, neurologic disorder, renal dysfunction, fever and fragmanted erythrocytes. Promoting factor is not known certainly, but common pathogenetic mechanism is excessive von Willebrand factor accumulation in plasma and platelet surface and thrombocytic gag in microvasculer bed. In acute attack there is a IgG type inhibitory against protease that breaks von Willebrand factor but in familial type there is a protease deficiency.Plasmapheresis is the first choice and effective treatment modality. Aims: We aimed to study clinical process, laboratory findings, response to therapy and prognosis of 12 TTP patients that were followed in our hematology clinic between 1998 and May 2005. Methods: Basic diagnostic parameters were thrombocytopenia, coombs negative microangiopathic hemolytic anemia, high LDH levels, neurologic findings, renal dysfunction and presence of fragmanted erythrocytes. Plasmapheresis was done by 1700-2800 cc plasma. At least 3 and at most 14 times plasmapheresis was applied. Results: Two patients needed a second period of plasmapheresis, one after 22 months and the other after 49 months. Three patients died. One of them was the patient that needed a second period of plasmapheresis after 22 months. The other 2 patients died at the time of diagnosis. The average platelet count of patients were 42.000/mm3,the average LDH levels was 479 IU/L. Five patients had fever at the time of diagnosis. Nine of 12 patients had

reversible renal functional deteriotement. Summary/Conclusion: We find that plasmapheresis is effective and tolerable treatment for TTP.

Abstract: 733 Poster: 640

CONTRAST-MEDIA INDUCED HEMORHEOLOGICAL ALTERATIONS IN NIGERIAN INTRAVENOUS PYELOGRAPHY (IVP) PATIENTS

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BACKGROUND: Intravenous pyelography is the injection of a radio-opaque liquid (contrast media) into the bloodstream which is first excreted by the kidney, opacifies the renal parenchyma and later the collecting system. This provides important structural information and also reveals the presence or absence of excretory function. There has been several reports of renal blood flow reduction due to contrast media injection (Donaldson,1968 and Caldicott et al, 1970). There is paucity of information about possible haemorheological changes in these patients. AIM: This study therefore is to ascertain the possible effects of the media on the flow properties of blood. MATERIALS AND METHODS: Ten selected patients among those going in for IVP who consented, were studied. Their blood samples were collected before (Pre-IVP), during the procedure (Pro-IVP) and after the procedure (Post-IVP) for analysis of packed cell volume(PCV), whole blood viscosity (WBV), plasma viscosity (PV), plasma fibrinogen concentration (PFC) and euglobulin lysis time using Standard methods. RESULTS: There were no statistical significant differences in PCV, WBV and PV in both Pre and Post-IVP samples but an enhanced fibrinolysis and a concomitant decrease in PFC in the Pro-IVP samples were observed ($P<0.005$) respectively while. The Pro and Post-IVP samples compared exhibited a parallel increase in all the parameters except in PCV ($P<0.005$) respectively. CONCLUSION: The enhanced fibrinolysis coupled with hypofibrinogenaemia after contrast injections could be an acute risk factors to bleeding while the effect on other flow properties of blood is insignificant provided the contrast is excreted. Therefore, the blood flow reduction earlier observed in these patients could be due to probable vascular response.

Abstract: 734 Poster: 641

CHILDHOOD THROMBOSIS

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Over the last few decades, better understanding of thrombosis in children and improvement of tertiary pediatrics care occurred. Conditions such as leukemia, congenital heart diseases and prematurity that considered lethal previously have become curable. That`s involved use of newer techniques and devices such as catheterization and prosthesis. Where thromboembolisms become more common. The Canadian registry of venous thromboembolism in children reported an incidence of 0.07 / 10,000 and 5.3 / 10,000 of hospitals admissions. Where only 4% was idiopathic and 84% had two risk factors, inherited prothrombothic disorders constitute the least frequent risk factor. Factor V leiden and prothrombin 20210A gene, only recently become characterized and becoming a common risk factor for venous thromboembolism. With estimated incidence of 7% among Saudi population. Epidemiology, risk factors, pathology, presentation, diagnosis and therapy of thrombosis in children has been discussed in this review.

Abstract: 735 Poster: 642

EFFECTS OF RESISTANCE TRAINING WITH DIFFERENT VOLUME ON HEMOSTATIC PARAMETERS IN YOUNG MALES

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Aim: It is revealed by various studies that physical exercise activates coagulation and increases fibrinolytic activity. However, there are different observations depending on the type, volume and intensity of the physical exercise. There are very

few studies on the effect of exercise on the coagulation inhibitors having different results. Studies in literature focus on the effects of acute and subacute effects of endurance exercises. This study aims to investigate the effects of resistance training with different volume but equal intensity on some hemostatic parameters. Method: 26 healthy male students were randomly placed into single set group (SSG; n= 14) and multiple set group (MSG; n= 12). MSG performed all exercises in 3 sets of 12-15 repeat maximum (RM) for the first three weeks; super sets and 3 sets of 8-12 RM were performed for the remaining 5 weeks; 3 days/week. SSG performed all exercises in one set. Pre and post-training values of protrombin time (PT), activated partial protombin time (APTT), fibrinogen (FIB), d-dimer (DD), factor (F) VIII, plasminogen (PLASM), protein C (PC), free protein S (PS), antitrombin (AT) were measured from plasma by coagulometer; thrombin activatable fibrinolysis inhibitor (TAFI) was measured via ELISA method. Results: After the exercise period, PT was shortened ($p<0.05$); FVIII and AT decreased ($p<0.05$); PS decreased ($p<0.01$); PLASM increased ($p<0.05$) and insignificant increase in FIB in SSG was determined. In MSG, PT was shortened; PLASM increased ($p<0.01$); PC decreased ($p<0.05$); PS decreased ($p<0.01$); TAFI increased ($p<0.05$); insignificant increases in FIB and DD; insignificant decreases in FVIII and AT were determined. Conclusion: No studies were found in literature comparing the effects of resistance training with equal intensity but different volume on the aforementioned parameters. Our results showed that two-month resistance exercises may increase the tendency for coagulation in healthy people. This form of exercise may be an additional risk for the people with PC, PS and AT deficiency. The increase in TAFI with the increased exercise volume may lead us to think about the inhibition of fibrinolysis. Despite the existence of studies on TAFI with the risk factors for cardiovascular and coagulation, no studies exist on its relationship with exercise. Exercise modes in which TAFI is studied with the other fibrinolysis parameters will be enlightening on this issue.

Abstract: 736 Poster: 643

EVALUATION OF PLASMA TISSUE FACTOR AND TISSUE FACTOR PATHWAY INHIBITOR LEVELS IN CHILDHOOD HEMANGIOMAS

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Purpose: To evaluate the plasma levels of tissue factor (TF), an angiogenic marker, and tissue factor pathway inhibitor (TFPI), an antiproliferative protein, in the childhood hemangiomas at proliferative and regressive stage. Patients and methods: The study included 30 patients with hemangiomas and 30 healthy children. Localization, number, stage, type, duration of growth, complications, and treatment modalities of the hemangiomas were determined. Venous blood samples from all individuals were collected into citrated tubes, supernatant plasma were separated, aliquated, and stored at -70oC until samples could be assayed. Plasma levels of TF and TFPI were measured with quantitative ELISA kits. Results: Plasma TF and TFPI levels did not show any significant difference between the study and control groups. Plasma TF and TFPI levels also did not show a statistically significant difference when patients with hemangiomas were divided into two groups according to gender, hemangioma size, type, and stage and compared to each other. Conclusion: Plasma TF and TFPI levels of our patients with hemangiomas were not different from healthy children and they did not show any correlation with clinical features, including proliferative and regressive stage. We believe that further studies investigating the plasma/tissue levels of TF and TFPI and evaluating the role of TFPI therapy in diffuse hemangiomatosis may provide strategic results in therapeutic approach and follow-up of those patients.

Abstract: 737 Poster: 644

PLATELET AGGREGATION ABNORMALITIES IN PATIENTS WITH ARTERIAL THROMBOEMBOLIC DISORDERS, VENOUS THROMBOEMBOLISM AND RECURRENT FETAL LOSS (A PRELIMINARY REPORT)

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The results of recent studies suggest that platelets have a major role in arterial and venous thrombosis and recurrent fetal loss. The purpose of this study is to evaluate the platelet aggregation abnormalities in patients with arterial thromboembolic disorders, venous thromboembolism and recurrent fetal loss. Results of two arterial thromboembolic events (two ischemic stroke), 13 venous thrombosis (10 deep vein thrombosis/pulmo-nary embolism, one hepatic vein thrombosis, one portal vein thrombosis and one retinal vein thrombosis) and 22 patients with recurrent fetal losses were compared with 59 controls in this preliminary report. Platelet aggregation was induced by adenosin diphosphate (5 micromole) (ADP), collagen (0,2 mg/ml), and epinephrine (10 micromole). The analyses were performed by using a Whole Blood Lumi-Aggregometer. Cases with arterial thromboembolic events were not evaluated as a distinct group in statistical comparison because of inadequate case number. The whole patient group (5/37 vs 0/59; p=0,007) and the group of patients with venous thromboembolism (2/13 vs 0/59; p=0,030) have significantly higher ratio of patients with high response to ADP than the control group. The whole patient group (7/37 vs 1/59; p=0,005) and the group of patients with recurrent fetal losses (5/22 vs 1/59; p=0,005) have a significantly higher ratio of patients with low response to ADP than the control group. The whole patient group (5/37 vs 1/59; p=0,030) and the group of patients with venous thromboembolism (3/13 vs 1/59; p=0,017) have a significantly higher ratio of patients with low response to collagen than the control group. The whole patient group (10/37 vs 2/59; p=0,001), the group of patients with venous thromboembolism (3/13 vs 2/59; p=0,038), and the group of patients with recurrent fetal losses (6/22 vs 2/59; p=0,004) have a significantly higher ratio of patients with low response to epinephrine than the control group. Sticky platelet syndrome (SPS) is characterized by hyperaggregability of platelets in platelet-rich plasma with ADP and epinephrine (type I), epinephrine alone (type II), or ADP alone (type III). SPS was detected in four cases (10,8%) of the patient group (one case with type I in recurrent fetal losses group, one case with type III in arterial thromboembolism group, two case with type III in venous thromboembolism group). Although we need data which will be obtained from many more cases for a certain evaluation, we suggest that in approaching the patients with thrombosis/recurrent fetal losses platelet functions screening should be applied according the results of this preliminary report.

Abstract: 738 Poster: 645

EFFECTIVE USE OF HIGH DOSE RECOMBINANT FACTOR VIIA IN THE TREATMENT OF HEMORRHAGIC CYSTITIS INDUCED BY CYCLOPHOSPHAMIDE IN A PATIENT WITH CLL

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Although it is very rare, hemorrhagic cystitis could be accepted as fatal clinical situation if left untreated. Major causes are as follows; chemotherapeutic agents like cyclophosphamide and ifosfamide, bladder cancer, pelvic RT, AIDS, antibiotics, various chemicals (dyes, insecticides), viruses like papova and adenovirus infections, persistent urinary tract infections and thrombocytopenia. Cyclophosphamide and ifosfamide have been the most popular reason for hemorrhagic cystitis which was induced by acrolein, major toxic metabolite of cyclophosphamide and ifosfamide. There has not been optimum treatment modality for hemorrhagic cystitis. Palliative approaches such as analgesic agents, antibiotics, blood products (fresh frozen plasma etc.), bladder irrigation with saline solutions, intravesical agents have been in practical use. Selective bladder arterial embolization, intravesical PGF2 application and cystectomy would be aggressive modalities in patient resistant to previous approaches. Recombinant factor VIIa (rFVIIa) has been recently established in the treatment of Hemophilia and life-threaten-ing bleeding disorders. We hereby present a 76 years old CLL patient who was treated with cyclophosphamide and developed hemorrhagic cystitis. He was admitted to hospital because of oliguria and hematuria after completing the treatment with cyclophosphamide. Grade 4 thrombocytopenia, acute renal failure and hemorrhagic cystitis were documented in the patient. Supportive treatments with several erythrocyte and platelet suspensions, and irrigation could not cure hemorrhagic cystitis. It was decided to use rFVIIa due to progressive and aggressive clinical course and, after the first bolus dose, hemorrhage was stopped and cistoscopy was performed. Cistoscopy revealed clear urine and hemorrhagic bladder epithelium. The requirement for erythrocyte suspension decreased after rFVIIa administration and hematuria disappeared. But the patient died because of sepsis induced by catheter

infection. rFVIIa was found to be effective in the treatment of refractory hemorrhagic cystitis.

Abstract: 739 Poster: 646

THE CORRELATION BETWEEN LOWER EXTREMITY DOPPLER ULTRASONOGRAPHY, PULMONARY PERFUSION SCINTIGRAPHY: CLINICAL PROBABILITY OF PULMONARY EMBOLI AND PLASMA D-DIMER `LATEX` MEASUREMENTS

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Background:Pulmonary thromboembolism is difficult to diagnose due to vague symptoms and non-specific clinical presentation. A high index of suspicion should be maintained in those with significant risk factors and a presentation compatible with venous thromboembolism. Two thirds of the cases are misdiagnosed. Aims:Thus it is a clinical entity with a high mortality rate in this study we evaluated the correlation between lower extremity doppler ultrasonography, pulmonary perfusion scintigraphy and D-dimer (latex) in cases with probable signs of pulmonary thromboemboli.We also investigated whether this test has a diagnostic value and could be used as an exclusion criteria in the diagnosis of pulmonary thromboemboli. Methods: Fifty three adult patients with clinical sign and symptoms of pulmonary and/or deep venous thrombosis are prospectively enrolled in our study. Twenty seven (51%) were females whereas 26(49 %) were males. Mean age was 67+-15 years (range between 22-93). Results: Twenty four (45.2%) had high, 20(37.7%) had intermediate and 9(16.9%) had low probability of pulmonary embolism. High probability group had D-Dimer positive in 22 (91.6%) cases, intermediate probability group had in 10(50%) cases and finally low probability group had in 4 (44.4%) cases. Twenty four of 26 cases (92.3 %) with high probability of pulmonary embolism had D-Dimer positive.Whereas 6 of 9 cases (66.6%) and 6 of 18 cases (33.3%) had D-Dimer positive with intermediate and low probability of pulmonary embolism respectively. Twenty six patients were undergone to ultrasonographic examination; 11 (42%) of cases had DVT and 7 of them had D-Dimer positive. Conclusion:We conclude that for the diagnosis of pulmonary emboli D-Dimer (latex) test has 92% sensitivity and 66% specifity whereas sensitivity is 63% and specifity is 53% for the diagnosis of DVT.

Abstract: 740 Poster: 647

THROMBOPHILIC MUTATIONS AMONG STEM CELL TRANSPLANTATION PATIENTS: EXPERIENCE IN A SINGLE CENTER FROM TURKEY

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The most frequent mutations associated with inherited thrombophilia, factor V Leiden (FVL) and prothrombin G20210A have a prevalence of 9 and 2.7 % respectively among the healthy adults in Turkish population. The frequencies of the CC, CT and TT genotypes for methylenetetrahydrofolate reductase gene (MTHFR) were also found to be 42.9, 47.4 and 9.6 % respectively in Turkish population. Here we analysed the prevalence and significance of thrombophilic mutations among patients who underwent stem cell trasplantation. Thirtyone patients (13 male/18 female, median age 43 years) referred to our transplant unit were screened for FVL, PT G20210A and MTHFR mutation. Patient population consisted of acute leukemia (n=10), lymphoma (n= 4), chronic myelogeneous leukemia (n=3), multiple myeloma (n=12) and apalstic anemia (n=2). Type of transplantation was allogeneic for 16 patients and autologous for 15 patients. Heterozygosity for FVL (n= 4), PT G20210A (n=3) and MTHFR (n=18) was 12.9, 9.7 and 58.1 % respectively. Homozygote mutation for MTHFR was detected in only 2 patients (6.45 %) but these patients did not have any thrombotic complication. In 2 of our patients concomitant heterozygote mutations have been detected; one with PT G20210A-MTHFR and the other with FVL- PT G20210A. These patients did not have any thrombotic complications. In our study population 8/31 patients have been recorded with thrombotic complications (6 with acute leukemia in complete remission and 2 with multiple myeloma) in which 3/31 were veno occlusive disease and 5/31 indwelling central venous catheter related thrombosis. Characteristics of patients with and without thrombotic complications are shown

in Table 1. Although patients recorded with thrombotic complications were all heterozygote for MTHFR, other 10 with heterozygote MTHFR did not have any thrombotic complication, so there were no statistically significant relation between them. We could not find a significant relation between thrombophilic mutations and thrombotic complications. In our study the only significant relation was between mocositis . grade 3 and thrombotic complications. When we analysed patients with mucositis, 4/8 patients (50%) with grade .3 mucositis and 4/23 (17.4%) patients with grade < 3 mucositis developed thrombotic complications (p=0.008). Mucositis . grade 3 were all detected in allo-SCT. Endothelial damage due to mucositis may the risk factor for thrombotic complications in our patient population. Upto date controversial results have been reported about the association of thrombophilic mutations and posttransplantation thrombotic complications. It is generally accepted that FVL and PT G20210A mutations are the most frequent mutations leading to thrombotic complications after stem cell transplantation. Although the number of patients in our study is small to draw a conclusion we were not able to find a relation with thrombotic complications and thrombophilic mutations in our patient population.

Abstract: 741 Poster: 648

SUCCESSFUL LEPIRUDIN TREATMENT OF A PATIENT WITH SERONEGATIVE HEPARIN-INDUCED THROMBOCYTOPENIA - TYPE II AND VENOUS THROMBOEMBOLISM RESISTANT TO DANAPAROID SODIUM

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We report the case of a 19-year-old male patient with left femoropopliteal deep vein thrombosis and FV Leiden heterozygous mutation in whom an extension of thrombotic process into v.iliaca accompanied by typical signs of pulmonary embolism was detected on the 16th day after introducing heparin and subsequent oral anticoagulant treatment with adequate therapeutic INR values. The reintroduction of heparin as a replacement for the oral anticoagulants resulted in further aggravation of the clinical state with the extension of thrombosis into v. cava inferior. On the 8th day of heparin therapy, the occurrence of heparin-induced thrombocytopenia - type II (HIT II) with platelet counts 48 x109/l and highly positive values of 4T`s score was diagnosed besides negative functional and antigen assays (heparin-platelet factor 4 antibodies). The progression of disease continued upon danaparoid sodium introduction although the in vitro danaparoid sodium aggregation assay was negative. Only upon lepirudin initiation on the 5th day of danaparoid sodium therapy was there an immediate and almost complete normalisation of the platelet count achieved. Current diagnostic assays failing to detect up to 5 to 10 percent of HIT cases and the HIT II diagnosis being primarily clinical, negative laboratory tests must not be a reason for the delay and slowing down of adequate therapeutic measures application. Upon detecting the resistance to the first-line nonheparin anticoagulants, another, possibly more potent, direct thrombin inhibitor or some of adjuvant therapeutic methods should be used as soon as possible.

Abstract: 742 Poster: 649

FACTOR V LEIDEN MUTATION AND DEEP VENOUS THROMBOSIS IN A PATIENT WITH HYPEREOSINOPHILIC SYNDROME: CASE REPORT

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The idiopathic hypereosinophilic syndrome (HES) is a rare multisystem disease characterized by elevated eosinophil counts and multiple organ involvement due to eosinophil cationic proteins (ECP)-induced organ dam-age.Patients with idiopathic HES are at increased risk for thrombosis which can be seen in the heart, spleen, lungs, kidneys, skin and cerebral vessels. On the other hand, factor V (FV) Leiden mutation is the most common gene defect that causes hereditary thrombo-

philia. The patient presented here indicates that the co-existence of HES with FV Leiden mutation may be associated with an increased risk of thrombosis. CASE:A 29 years old male patient presented with pain and swelling in the left leg, which had started two weeks ago and had increased since then. He indicated that he had experienced a similar condition 8 years ago that yielded a diagnosis of deep vein thrombosis (DVT) and HES. He had used prednisolone 1 mg/kg initially with a subsequent escalation to a lower dose, for 6 months and an additional oral anticoagulant medication. The physical examination of the patient revealed hepatomegaly (2 cm), a left leg diameter of 43 cm and a right leg diameter of 38 cm and a positive Homan sign on the left side. Routine hematologic examination was as follows: hemoglobin 14.7 g/dl, white blood cell count 18.6x109/l, absolute eosinophil count 10.8x109/l, platelets 139x109/l and eosinophilia in the differential. Bone marrow aspiration was performed and a hypercellular bone marrow with a 10/1 ratio of myeloid/erythroid cells and 52% of eosinophilic cells was determined in the microscopic examination. Cytogenetic analysis revealed a 46;XY caryotype. Philadelphia chromosome was negative by banding and FISH method. Scintigraphic examination markedly demonstrated segmental hotspots and collaterals of left leg. The patient was diagnosed as HES and recurrent DVT and subcutaneous LMWH and Hydroxyurea 500 mg/12 hour was initiated. Oral anticoagulant therapy was added on the 7th day of treatment. On the sixth month, two weeks after the discontinuation of coumarin treatment, protein C, protein S, antithrombin III levels were normal, prothrombin G20210A mutation was negative and FV Leiden mutation was heterozygote positive. Analysis of FV Leiden mutation in family members revealed that heterozygous FV Leiden mutation was present in the mother and her son. CONCLUSION:The presence of idiopathic HES may have contributed to the prothrombotic effect of heterozygous FV Leiden mutation in our case. In conclusion, investigation of thrombophilia in cases with idiopathic HES with recurrent thromboemboli will be appropriate.

Abstract: 743 Poster: 650

ANALYSIS OF THROMBOTIC COMPLICATIONS IN PATIENTS WITH ONCOHEMATOLOGIC DISEASES

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Decompensated disorders of hemostasis with hemorrhagic and thrombotic complications impede with course and treatment of many diseases and often are the cause of fatal outcome. That`s why it is necessary to spare enough respect to work under prevention, early detection, and adequate treatment of such disturbances. Taking into consideration that the incidence of thrombotic complications has increased with presence of malignancies we analysed cases of thrombosis in patients with oncohematologic diseases. We studied 18 cases of thrombotic complications in patients with the following diagnoses: chronic lymphocytic leukemia - 3, non-Hodgkin`s disease - 5, acute myeloblastic leukemia - 1, multiple myeloma - 5, polycythemia vera - 4. There were 5 women and 13 men, aged from 41 to 73 (middle - 60 years). Thrombosis of deep veins of lower extremities was diagnosed in 17 patients. Only in one patient, who had polycythemia vera, the disease was complicated with arterial thrombosis (the left femoral artery). 5 patients died due to development of pulmonary thromboembolism. According to the investigation data the main risk factors of thrombotic complications in patients with hematooncologic diseases are the following: age over 40 years; disease progression (the late stage of a disease); systemic symptoms of tumor intoxication (fever, weight loss, sweating); cytostatic treatment; degree of disorders of blood rheology (in mul- tiple myeloma - a total protein level, in polycythemia vera - hematocrit value). The obtained results substantiate, that in all hematooncologic patients in age after 40 years the following studies should be performed for estimation of hemostasis condition both on a step of diagnosis and treatment/rehabilitation process: platelets count (in hyperthrombocytosis - platelets aggregability), fibrinogen, fibrin-monomers, fibrin degradation products. Character and severity of detected disorders will determinate the fol-low-up systematic examination and providing of adequate correction of hemostasis in an every concrete case.

Abstract: 744 Poster: 651

THE FREQUENCY OF FACTOR V LEIDEN IN A WOMEN WITH HISTORY OF ABORTION

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Background: Abortion is the most significant problem in pregnant women. Currently it is mentioned that abortion leading to maternal morbidity and somtimes mortality are due to thrombosis, hemostasis disorders and plasental vascular anomalies. Aims: Our aim is to investigate the frequency of factor V Leiden (FVL) gene mutation in a women with history of abortion. Methods: One hundred eighteen patients with abortion and 112 healthy pregnant women were evaluated for FVL.The study was carried out on a basis of case-control. Student-t test and Chi-square method were used for stastistics. Results: Heterozygous FVL was found in the 10% of patients group and in 4% of control group. Homozygous FVL was not found in the two groups. Summary/Conclusion: The role of hereditary thrombotic risk factors in a women with history of abortion is still controversial. In our study, we find that the frequency of heterozygous FVL mutation in women with history of abortion was higher than control group.

Abstract: 745 Poster: 652

COEXISTENCE OF FACTOR V LEIDEN MUTATION AND ESSENTIAL THROMBOCYTHEMIA RESULTING WITH RECURRENT CORONARY OCCLUSIVE EVENTS: A CASE REPORT

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Essential Thrombocythemia (ET) is a myeloproliferative disorder with frequent thrombotic and hemorrhagic complications. Thrombosis is often the cause of mortality in ET. Thrombosis can be detected in these patients with the ratio of 18-84 %. Additional coexisting thrombopilic conditions could promote the thrombotic events. We hereby report a case with Essential Thrombocythemia and recurrent coronary events. Sixty three years-old man with a history of frequent chest pain was hospitalized due to angina pectoris. During this hospitalization, the platelet count was over 1 million per cubic millimeter. Physical examination, laboratory evaluation and bone marrow aspiration/biopsy revealed diagnosis of essential thrombocythemia. Although the platelet count was kept under 450000/mm3 for the next a couple of years during the follow-up period, patient had 3 more coronary occlusive events and coronary artery by-pass grafting surgery. Pre-thrombotic risk factors including hereditary thrombophilia were investigated and the PCR results confirmed the presence of heterozygous factor V Leiden (FVL) mutation. The patient has been treated with anegralide HCl, aspirin and coumadin for the last one year without any additional thrombotic attack. Although no directly relationship has been established between the presence of FVL and arterial thrombosis, the presence of FVL is the most common cause of hereditary thrombophilia. Coexistence of FVL mutation and ET is related to a higher probability of developing recurrent coronary occlusive events such an acute myocardial infarction. These results have generated two more questions to be elucidated: 1-Is convential antiplatelet therapy for the prevention of Coronary Artery Disease always safe in the patient with chronic myeloproliferative disorders especially patient with Essential Thrombocythemia and heterozygous FVL mutation carriership? 2. Is keeping the platelet count under physiological range enough and safe for these patients?

Abstract: 746 Poster: 653

HEPARIN INDUCED THROMBOCYTOPENIA-POTEN-TIAL POSIBILITY FOR FATAL SIDE EFFECTS

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HIT (heparin induced thrombocytopenia) is a rare complication of heparin therapy. HIT type II is defined by peripherial thrombocytopenia combined with thrombotic and thromboembolic events. We report a case of a 72year old male patient who was admitted to the hospital because of a right femoral vein thrombosis. The therapy was started with standard (unfractionated) heparin in continuous i.v. infusion 40 000 IU per day for 5 days and then the same daily dose as a bolus injection every 6 hours The femoral thrombosis improved soon but 11 days after starting the therapy, the patient`s clinical state worsened with respiratory complications and the patient was

transmitted to the Intensive care unit. Pulmonary embolism was confirmed. A fall in the platelet count was noted from 200x10(9)/l initially to 35x10(9)/l. HIT was suspected and the treatment with unfractionated heparin was immediately stopped. Oral anticoagulant therapy with coumarin derivate (Sintrom 4mg) was started overlapping the next 5 days with low-molecular weight heparin (LMWH)-Clexane.We noticed a raise in the platelet number progressively, reaching 95x10(9)/l the eihgt-th day after heparin cessation. Twelve days afterwards, the patient was dismissed with a rapid clinical improvement. Discussion: The occurrence of HIT associated with thrombosis and thromboembolism leads to cessation of standard heparin therapy. In an absence of alternative direct thrombin inhibitor, the treatment of pulmonary embolism in our case improved with LMWH together with coumarin derivate. However, sometimes there is a cross-reactivity of standard, unfractionated heparin with LMWH-s, so this substitution therapy is not strongly recommended. Conclusion: HIT type II is a rare complication but life-threatening events can occur. That`s why the platelet count check-up during heparin therapy must be systemic.

Abstract: 747 Poster: 654

THROMBOTIC THROMBOCYTOPENIC PURPURA AND BONE MARROW NECROSIS AS THE INITIAL PRESENTATION OF LUNG CANCER

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Thrombotic thrombocytopenic purpura (TTP) is a disseminated form of thrombotic microangiopathy. Although most cases are held to be idiopathic, its association with malignancy is well recognized and it usually occurs at the terminal stage of cancer. Bone marrow necrosis (BMN) is another rare disorder defined pathologically as the necrosis of myeloid tissue and medullary stroma with preservation of bone. While hematologic malignancy is the most common underlying disease associated with BMN, it can also be caused by solid tumors. A 53-years-old man was admitted to emergency room with complaints of fever, weakness, and generalized ecchymosis. The fever was accompanied with night sweats and feeling of weakness for the previous month. His medical history was unremarkable. On physical examination, pale conjunctivas and generalized ecchymosis especially on the lower extremities were observed. His temperature was 37.9 °C, blood pressure was 100/55 mmHg, and the pulse was 110/min. Laboratory examination showed: Hemoglobin: 4.3 gr/dl, the white blood cell count; 9500/mm3, and the platelet count was 10.000/ml. A blood smear showed reticulocytosis, poikilocytosis, and numerous schistocytes. In order to investigate the etiology of pancytopenia, a bone marrow biopsy was planned. It was consistent with ischemic necrosis in the bone marrow. By the time, we investigated the etiology of bilateral pleural effusion and hilar opacities that was encountered on the chest X- ray. Therefore, thorax CT scan was performed that showed multiple paratracheal, precarinial and aorticopulmoner lymphadenopathies, bilateral pleural effusion and col-lapse-consolidation areas and multiple minimal nodular opacities. Fiber optic bronchoscopy was performed and multiple biopsies were taken to investigate the underlying pathology. Pathological examination showed malignant epithelial cells in the bronchial mucosa consistent with non-small cell lung cancer. The occurrence of TTP with BMN associated with lung cancer has not been reported in the English literature. We first describe a patient with the rare association of TTP and BMN displayed as the first manifestations of a lung cancer.

Abstract: 748 Poster: 655

SUPERIOR SAGITTAL AND TRANSVERSE SINUS THROMBOSIS IN A CHILD WITH NHL AND CONGENITAL THROMBOPHILIA

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There is increased risk of thrombosis in childhood malignancies, due to various reasons such as hyperleukocytosis, administration of chemothera-

peutic agents, use of central venous catheters, procoagulant activity of tumour cells and/or congenital thrombophilia. We report a case of partial superior sagittal and transverse sinus thrombosis in a 4-year-old boy with B-cell non-Hodgkin`s lymphoma of the right tonsil. The patient was referred to our department after tracheostomy because of pharyngeal obstruction and tonsil biopsy which confirmed diagnosis. He started treatment with MRC 902 protocol (vincristine, cyclophosphamide, prednisolone, methotrexate and doxorubicin). After his first cycle of chemotherapy the size of the tumour was dramatically decreased and the boy was in generally good overall condition. He only complained of dizziness and sleepiness, with no signs of infection. Head and neck magnetic resonance imaging showed a decrease in size of the tumour, but revealed partial thrombosis of the superior sagittal and transverse sinuses. Past history of the child was negative. His grandmother suffered from thrombotic infarctions, starting at the age of 45. He started therapy with low molecular weight heparin (clexane) at a dose of 100iu/kg and the symptoms disappeared within a few days. MRI 15 days later showed complete resolution of the thrombi. Evaluation of the prothrombotic risk factors revealed increased activity of factor VIII (208%) and heterozygosity of MTHFR. Antithrombotic therapy lasted one month after the completion of the chemotherapeutic protocol with no complications. We believe that detailed study of prothrombotic risk factors may be useful in all patients with malignancies, especially in those with positive family history, before starting chemotherapy.

Abstract: 749 Poster: 656

HETEROGYNOUS FACTOR V LEIDEN DEFICIENCY IS A RISK FACTOR FOR ISCHEMIC STROKE IN YOUNG WOMEN?

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INTRODUCTION: Factor V Leiden mutation is a well-established risk factor for venous thrombosis. The relative risk of thrombosis in factor V heterozygotes is at least 3 times higher than in general population, whereas the increased risk of thrombosis in heterogygotes is estimated to be 50 to 80 fold greater than those without the defect. Factor V Leiden`s influence on the arterial circulatory system remains controversial. An increase of the risk for myocardial infraction and ischemic stroke, particularly among younger patients and women can be associated with the presence of the F V Leiden mutation, but the overall association is only modest. Factor V Leiden has also been linked to preeclampsia, pregnancy loss and fetal growth restriction. We present here the cases of a 39-year-old and a 27-year-old female. The first woman reported in her individual background 2 natural child deliveries and no miscarriages. One year ago presented headaches and 6 months ago formications of the hands. Her father had arterial blood hypertension and cerebrovascular disease; her mother and her sister were completely healthy. The MRI of the brain reviled diffused ischaemic vascular disorders. An extensive coagulation examination took place with the following results: PT 11.5 sec, APTT 26.3 sec, Fibrinogen 290 mg/dl, number of platelets 160000 cmm, ATIII 125%, Pr C 92%, FV 170%, F VII 149%, FVIII 210%, F IX 91.6%, FXI 113.4%, FXII 106.5%, Plasminogen 102.5%, APCR 57.6, ACA and lupus anticoagulants were negative. The second woman reported a natural child delivery but from the second month of pregnancy had formications of the hands and headaches. In her familiar background her mother had 1 miscarriage, a placental detachment and breast cancer. The brain CT and the angiography were negative and the brain MRI reviled vascular micro thrombosis.The laboratory tests showed abnormal levels of APCR 78.5%; all the other results were in the normal range. In both women the biochemical tests showed no evidence of hyperlipidaemia and the molecular analysis of FII 20210 G-A, F V Leiden mutations and MTHFR C677T, showed a heterozysity for factor V Leiden mutation in both cases. MATERIAL AND METHODS: Coagulation factors levels measurement became with a chromogenic substrate method. Detection of F V Leiden gene polymorphism: a PCR product spanning the polymorphic site was generated of 120 bp lengths. DISCUSSION: The contribution of gene abnormalities and the ischemic stroke in young women remains poorly explored. Here we present 2 cases where symptoms of nubness and cerebrovascular disease are associated with heterozygosis of F V Leiden, a mutation responsible for ischemic stroke. A more extensive study addressing the occurrence and significance of the mutant FV Leiden mutation in patients with vasospastic cerebrovascular diseases seems to be warranted.

Abstract: 750 Poster: 657

FACTOR V LEIDEN, FII G20210A, MTHFR C677T MUTATIONS AND IDIOPATHIC REPEATED EARLY MISCARRIAGES

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Recurrent fetal loss is a frequent health problem, affecting up to 5% of women in the reproductive age. Data accumulated over the past years suggest a possible association between thrombophilia and fetal loss. Thrombophilia is multifactorial disorder in which acquired and genetic risk factors may play important roles. The most frequent genetic risk factors are: factor V G1691A (FV Leiden), factor II G20210A (FII G20210A) and methylenetetrahydrofolate reductase C677T (MTHFR C677T) mutation. Purpose of our study was to establish the prevalence of these genetic risk factors in group of 15 women with two or more idiopathic pregnancy losses in the first trimester. Patients with antithrombin III, protein C or protein S deficiency, malignancy or immunological disorders were excluded from the study. Factor V Leiden mutation was not detected in any of the patients. For the FII G20210A mutation one heterozygous carrier was identified, giving the frequency of 6.7%. The MTHFR C677T mutation was observed in 11 patients (8 heterozygous and 3 homozygous carriers) which gives the frequencies of 53.3% and 20.0%, respectively. We found increased frequency of MTHFR C677T mutation, but not FV Leiden and FII G20210A mutations. Our results suggest association between MTHFR C677T and repeated idiopathic early miscarriages.

Abstract: 751 Poster: 658

HYPERHOMOCYSTEINEMIA AND DEEP VEIN THROMBOSIS IN METFORMIN-TREATED DIABETIC PATIENTS ¡V A CASE REPORT

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Background Hyperhomocysteinemia is known to be an independent risk factor for arterial thrombosis and venous thrombosis. The most common genetic defect that results in hyperhomocysteinemia is a C677T homozygous mutation in methylenetetrahydrofolate reductase (MTHFR) gene, especially when lower plasma folate, B6 or B12 levels coexists. Thus MTHFR homozygous mutation and deficiency of the vitamin cofactor may cause deep vein thrombosis clinically. Aim We have seen a metformin-treated diabetic patient who presented with deep vein thrombosis, hyperhomocysteinemia and megaloblastic anemia. We analysed the cause of hyperhemocysteinemia and treated the patient successfully to attest the above described facts. Methods Detection of C677T mutation of the MTHFR gene was performed by the method described by Frosst et al. (Nature Genetics 1995; 10:111-3). The measurement of total homocystein(tHcy) concentration was based on fluorescence polarization immunoassay on an Abbott IMX analyzer. Folate and vitamin B12 levels were assayed on an Abbot AxSYM System based on microparticle enzyme immunoassay. Results We report a 65 year-old woman native of Taiwan who had suffered from swelling of left lower leg and left thigh and numbness of both palms for 2-3 months, as well as pale face and general weakness for 1-2 months before she was admitted on June 22, 2004. She was found to have type II diabetes mellitus since 1999 and treated with metformin(a biguanide) since April 2003. Ascending venography performed in this patient revealed an intraluminal thrombus at left popliteal vein and almost complete occlusion of left common femoral vein. Laboratory examinations on May18 2004 showed that Hb was 6.9 g/dl, MCV 134fl, WBC 4400 /£gl, platelet 110000 /£gl, reticulocyte count 1.4 %; vitamin B12 level 86 pg/ml (normal ranges, 2721078 pg/ml), folic acid 32 ng/ml (5-26ng/ml), serum iron 29£gg/dl (female, 49-177£gg/dl), TIBC 293£gg/dl (256-428£gg/dl), ferritin 69.8 ng/ml (female, 19-319ng/ ml); homocystein 32.4£gmol/L (<12£gmol/L). Protein C, protein S and antithrombin III functional activities were all within normal limits; anticardiolipin antibody was also within normal limits; antiparietal cell antibody was negative. Bone marrow aspiration disclosed a picture of megaloblastic change. Gastroendoscopic examination displayed no evidence of gastric atrophy. MTHFR C677T homozygous mutation was detected by molecular study. Metformin-induced vitamin B12 deficiency was highly suspected, therefore insulin injection was substituted

for metformin to control her hyperglycemia. Macrocytic anemia was corrected after vitamin B12 was supplemented. Hyperhomocysteinemia was also rapidly converted to normal level. Deep vein thrombosis responded fairly well to anticoagulant therapy. Conclusion Deep vein thrombosis in this patient was probably related to hyperhomocysteinemia caused by metformin-induced vitamin B12 deficiency and MTHFR (C677T) homozygous mutation.

Abstract: 752 Poster: 659

A CASE OF SEVERE THROMBOTIC THROMBOCYTIC PURPURA NON RESPONDING TO TREATMENT WITH VINCRISTINE

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Background: Thrombotic thrombocytopenic purpura (TTP) is a rare and potentially fatal disease with an acute onset and multisystem involvement. Aims: This case report describes non responding to treatment with vincristine in TTP Case Report:A 25-year-old previously healthy male, with no history of recent infection or drug use, was admitted to the emergency department in february 2005. There was 10 day history of malaise, dark urine, headache and vomiting. He had moderate confusion, low mood, dysartria for 10 days prior to admission. On Examination he appeared chronic ill and was unable to speak.Vital signs were normal except for a temperature of 38.50C. He was anaemic but had no clubbing, lymphadenopathy, skin rash, joint swelling. His sclera were icteric, and petechial-purpuric skin lesions were present in both legs. Neurological examination revealed diminished consciousness with glasgow coma scale of 7, +1 neck rigidity. Respiratory and cardiovascular system was unremarkable. The family history was unremarkable for diabetes mellitus and hypertension. Chest radiography and abdominal ultrasonography were both normal. Laboratory data revealed severe anemia (Hb 7g/ dl), thrombocytopenia (platelets: 6000/mm3), reticulocytosis of 33% and normal WBC (9800/mm3), bilirubin 8.5 md/dl with an indirect reacting fraction of 6.9mg/dl, LDH 6136 U/L (normal <450 U/L); haptoglobin was not detectable. A peripheral blood smear showed 30% schistocytes. Erythroid and megakaryocytic hyperplasia was present in the bone marrow aspirate. Urinalysis revealed microhaematuria with proteinuria. A Coombs test, both direct and indirect, was negative. Results of the immunological tests (serum complement levels, antidsDNA antibodies, antinuclear antibodies) and coagulation parameters (activated partial thromboplastin time, prothrombin time, plasma fibrinogen) were normal but D-dimer, AST, ALT were elevated. Blood, urine and stool cultures remained sterile. Serological tests to viruses (HIV,hepatitis A, B, C) and Mycoplasma pneumoniae were negative. On the basis of these findings a diagnosis of TTP was established. Steroids (methylprednisolone 1 mg/kg) were commenced immediately; PE with fresh frozen plasma replacement started on the second day. Therapeutic PE was performed using a Haemonetics MCS 3P. On the 5th day after the 7th PE, the patient developed worsening neurological symptoms (agitation, convulsion). Treatment was intensified with PE increasing to two sessions per day, combined with an increase in corticosteroid dosage (2 mg/kg). Unfortunately, the patients do not respond to this intensive treatment. it was administered to patient 1 mg vincristine on the 12th and 17th days. We could not give a response from vincristine therapy. After approximately 110 liters of plasma were exchanged during the teatment, platelet count began to increase, to a level greater than 100.000/mm3 at day 32; this was accompanied by clinical improvement. The patient achieved complete remission, and remains well at follow-up 3 months. As side effect of VCR therapy fallen foot was observed. This report adds to the evidence that VCR has not efficacy in nonfamilial TTP and warrants further study.

Abstract: 753 Poster: 660

THE COMPARISON OF THE IMPACT OF ABLATIVE VS REDUCED INTENSITY CONDITIONING REGIMENS ON THE ERYTROCYTE RECOVERY AND THE EARLY TRANSPLANT OUTCOME IN PATIENTS ALLOGRAFTED FROM AN ABO INCOMPATIBLE DONOR

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ABO blood group incompatibility between the recipi-ent-donor pairs in allogeneic hematopoietic cell transplantation (Allo-HCT) may cause various immunological disorders such as acute hemolytic transfusion reaction, prolonged erythroid aplasia or delayed type hemolytic anemia. Aim: Twenty-six patients who underwent allo-peripheral SCT from their HLA-identical, but ABO incompatible donors were retrospectively evaluated for the influence of ABO incompatibility on erythroid engraftment, the time period for switching of ABO blood group, and immune-or nonimmune-hematological complications and were compared early transplant-related morbidity and mortality between ablative (ACR) (n=13) and reduced intensive conditioning regimen (RICR) (n=13) in a case-control design. Results: Although both neutrophil and platelet engraftments were significantly shorter in RICR group than ACR, the probability of reticulocyte engraftment on day +30 were similar in both groups including major versus minor ABO mismatched groups and ACR versus RICR groups (Figure 1a and 1b). Conditioning regimen intensity did not have any impact on the switching of the ABO blood group (ACR: 76.9% vs RICR: 61.5 %, p=0.3), but this period was shorter in the major ABO incompatibility group compared with the minor group (median 49 days vs 147 days)(p=0.0004). The quantity of packed RBC transfusions at day +30 or +100 was neither affected by the conditioning regimen intensity nor the ABO incompatibility. In none of the patients, acute hemolytic transfusion reaction was observed. Delayed-type hemolysis, however, was encountered in seven of 26 (26.9%) patients, but this complication was affected neither form the conditioning regimen intensity nor ABO incompatibility. Pure red cell aplasia was detected in one of the patients who received an ablative dose regimen and allografted from a major ABO-incompatibility donor. Besides, in a patient conditioned with a reduced intensive regimen and allografted from an ABO-major incompatibility donor thrombotic thrombocytopenic purpura was developed. The incidence and severity of acute graft versus host disease and early-transplant related mortality (TRM) were not different between ACR and RICR (Acute GvHD: 46.2% vs 46.2%, p=1.0;TRM: 23.1% vs 15.4%, p=0.62) or major and minor ABO incompatibility groups (Acute GVHD: 35.7 % vs 58.3%, p=0.25 and TRM: 21.4% vs 14.7%, p=0.76) Conclusion: We showed that the intensity of the conditioning regimen in ABO incompatibility did not have any adverse effect on erthyroid recovery. Also, any negative impact of the incompatibility on the early-transplant-related morbidity or mortality was observed. But the type of ABO incompatibility did affect of the switching period of recipient-donor ABO blood group. Therefore, our findings should be evaluated in a prospective study in large recipient-donor pairs with ABO incompatibility. Figure 1. The probability of reticulocyte engraftment according to ABO incompatibility (1a) or the conditioning regimen type (1b)

Abstract: 754 Poster: 661

RELATIONSHIP BETWEEN LEUKOCYT E-DEPLETED ERYTHROCYTE CONCENTRATES AND CYTOKINES IN CARDIAC SURGERY?

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BACKGROUND Patients undergoing cardiac surgery are receiving high amount of blood transfsuions and are at risk for the development of infections and Multiple-Organ-Dysfunction-Syndrome (MODS), these complications are influencing the survival of the patients. During cardiac surgery pro-and anti-inflammatory cytokines are released. We observed in a randomized trial in cardiac surgery a significant reduction in infections and mortality due to MODS by transfusion of leukocyte-depleted erythrocyte concentrates (LD) compared to leukocyte-contain-ing, buffy-coat depleted erythrocytes (PC). AIMS In this study we investigated the effect of LD in the concentration of pro-and anti-inflammatory cytokines in relation to clinical outcome and complications after cardiac surgery. METHODS In 474 participating patients blood samples were taken before and after surgery. Using ELISA methods IL-10 and IL-12 were measured in these samples. The results were linked with the endpoints of the randomized trial: postoperative infections, MODS and in-hospital mortality. RESULTS All preoperative concentrations of IL-10 and IL-12 were low. Mean postoperative IL-10 level was 70 +/- 121 and IL-12 57 +/- 74. Compared with patients without MODS and without infections and survived patients only the IL-10 was significant higher in patients who died and in patients with MODS. There were no differences in mean levels related to LD and PC. The levels of IL-10 were higher in patients receiving more then 10 units

blood transfusions compared to 0 transfusions. CONCLUSION There is an association between MODS and mortality and IL-10, not with IL-12. LD has no influence of LD in mean levels of IL-10 and IL-12. There is a correlation between transfusion of more then 10 units and IL-10, not with IL-12. This suggests that T helper 2 (Th2) type response is activated by allogeneic blood transfusions independent of donor leukocytes.

Abstract: 755 Poster: 662

THE EFFECT OF EXTRACORPOREAL PHOTOIMMUNOTHERAPY (ECP) ON SERUM TNF-A LEVELS IN CHRONIC GRAFT-VERSUS-HOST DISEASE (GVHD)

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Bacground: GvHD is the most important cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation.(Allo-HCT). ECP is an alternative therapeutic modality in steroid and/or cyclosporin-A refractory chronic GvHD developing after Allo-HCT. In this study, we aimed to evaluate whether there was any correlation between serum TNF-a levels and the response of ECP in patients with steroid refractory extensive chronic GVHD. Materials and Methods: Between March 2001 and August 2003, seven patients (male:1, female:6) who were carried out ECP for treatment of steroid refractory extensive chronic GvHD and age- and gender-matched five healthy volunteers as control group were included in this study. Age of the patients ranged from 18 to 49 years. All patients were allografted from an HLA-identical sibling donor. Given median ECP sessions were 10 (8-36), consisting of sequential two cycles monthly. Peripheral venous blood samples were obtained prior to ECP (basal) and after first- and second- and in five patients after the tenth-sessions for the measurement of TNF-a levels. TNF-a levels were measured by using ELISA.(Quantakine HS, R&D system, UK). Results: ECP was given at a median of 5.8 months (1 to 14 months) after allo-HCT. We did not observe any serious complications during or after the ECP procedures. Median operational time of ECP sessions was 183 (135-259) minutes. Median volume of Uvadex used per each session was 4.40 ml (3.61-5.61). Basal mean level of TNF-a was higher in patients than the control group (2.47±0.83pg/ml vs. 1.75±0.06, p=0.05). Mean TNF-a levels decreased from 2.47±0.83 pg/ml to 1.77±0.93 pg/ml after first day (p=0.045) and from 2.32±0.92pg/ml to 1.69±0.93pg/ml after second day of the sessions (p=0.015). After the completion of ECP sessions, extensive chronic GvHD was recovered in only three patients. In clinically responsive patients, TNF-a levels were significantly reduced both after second and tenth sessions. On the contrary, in two patients not responding to ECP therapy, TNF-a levels increased. Conclusion: The decrease in the TNF-a levels after the first and second cycles of ECP therapy may be an early predictor of response to cGVHD. Large patient populations studies are needed for precise assessment.

Abstract: 756 Poster: 663

ANALYSIS OF TRANSFUSION MEDICINE PHYSICIANS` CALLS

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Background: Adequate knowledge of Transfusion Medicine (TM) practices can improve clinical care and reduce health care costs; additionally, on-call experiences are a useful educational and quality assurance tool. This study evaluated the appropriateness of blood product requests from hospital-wide calls in an effort to further staff education, improve patient care and reduce health care costs. Material and methods: The Blood Utilization Review Committee (BURC) at Parkland Memorial Hospital, University of Texas at Dallas, Texas has established transfusion criteria and defined indications for fresh frozen plasma (FFP), platelets, and cryoprecipitate. When requests do not meet BURC criteria or when special circumstances arise, Blood Bank technologists call the TM physician. Results: From October 2003 to February 2005, 1,304 calls generated 1,326 blood component requests that required TM resident intervention. During this period 44,939 blood components were transfused. Of the total requests, 1159 (87%) did not meet BURC criteria; 116 (9%) were for special products; 9 requests (0.7%) were for neonatal transfusions; 27 (2%) were for transfusions to patients with red cell antibodies (both auto and allo); and, 15 (1.1%) were for transfusion reactions. All 1159 triaged

requests were divided into three groups according to BURC guidelines: requests approved (632 or 54.5%), requests partially approved (87 or 7.5%), and requests denied (440 or 38%). Recommendations for additional/alternate products or blood components were made in 93 cases (8%); cryoprecipitate was recommended in 49 cases (53%). FFP, the most frequent inappropriately ordered product, was denied in 220 cases (51%); platelets were denied in 202 cases (31%). TM staff intervention resulted in savings of at least $160,000 in blood product cost alone. Effectiveness of medical staff education was evaluated for 3 consecutive months at both the beginning and the end of the study. Analysis showed no change in platelet ordering practice, number of triaged units, and percentage of orders denied. While inappropriate FFP orders did decrease by 61%, the percentage of triaged FFP orders that were denied increased from 37% to 66%, (112/169 to 110/296). Conclusion: While the decrease in the number of FFP and CRYO orders demonstrates the effectiveness of education on appropriate FFP use, further analysis indicates a significant need for ongoing medical staff education in transfusion practices

Abstract: 757 Poster: 664

MANNOSE-BINDING-LECTIN (MBL) LEVELS AND BLOOD TRANSFUSIONS RELATED TO POSTOPERATIVE COMPLICATIONS AFTER CARDIAC SURGERY

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BACKGROUND It has been accepted that during cardiac surgery the complement-system is activated which enhances ischemia-reperfusion injury, leading to postoperative complications as infections and organ failure. The lectin pathway is one of the mechanisms that can activate the complement-system, this pathway can be mediated by mannose-binding-lectin (MBL). The level of MBL in serum shows a wide variation. A low level of MBL can lead to more infections in some conditions and a high level to tissue damage after ischemia-reperfusion injury. The effect of transfusions of erythrocyte-concentrates on the MBL levels and on complications after cardiac surgery are not known. AIMS In this study we investigated the role of MBL levels and the effect of transfusions on postoperative complications after cardiac surgery. METHODS In a randomized controlled trial 474 cardiac surgery patients were included and blood samples were taken pre- and postoperatively. MBL measurements were performed by ELISA assays. The data were linked with postoperative complications as mortality, infections and multiple-organ-dysfunction-syndrome-MODS and with peri-opera-tive erythrocyte and plasma transfusions. RESULTS The mean pre-operative MBL-level was 837+/-796 and postoperative 456 +/- 347 microg/ml. There were differences in MBL levels between patients with infections or MODS and the non-infected and non-MODS patients. The difference in pre-operative MBL between non-survived (672 +/- 587) and survived patients (853 +/- 812) was not significant (p=0.20). Patients with low MBL levels who received blood transfusions had a small increase in their MBL levels. Patients with high MBL levels who received blood transfusions and patients with low MBL levels without blood transfusions had a significant decrease in their MBL levels. CONCLUSIONS Pre-and postoperative MBL levels in cardiac surgery are not related to postoperative infections, MODS and hospital-mortality. Blood transfusions have a small effect on MBL levels and probably no effect on outcome related with the lectin pathway.

Abstract: 758 Poster: 665

NITRIC OXIDE AND NEUTROPHIL APOPTOSIS IN SICKLE CELL VASOOCCLUSIVE CRISES

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Neutrophils are important effector cells in immunity to microorganisms. Leukocytosis correlates with clinical severity and early deaths in patients with SCD. The balance between productions and death of cells is important in the control of cell numbers within physiologically appropriate ranges. Human neutrophils constitutively undergo apoptosis, process which is critical for the successful resolution of inflammation by the safe removal of effete cells. There is evidence that in

sickle cell disease (SCD) vascular production of nitric oxide (NO) is elevated to maintain vasodilatation. Nitric oxide can also act on neutrophil apoptosis. We aimed to investigate the effects of NO on the neutrophil apoptosis before and after sickle cell vasoocclusive crises ended, and to define the effects of vasoocclusive crisis on the plasma NO concentration and neutrophil apoptosis. Stable NO product (nitrate, and nitrite) and PFH level in human plasma were measured by using spectrophotometric methods. Flow cytometric measurements of neutrophil apoptosis were performed according to standard techniques by using Annexine V-FITC (ANXV), and Propodium iodide (PI). Seventeen patients (13 M, 4 F) with sickle cell vasoocclusive crisis were included to study. Their ages were between 18-48 years. Mean NO values were 21.19 ±8.95 µmol/L before vasooclusive crisis and 19.75± 10.39 µmol/L after vasooclusive crisis ended. Mean Neutrophil apoptosis were 4.13± 3.23 % for ANXV, 0.40± 0.36 % for ANXV/PI, and 0.15± 0.26 % for PI before vasoocclusive crisis, and 6.25± 6.79 % for ANXV, 0.78± 0.0.94 % for ANXV/PI, and 0.40± 0.0.66 % for PI after vasoocclusive crisis ended. There were no statistically significant differences in regard to NO concentration and neutrophil apoptosis levels before and after vasoocclusive crisis ended (P > 0.05, for both), and either we did not find significant correlation of NO concentrations and neutrophil apoptosis levels before and after vasooclusive crisis ended (P > 0.05). This study is the first to investigate the association between plasma NO concentration and neutrophil apoptosis in patients with SCD. We showed that plasma NO concentration has any effect on the neutrophil apoptosis before and after vasooclusive crises ended. Data obtained have not supported the theory that neutrophil apoptosis might be an indicator reflecting vasoocclusive crisis in patients with SCD

Abstract: 759 Poster: 666

WHEN TO START G-CSF AFTER MOBILIZATION REGIMEN? ANY IMPACT ON STEM CELL COLLECTION EFFICIENCY

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Aim: Autologous peripheral blood stem cells (PBSC) provide rapid and sustained hematopoietic recovery following high-dose chemotherapy in patients with various hematological malignancies and solid tumors. There is no consensus on type and timing of growth factor(s) used for mobilizing PBSCs. In the aim of finding the optimal schedule for collection of PBSCs after G-CSF, we retrospectively analyzed the feasibility of initiation day of G-CSF day +4 vs day +7 in our patients receiving chemotherapy-based mobilization regimen. The diagnoses were malignant lymphoma (n=19) or myeloma (n=17) in total of 36 patients (Table 1). According to the G-CSF initiation schedule 17 patients received G-CSF on the seventh day (Day 7), the remaining on the fourth day (Day 4). There are 22 male and 17 female with a median age of 46 years (range, 1568). The mobilization regimen used was CY-VP16 (CY 4g/sqm iv on day one and etoposide 200mg/sqm iv on days 1-3). A total dose of 4x10e6/kg CD34+ cells/kg per recipient BW was targeted. Stem cell mobilization and collection failure was observed in five patients (13.9 %). Median time interval between start of G-CSF and first day of apheresis procedure was shorter on Day 7 than on Day 4 (9 days vs 10.5 days, p<0.05). But we were not able to reveal any significant difference for the time interval between start of mobilization regimen and initiation of apheresis. We were not able to show any significant difference for the median numbers of apheresis cycles, total CD34+ cells collected, and total nucleated cells collected in both groups (table). Consequently, the initiation of GCSF use on day 7 has apparently no negative impact on PBSC collection efficiency in comparison to day 4. The reflection of this three-day`s reduction on the cost should be evaluated in a larger and more homogenous disease group using a prospective cost analysis design.

Abstract: 760 Poster: 667

CHANGE OF COAGULATION PARAMETERS AFTER DOUBLE APHERESIS

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Objective:Apheresis is a relatively safe procedure, frequently used for donation and therapeutic purposes. It has a low complication rate (4.8 %) and majority of the side effects are well tolerated and reversible. In the previous studies, AT-III, plasminogen and protein C levels were reported to be reduced and F VIII, vWF activity and fibrin monomers levels were found to be increased folowing automated aphreresis leading to a hipercoagulable state. Conversely, some authors showed decreased platelet counts, plasma F II, F V, F VII and F IX levels and elevated PT and PTT following plasmapheresis, causing bleeding tendency. We tried to find out changes in coagulation parameters after double apheresis in this study. Materials and Methods: Forty-five subjects (45 double thrombopheresis) were recruited to the study, and coagulation parameters including prothrombin time (PT), partial thromboplastin time (PTT), protein-C, protein-S, antithrombin-III, factor V, factor VII, factor VIII, factor IX, factor X and fibrinogen were assessed before and after apheresis. Results: Table 1 shows results of coagulation parameters before and after double apheresis procedure. After double thrombopheresis, fibrinogen, factor V, VIII and IX were decreased compared with the values before apheresis. PTT, PT, plasma levels of protein-C and S, antithrombin-III, factor VII and factor X did not change prior and after the procedure. Conclusion: Statistically significant changes were observed in some coagulation parameters after double apheresis. Although serum levels of this coagulation parameters are decreasing, they are still in the normal limits. Therefore, we suggest that double apheresis is a safe procedure for healthy volunteers.

Abstract: 761 Poster: 668

THERAPEUTIC PLASMA EXCHANGE PLUS CORTI COSTEROID FOR THE TREATMENT OF THE THROMBOTIC THROMBOCYTOPENIC PURPURA: A SINGLE INSTITUTION EXPERIENCE IN THE SOUTHERN MARMARA REGION OF TURKEY

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Background. Thrombotic thrombocytopenic purpura (TTP) is a classic, but not a common disorder of hematology. Plasma exchange (PE) was shown to nearly reverse its %90 mortality rate. However, there are still some fatal outcomes in this dramatic disease. Searching of additional treatment modalities is going on and treat-ment is still not standardized and varies considerably except for daily PE Aimes. Currently there is no published local epidemiological data on TTP and its treatment. We present our experience of plasma exchange plus corticosteroids for the treatment of TTP in our hospital. Methods. Patients with TTP diagnosed between January 1996 and January 2005 were identified by a retrospective review of records of the Uludağ University Hospital, Bursa (the largest referral center for adults with this disorder in this region with an estimated 2.2 million residents), which performed all therapeutic PE in the southern Marmara region in Turkey. Results. A total of 11 (6 male, 5 female) patients were treated for TTP during this period. The median age was 39 years (range 18-49). Eight patients presented with central nervous system manifestations ranging from focal motor and sensory deficits to altered consciousness and convulsions. Four patients had fever and 2 had renal failure; one them required dialysis at presentation. The median hemoglobin level was 8.5 g/dl (range 4.8-11.6) and the median platelet count was 15 000/mm3 (range 680064000). The classical pentad picture was present only in one case. The median clinical severity score was 5, with a range of 4 to 7. One plasma volume exchange daily plus steroid was the principle treatment in all patients. The length of time from the admission to the first PE was six hours or less in 5 patients and twelve hours or less in 3 patients and one day in 3 patients. A total of 295 PE sessions were performed. We have obtained 6 complete responses (CR) and 3 partial responses (PR) with daily PE and steroid (response rate 9/11). The earliest maximum response was noted after three days and the latest one was noted after 25 days (median 11 days). One of our primary refractory patients was saved with pulse steroid+cyclosporine+vincristine. Now he is free of disease over one year. The other refractory patients did not develop any response to salvage therapy and expired in 15th day with status epilepticus and ventilator related pneumonia (mortality rate 1/11). A CR was obtained with adjuvant treatments in all 3 PR patients. Only one CR patient developed an early relapse (early re-

lapse rate in CR patients 1/6). She was treated successfully with daily PE plus vincristine. It must be noted that in 2 CR patients very slow tapering schedule was needed. We have only one real relapsing patient in this series (relapse rate in CR patient 1/10). She developed four isolated relapses in 108 months. After her each relapses a CR was achieved with different treatment modalities. Our median follow up period was 25 months (Range 9-108). Conclusions. Considering our local population, our annual incidence is only about 0.63 new cases per one million people. This figure is highly less than the data from US, which indicated an incidence of 3.7 cases per 1 000 000. To our knowledge there is no high variability in the incidence of TTP in the different geographical regions of the world. It suggests that considerable number of patients escaped notice. We hope that, demonstrating the successful outcome, this article served to urge primary physicians to keep in mind the diagnosis of TTP and refer of suspected cases urgently.

Abstract: 762 Poster: 669

EXCHANGE TRANSFUSION BY CLOSED SYSTEM APHERESIS IN CHILDREN WITH SICKLE CELL ANEMIA: A PRELIMINARY REPORT

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Background: Automated red cell-exchange (ARCE) is a procedure exchanging approximately 60% of the patient`s red cells. In childhood sickle cell anemia, exchange transfusion (ET) was performed for a number of situations such as stroke, preoperative preparation, and severe vasoocclusive crisis. However, there is little experience with exchange transfusion by ARCE. Aims: We report our experience with ET by ARCE in 7 children with sickle cell anemia. Methods: Using an automated system (Cobe Spectra, Lakewood, CO.,USA) which separates cells with continuous blood flow, 60-70% of the patients` red cells was exchanged with cross-matched new red cells in order to decrease hemoglobin S levels of the patients below 30%. Leucofiltered red cell suspensions preserved in CPD (citrate-phosphate-dextrose) for 1-7 days with hematocrit about 75% were used for the procedure. Total blood volume was calculated by body weight, and erythrocyte volume was calculated by hematocrit values of the patients. Complete blood count, hemoglobin electrophoresis and calcium levels were performed before and after the procedure. Venous access was provided by central catheters in 5 children. Results: A total of 7 children (5 girls and 2 boys, aged 3-17 years, weighed 15-70 kg) with sickle cell anemia received 14 ET by ARCE. Indications included preoperative preparation in 3 (1 splenectomy, 1 heminephroureterectomy and splenectomy, 1 cholecystectomy), severe vasoocclusive crisis in 2, acute chest syndrome in one, and avascular necrosis of femur in one patient. Each procedure lasted in 1-1.5 hours without complications other than venous access problems in two patients. Conclusions: ARCE may be used safely for ET in children with sickle cell anemia.

Abstract: 763 Poster: 670

LOCAL EXPERIENCE WITH THROMBOTIC TROMBOCYTOPENIC PURPURA FROM WEST PART OF TURKEY

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Thrombotic thrombocytopenic purpura (TTP) is a fatal disorder if untreated. Therapeutic plasma exchange (PE) has resulted excellent remission and survival rates in these patients. But in the few of TTP patients PE therapy is not enough to get response, and there is need for alternative immunomodulatory treatments. We demonstrated a descriptive, retrospective study of 25 (14 female, 11 male) adult patients with a median age of 32 with TTP admitted to our hematology unit. Upper respiratory tract infection in 2 patients, salmonella typhus infection in 1, urinary tract infection with E. coli in 1 patient were observed as initiating factors of TTP. One of the patients symptoms were started during the pregnancy and SLE associated with TTP in one of the patient. 2 patients were got diagnosis of TTP after the allogeneic stem cell transplantation. All the patients were treated with immediate PE and standard dose corticosteroid (1mg/kg prednisone) therapy other than one who was admitted with upper gastrointestinal bleeding. Other treatment modalities were added if complete remission was not achieved within 30 days. Within the responders to treatment improvements of clinical sta-tus, platelet

counts and serum LDH levels were after the median 13, 14 and 3.5 PE sessions respectively. Mortality rate was % 12 (3 patients) and 2 of them were resistant acute leukemia cases who were treated with allogeneic stem cell transplantation from full match sibling donor and presented with signs and symptoms of TTP. Both of them died before engraftment with multiple clinical complications. In our series 2 patients were relapsed cases. Median 7 years clinical follow-up, all the other patients are still in complete remission. Only one patient is chronic relapsing form of TTP and now her symptoms are under the control with cyclic fresh frozen plasma transfusion. Her 16 years old brother has also diagnosed with TTP and treated in another hospital. Although we did not performed an antibody screening or genetic test, a hereditary form of TTP was the most likely diagnosis This study showed that prompt and aggressive PE therapy is life-saving in the treatment of adult patients with TTP. Application of early corticosteroid treatment could maintain the early and the durable response without significant side effects. But, few of patients need addition of other alternative immunosuppressive treatment to get a long term complete response.

Abstract: 764 Poster: 671

PLATELETPHERESIS ACTIVITY IN YEAR 2004: A SINGLE CENTER EXPERIENCE

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In recent years there has been a greater reliance on the use of platelets collected by apheresis.Thus it is important to establish the efficiency of platelet production by different apheresis systems. In our center between January 01, 2004-December 31,2004 a total of 2826 apheresis unit platelets were collected by using Amicus (1697), Fresenius ASTEC 204 (472), Haemonetics MCS (299),Dideco Excel (271) and Cobe Spectra (77). All donors (2800 male,26 female) were required to meet the eligibility criteria defined by Council of Europe,Guide to the preperation use and quality assurance of blood components.From 2826 procedures 150 procedures,30 procedures for each apheresis machine with similar pre-procedure platelet counts, were evaluated.Table presents the mean donor and procedure characteristics of the final sample. The adverse reactions encountered during the study were minimal and related to citrate toxicity and hypotension in Haemonteics group. In our experince Amicus gave reliable platelet counts and allowed to perform double units plateletapheresis. All machines found to be operator friendly and safe.

Abstract: 765 Poster: 672

HEPATITIS B SCREENING AND TRANSMISSION KNOWLEDGE AMONG BLOOD DONORS

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Background: Increased knowledge of Hepatitis B (HB) transmission and detection by donor screening could potentially decrease the number of at risk donors. Method: Knowledge of HB transmission, screening, the association with demographics, screening test reactivity and the vaccination program was assessed by a questionnaire asked to full out by 5010 (4279 Male, 731 Female) donors, of whom applied to Süleyman Demirel University Blood Bank. Donors were asked about their understanding of routine HB screening procedures at blood banks and whether donating or receiving blood poses a risk. (Table) Demographics, educational level, donor status (first time / repeated), a volunteer donor or donating to a relative were compared between donors who answered correctly and who answered incorrectly, using Chi-square test. Results: The donors` responses are represented in the table. Groups most likely to give incorrect response were more than 45 years old, less than high school (HS) education, first time donors and volunteers not donating to his/her relatives. Donors who said they `do not know` were more likely to be older age and less educated. The 3-6th questions about screening tests and vaccine program were highly answered as `do not know`. Conclusion: Many blood donors still lack knowledge regarding HB virus transmission, screening and vaccine program. Innovative

ways to increase donor knowledge should be developed. The risk behaviors, transmission routes, the tests and their limitations, vaccine program should be briefly explained to the donors. To improve the safety of the blood supply increasing efforts are required to educate blood donors about testing limitations and the need for deferral if she/ he had risky experience.

Abstract: 766 Poster: 673

MOLECULAR TYPING FOR KIDD BLOOD GROUP IN TAIWAN

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Background:The Kidd (JK) blood group system is clinic-ally important in transfusion medicine. Alloantibodies to antigens in this system may be produced following blood transfusion or during pregnancy and can result in serious hemolytic transfusion reactions and hemolytic disease of the newborn (HDN). The two major codominant alleles of the JK gene, Jka and Jkb, have a similar frequency in Caucasian populations (0.51 and 0.49, respectively) and define 3 common phenotypes Jk(a+b+), Jk(a+b-),Jk(a-b+), while frequency of Jk(a-b-) or Jknull phenotype is exceedingly rare. Many individuals of Polynesian extrac-tion have been identified as Jknull. Its frequency and molecular characterization for Chinese people in Taiwan, however, has not yet been clarified. Study design and methods: By using the lately developed single-tube allele-specific primer/multiplex PCR technique, a total of 320 random whole blood samples were analyzed. In addition, three samples already serologically proven as Jknull phenotype in our Lab were also investigated. Results: None of the 320 random whole blood samples was serologically typed as Jk(a-b-), while the frequencies of three other phenotypes were 47.5% for Jk(a+b+), 23.1% for Jk(a+b-), and 29.4% for Jk(a-b+). Interesting-ly, two Jka/Jk and four Jkb/Jk were identified, resulting in a gene frequency of Jka ¡V 46.72%, Jkb ¡V 52.34% and silent Jk ¡V 0.94%. As for the three samples of Jknull phenotype all belonged to the so-called Polyne-sian type, i.e.3¡¦-acceptor splice site G->A mutation of intron 5 that resulted in the skipping of exon 6 (called muta-tion JK£G6). Conclusion: The present study confirms that the single-tube allele-specific primer/mul-tiplex PCR technique has enabled genomic typing of the Kidd blood group easier and reliable. The frequency and molecular characteriz-ation of JK phenotypes for Chinese people in Taiwan have been clearly characterized.

Abstract: 767 Poster: 674

DETECTION OF THE BEHAVIOURS OF MEDICAL AND HEALTHCARE STUDENTS ABOUT THE BLOOD DONATION

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Aim: Cross-sectional study was planned to detect the knowledge and behaviours of the students in the departments of health area in the Celal Bayar University about the blood donation (BD). Method: The research contents 599 students from CBU Faculty of Medicine (FM) (n=244), Health High School (HHS) (n=318) and Healthcare High School (HCHS) (n=37). In this research, through reaching 75% of the students, a self reported questionnaire was used for data collection. This questionnaire includes the social demographic characteristics of the students and the questions which inquires their knowledge and behaviours about the BD. Data were analyzed using SPSS for windows statistical programme, chi-square test, trend chi-square test, Fisher`s exact test and logistic regression analysis were used for statistical comparisons. Moreover, multivariate OR (%95 CI) is calculated with the logistic regression analysis. Results: While 33.1% of the survey group was composed of men, 66.9% of the survey was composed of women. 7.3% of the students were 18 or under the age of eighteen, 34.1% were at the age of 19 and 20, 33.1% were at the age of 21 and 22, and 25.5% were 23 or above. 40.7% of the students were at FM, 53.1% were at HHS and 6.2% were at HCHS. In addition, it was determined that 3.5% of the students have a transfusion history, 44% of the students` relations have a transfusion, 12.3% has donated blood before. 58.5% of the students have done a blood count before, 73.9% of them have a blood test for hepatitis and 95.9% were of the

opinion that BD is useful. On the contrary, 22.2% of the students were abstaining from BD and 87.9% stated that they want to donate blood now or later. When all the research group was examined, it could be concluded that, in the male group, whose age is older than the others and whose fathers are more educated, the rate of the BD is much higher ($p<0.05$). Being younger and not being a blood donor before are effective factors on abstaining from BD ($p<0.05$). When the factors about the BD were evaluated considering the students of medicine, it was found that the rates of BD were much higher in males and in the 4th, 5th and 6th classes ($p<0.05$). Conclusion: Even if the rates of BD are much higher in the survey group than the community, the fear/ hesitation from the BD is common. The positive attitude to BD has a relation with the age, socioeconomic level and education. Blood transfusion course that is given to the 4th year students may be effective in the increase of the rates of BD in the last three years rather than the first three years in the group of FM. After beginning the clinical training, being in the same place with the patients who needs blood could also be effective in that increase. It can be thought that this group whose majority has examined by the blood tests and has a positive attitude to blood donation can be possible blood donors with the education that resolves the hesitations.

Abstract: 768 Poster: 675

THERAPEUTIC PLASMA EXCHANGE IN THROMBOTIC THROMBOCYTOPENIC PURPURA

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Introduction: Thrombotic Thrombocytopenic Purpura (TTP) is a rare syndrome with fatal outcome if not diagnosed and treated properly. TTP has classically been characterized by the pentad of fever, microangiopathic hemolytic anemia, neurologic symptoms, renal dysfunction and thrombocytopenia. The pathogenesis of the disease has been a mystery until recently a von-Willebrand Factor(vWF)-cleaving metalloprotease has been found to be reduced or absent in most patients with TTP. Objectives: Medical treatment of TTP includes glucocorticoids, immunosuppression, splenectomy and antithrombotic drugs. However the most beneficial treatment remains to be Therapeutic Plasma Exchange (TPE). As it has been reported that the above-men-tioned vWF-cleaving metalloprotease is present in fresh-frozen plasma(FFP) and cryoprecipitate-depleted plasma (cryosupernatant). Infusions of these plasma products would stop or prevent TTP episodes in the patients. Methods: We retrospectively investigated the laboratory findings, clinical outcome, apheresis procedure parameters and response to TPE of 25 newly diagnosed TTP cases who were admitted to various departments of our hospital between 1999-2005. The TPE procedures were carried out by the cell separators found in our unit: COBE Spectra (COBE BCT, Lakewood, IL USA) and Fresenius AS204 (Fresenius AG, Germany). Mean age and M/F ratio of the patients were 44 years (25-70) and 17/8 respectively. Results: A total of 248 TPE cycles were performed for all patients. Median no. of TPE procedures for each patient was 11 (1-33). Median volume of plasma exchange was 3 (2.5-4.0) L/cycle. ACD volume used during each procedure was a median of 350 (250-600)ml. Median apheresis duration for each cycle was 100 (60-120) minutes. The median values of laboratory results before and after TPE are given in table. Except three patients who were exchanged with FFP + 5% albumin, all received FFP. Fourteen (56%) patients received methylprednisolone ± cyclosporine-A ± IVIg treatment in addition to TPE. Fourteen (56%) patients achieved complete remission while eleven (44%) patients showed no response to TPE. No grade III-IV complications arose during the procedures. Conclusion: TPE is a successful treatment modality in patients with TTP if applied as soon as the diagnosis is established. The results of our study support the evidence that TPE with or without additional treatment is a reliable and successful therapy in TTP. Replacement of the inhibited (or otherwise inactive) vWF-cleaving metalloprotease by plasma infusion, as well as removal of unusually large vWF multimers by plasmapheresis may explain the effectiveness of plasma exchange.

Abstract: 769 Poster: 676

ABSENCE OF ANTI-D ALLOIMMUNIZATION IN HAEMATOLOGICAL PATIENT AFTER D-

INCOMPATIBLE PLATELET TRANSFUSIONS

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Background: Alloimmunization with Rh antigen is possible after transfusion of Rh incompatible blood or blood components. Following application of Platelet Concentrates (PC), although Rh antigens are not present on the platelet membrane, alloimmunization to D-antigen is possible due to presence of Erythrocytes in the PC. PCs contain more or less RBCs whose antigens can be the cause of anti-D immune response. The frequency of aloimmunization in immunosuppressed patients was found to be up to 19%. Material and methods: The study included 10 Rh (D) negative patients with haematological diseases treated at the Haematology Clinic. Because of the decreased platelet number, in deficiency of Rh-negative PCs, the patients were administered platelet concentrates of positive donors. PCs were prepared from random whole blood donors (PRP method) or using a cell separator (Single Donor Platelets). Prior to application, the routine screening test detected no anti-D antibodies in any patient. Following PC application, every patient was treated with a single dose IgG anti-D every 2 weeks. Results: The 10 immunosuppressed patients with thrombocytopenia, treated with Rh incompatible PCs, were being followed during a period of over 3 months. There was no Rh alloimmunization detected in any of the 10 patients. Conclusion: The analyses of this group of haematological patients showed that there is a insignificant risk of developing anti-D alloimmunization in immunosuppressed patients.

Abstract: 770 Poster: 677

PREVALENCE OF DIFFERENT CAUSES OF REJECTION IN BLOOD DONORS ADMITTED TO KHUZESTAN TRANSFUSION SERVICE

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The donor screening process is one of the most important steps in protecting the safety of the blood supply. The health of blood donors has important role in patient and public health. The easiest way to excluded of infected or suspected blood donors from healthy donors are physical examination. Determination causes of blood donor rejection shows the important problems that hygienic systems and blood transfusion that should be emphasis. We studied 11584(10849 male, 735 female; 3541 first time donors, 5391 prospective donors,2652 repeated donors)of blood donors admitted to Khuzestan blood transfusion service that of them 2257(28 %) donors were rejected(permanent or temporary) The major causes of reject determined in this population. (Non random simple sampling) The major causes of reject was as following: high risk behavior (1568/2257;69%),hyper or hypotension(408/2257;18 %),medication(254/2257; 11%),blood disorder (147/ 2257;6%), anemia (134/2257;5 %),phlebotomy(108/ 2257;4%),renunciation (77/2257; 3 %),vascular heart disease (70/2257; 3%),travel(56/2257; 2 %). The rejection rate was very high in comparison with previously reported rate(12 %). we also found that the high risk behavior was significantly low in repeated donors comparison with first time donors.[first time donors(754/ 1568;40.09 %), prospective donors (569/1568;38.01 %),repeated donors(218/1568;13.9%).attention to above results,importance of sexual transmitted disease in the threatening of blood safety and existence of window period in most of this disease training the blood donors about the risk must be pay attention to it.

Abstract: 771 Poster: 678

PREVALENCE HBS-AG+ IN BLOOD DONORS REFERRED TO KHUZESTAN BLOOD TRANSFUSION SERVICE

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Nowadays, chronic hepatitis is the most important in social hygienic and the most common infections and contagious disease after Tuberculosis and malaria. The complications of hepatitis are varied from chronic hepa-titis to cirrhosis and hepatocarcinoma. In Iran, The most common agent of chronic hepatitis is hepatitis B virus (70-

80%), as the result it is the most important cause of mortality and morbidity due to liver disease in this study, we determined the in HBS Ag + prevalence healthy blood donors referred to Khuzestan blood transfusion service. According to prevalence of HBS Ag+ in cities of regional Khuzestan[(82/3979);1.32%]and comparison with other countries data seems that should be to give priority to this matter (Table 1).

Abstract: 772 Poster: 679

EFFECTS OF PLASMA DILUTION WITH CRYSTALLOID OR COLLOID SOLUTIONS ON BLOOD COAGULATION

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Massive transfusions of crystalloid and/or colloid plasma expanders are often complicated by dilutional coagulopathy, which is thought to be due to decreased concentrations of coagulation factors. However, as follows from the available clinical data and existing mathematical models, most of the coagulation factors are present in plasma in vast excess; therefore, their levels can drop by a factor of 5 to 10 without affecting the coagulation. On the contrary, with a decrease in the coagulation inhibitor concentration, the coagulation rate linearly increases. Obviously, plasma dilution with solutions containing nighter coagulation factors nor inhibitors would accelerate coagulation because the remaining concentrations of its inhibitors are low. In this study, the effect of plasma dilution was studied using a thrombin generation assay and an experimental in vitro model of spatial clot growth. If Ñà+2 was kept at 1.5-2 mM, and ğÍ at 7.4, normal plasma diluted 1.2- 4.0 times with various plasma expanders and activated whether via the extrinsic or intrinsic pathway exhibited an increase in the endogenous thrombin potential, accelerated spatial clot growth, and enhanced formation of spontaneous foci of clotting. At higher dilutions, these parameters decreased in some plasmas. On the contrary, the standard clotting times (APTT and PT) were prolonged at all plasma dilutions. Similar results were obtained in experiments with healthy volunteers who received HES transfusions (12 ml/kg; approx. 1.15-fold plasma dilution). These data suggest that plasma substitution should be avoided when blood loss is below 500600 ml because of potential thrombotic complications, especially when coagulation activation.is suspected This work was partially supported by the Russian Foundation for Basic Research, project no. 03-04-48338.

Abstract: 773 Poster: 680

EVALUATION OF PLATELET PARAMETERS IN HEALTHY APHERESIS DONORS USING ADVIA120TM

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Platelet apheresis donors are volunteer most of the time, and it is accepted that no clinically important change is observed after apheresis procedure. The changes in complete blood count parameters had been studied extensively, but obtaining reliable platelet counts with conventional hematology analysers could not be reached in certain instances. A recently developed automated hematology analyser (the ADVIA 120, Bayer Corporation, Tarrytown, NY, USA) provides not only a more accurate platelet count but also new parameters which describes both platelet morphology and function. We studied the changes in platelet parameters of 35 healthy volunteer platelet apheresis donors using ADVIA 120. We found a 30% decrease in platelet counts after apheresis, which was statistically significant but expected. Ther was no change in mean platelet component value, which was proposed to show platelet activation, as compared before and after apheresis. Mean platelet component value of the product was lower than the values obtained before and after apheresis, and this decrease was statistically significant which could be attributable to the activation of platelets when stored in citrate. We conclude that no remarkable changes were noted except the reductions in platelet numbers and plateletcrit which were expected to return normal values in a few days.

Abstract: 774 Poster: 681

THE EFFECT OF DOUBLE DOSE PLATELET APHERESIS ON PLATELET ACTIVATION IN HEALTHY DONORS

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BACGROUND and AIMS: The wide diffusion of multicomponent collectionin donor apheresis has led to the yielding of different components, such as doubledose plateletpheresis (DP). In recent years some investigators have shown that platelet activation may play a critical role in the pathogenesis of thrombotic and hemorrhagic disorders. The aim of this study was to determine the effect of double dose platelet apheresis on platelet activation. METHODS: In this study, we investigated the effects of DP with two different devices (continuous-flow automated blood cell separator Fresenius AS.TEC 204 n= 15 and intermittent-flow blood cell separator MCS Plus n=15) on in vivo platelet activation in 30 male volunteer donors. Peripheral blood samples were taken immediately before and after apheresis and on the 1th, 7 th days. Activation of platelets was determined by quantitating the amount of platelet P-selectin (CD62)expression with mean fleurosans intensity (MFI) of CD62P using a whole blood method on flow cytometry. RESULTS: We concluded that the platelet pheresis procedure did not cause an increase in platelet activation in donors. On the contrary, circulating activated platelet counts were decreased significantly immediately and first day after apheresis that may be due to the selective collection of activated platelets in the collection bag or removel of activated platelets from circulation by adhesion to leukocytes or reticuloendothelial system. CONCLUSIONS: Although clinical significance of these findings are not known, further studies are needed to elucidate whether DP is with an increase risk for donors with frequent apheresis, history of thromboembolism or other factors such as smoking.

Abstract: 775 Poster: 682

SINGLE DOSE PLATELET PREPARATION (OUR EXPERIENCE)

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Background: The preparation of Platelet Concentrates of Random Donors (PCRD) of whole blood is in constant increase. In the past 15 years (1990-2004) it has marked an increase from 1705 to 8589. The Single Dose Platelet (SDP) unit preparation is, however, a "conditio sine qua non" especially in patients in stages preceding, during and following Peripheral Stem Cell (PSC) transplantation, as well as in patients not responding to platelet transfusions. The report shows our experience in SDP preparation during 110 procedures. Material and methods: Cell separator Baxter CS 3000 Plus, Closed System Apheresis Set; End point volume of processed blood -5000 mL, whole blood-ACD relation 9-11:1; Blood flow rate 50mL/min (45-60); double venous access have been used. Results: 110 SDP units have been analyzed for the purpose of the study. The provision of Platelets in 200ml SDP is 557 x 10e9 (408-1028); Platelet count in donors was 264 x10e9 (184-406) preceding procedure realization and 178 (128-224) following the completion of procedure. Platelet depletion in donors was found to be 28% (11-46). SDP were controlled daily for the swirling and shimmering phenomenon, SDP pH did not undergo decrease under 6, 4 during 5 days. A patient having undergone 16 SDP transfusions was monitored and status-analyzed. The issues occurring during SDP preparation were divided into: problems arising prior to procedure onset - 1 occasion (without procedure cession) and problems occurring during the course of procedure, related to the donor - 3 occasions (procedure cessions: 1 -due to appearance of chylous plasma, 1 - due to onset of subjective symptoms, 1 - due to flow decrease). Minor side effects, such as hypocalcaemia, have been corrected with Calcium effervescent tablets. Conclusion: Our experience from 110 SDP procedures, makes the platelet obtaining method a routine procedure for providing sufficient amounts of high quality platelets; proves the procedure tolerable by donors and confirms it efficient as platelet supplement procedure in patients.

Abstract: 776 Poster: 683

THE RESULTS OF MICROBIOLOGIC SCREENING TESTS IN BLOOD DONORS IN MERSİN / TURKEY

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The tests for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and syphilis are routinely screened in blood donors. The results of 88222 screened blood donations from blood centres in the Mersin (Mersin University Hospital Blood Centre and Mersin State Hospital Blood Centre) between 1 January 1998 and 31 May 2005 for HBV, HCV, HIV and syphilis were analysed retrospectively. Testing for HBsAg, anti-HCV and anti-HIV has been done by using commecially available micro and/or macro enzyme immunoassays, and syphilis reagin antibody test by latex agglutination method. The positive blood samples with anti-HIV were sent to the reference laboratory. The results of screening for HBV, HCV, HIV and syphilis were 2.39% (2114), 0.50% (444), 0.05% (51) and 0.02% (107) respectively. Reference laboratory reported that 4 patients were HIV positive (0.004%).

Abstract: 777 Poster: 684

THYROID FUNCTIONS IN THALASEMIA MAJOR PATIENTS

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Ninety children with beta-thalassemia major (55 males and 35 females; mean age, 7.17 ± 3.78 years; age range 1-18 years) were enrolled into study. These patient were regularly transfused and desferioxamine chelated, and followed in our department with diagnosis of beta-thalassemia. Thyroid function and iron-load status were evaluated by measurements of free thyroxine (FT4), free triiodothyronine (FT3), thyrotropin (TSH), and serum ferritin levels. In 3 patients serum TSH levels were elevated and FT3, FT4 levels were found to be in normal limits for age groups. TRH stimulation test revealed maximal TSH response in early phase in those three patients. All cases were accepted to have compansated hypothyroidism. In beta-thalassemia major thyroid dysfunction may be seen even in early phases of disease. In this study we found that the thyroid dysfunction was related with transfusion intervals and serum ferritin levels. In conclusion thyroid function may be routinely evaluated in children with beta-thalassemia major.

Abstract: 778 Poster: 685

EARLY COMPLICATIONS OF TRANSFUSING BLOOD COMPONENTS IN HOSPITALIZED PATIENTS OF HEMATOLOGY AND ONCOLOGY CENTER IN SHAHID GHAZI HOSPITAL DURING 2002-2003

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Background: Cancer patients require appropriate blood components transfusion due to bone marrow suppression, sepsis, and etc, while there are risks of reactions due to blood components. These risks are influenced by multiple factors observed in different geographic regions and medical centers. Objective: This study was performed to determine incidence of early reactions and their clinical symptoms and signs in cancer patients, as well as correlation between these adverse reactions and some demographic data and characteristics of blood components. Methods: In this descriptive-analytic study, 39 reactions from 4023 transfusions were assessed. Patients were monitored for symptoms and changes in vital signs during 24 hours. Data analysis was performed according descriptive and inferential statistics (X2 and ANOVA). Results: The majority of reactions belonged to platelet (56.42%) and packed cell (43.58%) transfusion. The most common symptoms were shown to be rigors (2.72%), and increase in body temperature (2.33%). The incidence was estimated to be 2.7% for FNUTR, and 2.1% for allergic reactions. Haptoglobin deficiency was found in 0.8% of FNUTR. A correlation was shown between sex and higher rates of previous reactions to transfusion of blood components. Conclusion: These findings indicated that incidence of reactions and clinical symptoms were correlated with other studies. Reaction incidence in women and individuals with previous history of repeated transfusions was shown to be greater. Transfusion of packed cell was associated with allergic reaction and high platelet lifetime, associated with pulmonary reaction. To reduce these reactions, it is suggested to use modified blood products and components with short period of preservation.

Abstract: 779 Poster: 686

ROLE OF BONE MARROW EXAMINATION IN PATIENTS WITH ASYMPTOMATIC LEUKOPENIA

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Background. Persistent asymptomatic leukopenia is a common finding encountered at outpatient setting. Aims: The present study was designed to evaluate the role of bone marrow study in the patients with asymptomatic leukopenia. Methods. We performed a prospective study in 25 patients with isolated, persistent and asymptomatic leukopenia (defined as white blood cell count < 4x10^9/ L, but with normal hemoglobin and white cell count, at least two times in different periods longer than one month). The initial complete blood count was recorded. After excluding obvious causes of leukopenia, bone marrow aspiration and/or biopsy were performed. Bone marrow finding was recorded and incidence of abnormal bone marrow finding was calculated. Different variables of these leukopenic patients were compared and analyzed to find out whether there were any correlations among them. Results. Totally 25 patients were enrolled from May 2001 to December 2004 in the Hematology outpatient clinic, with mean age 59.5 years; 12 were male. Mean white blood cell count was 3.40 +/- 0.44 x10^9/L and mean absolute neutrophil count was 1.78 +/- 0.39 x10^9/L. Bone marrow studies were all within normal limits with mean cellularity 30.2 +/- 9.5% except a case found to have serous atrophy. Age, but not absolute neutrophil count, was correlated with bone marrow cellularity. Conclusions. Bone marrow study may provide little help in evaluating patients with isolated asymptomatic leukopenia and routine examination was not mandatory.

Abstract: 780 Poster: 687

SPLENIC INFARCTION RECOVERED WITH ANTIPLATELET TREATMENT AND PLATELETAPHERESIS IN POLYCYTHEMIA VERA

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Background: Thromboembolic events, seen in 27-45% of patients with polycythemia vera, occur in coronary and peripheral arteries, cerebral, pulmonary, portal, hepatic, and deep veins. Case presentation: A 79-year-old man was admitted to hospital, with complaints of pruritus especially increasing from bath and left upper abdominal pain radiating left shoulder.for two months. On physical examination, there were ruddy and hyperemic appearences of his face and konjunctiva, tenderness of left upper quadrant, and splenomegaly. Hemoglobin level was 16.6 g/dl, hematocrit 53.8%, white blood cell count 26x109/l, and platelet count 1.032x109/l. Bone marrow aspiration and biopsy reveled hypercellularity, megakaryocytic hyperplasia and dyplasia. The leukocyte alkalen phosphatase score was 190. The levels of serum vitamin B12 and D-dimer were 316 pg/ml and 744 ng/ ml, respectively. Arterial O2 saturation was 96%. Red cell mass was measured as 43 ml/kg.. On cytogenetic analysis, deletion of 20q was found. Computed tomography of whole abdomen showed diffuse splenomegaly and two hypodense areas due to splenic infarction in 2.5x2 and 3.5x3 cm. diameters in region of near to capsule of the spleen. The patient was treated with therapeutic plate-letapheresis, 40 mg/day aspirin, analgesic drugs, and 3 g/day hydroxyurea. After 1.5 months, platelet count dropped less than 500x109/l and splenic infracts were not detected on computed tomography. Figure.a and b. show Pre-treatment and Post-treatment of abdominal computed tomography. Conclusion: Splenic infarction may be first evidence of thrombosis in polycythemia vera. The reduction of platelet count with plateletapheresis, anti-platelet drugs, and carefull clinical observation may be enough in the treatment of splenic infarction.

Abstract: 781 Poster: 688

INDUCTION OF NK CELLS` FUNCTIONALITY BY THE USE OF APIGENIN

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Introduction: Natural killer cells (NK Cells - NKCs) are a subpopulation of lymphocytes that play an important role in immunotherapy. Apigenin is a phytoestrogen, an ingredient of many plants. Purpose: The investigation of possible induction of functionality of NK cells by the use of apigenin. Material and Methods: 18 healthy volunteers participated in the study. The methodology of quantification of cytotoxicity of NKCs was used in the in vitro study, which included four stages: a) Isolation of PBMC`s from blood and their quantification, b) Quantification of cancer cells (leiomyosarcoma-Wistar rats), which were used as cancer target cells (CTCs), c) Incubation of NKCs with CTCs in CO2 chamber in the ratios 12.5:1, 25:1, and 50:1 and d) Determination of cytotoxicity by flow cytometer Epics XL-MCL of Beckman-Coulter Co. The same trials were repeated after the addition of apigenin during stage c. Results: The cytotoxicity of NKCs against CTCs indicated an increase of 320%, 480%, average rate in the ratios 25:1 and 50:1, while no increase in cytotoxicity observed in the ratio 12.5:1. Conclusion: Apigenin seems to have important anticancer properties against cancer cells and its use in clinical trials should be seriously considered in the future.

Abstract: 782 Poster: 689

RESVERATROL, AN INGREDIENT OF MANY PLANTS, THAT INCREASES NK LYMPHOCYTES` CYTOTOXICITY AGAINST CANCER CELLS

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Introduction: Natural killer cells (NK Cells-NKCs) are a subpopulation of lymphocytes that play an important role in immunotherapy. Resveratrol is an ingredient of many plants, with antioxidant properties. Purpose: The investigation of possible anticancer actions of resveratrol by stimulation of NK cells. Material and Methods: 18 healthy volunteers participated in the study. The methodology of quantification of cytotoxicity of NKCs was used in the in vitro study, which included four stages: a) Isolation of PBMC`s from blood and their quantification, b) Quantification of cancer cells (leiomyosarcoma -Wistar rats), which used as cancer target cells (CTCs), c) Incubation of NKCs with CTCs in CO2 chamber in the ratios 12.5:1, 25:1, and 50:1, and d) Determination of cytotoxicity by flow cytometer Epics XL-MCL of Beckman-Coulter Co. The same trials were repeated after the addition of resveratrol during stage c. Results: The cytotoxicity of NKCs against CTCs indicated an increase at 320%, 440%, 67% average rate in the ratios 12.5:1, 25:1 and 50:1 respectively. Conclusion: Resveratrol seems to be an important NK stimulator against cancer cells in vitro and therefore further clinical studies using this substance should be performed for more convenient prevention and therapy of cancer.

Abstract: 783 Poster: 690

EFFECT OF AEROBIC AND ANAEROBIC EXERCISES ON NATURAL KILLER CELL NUMBERS AND ACTIVITIES IN HEALTHY ADULT HUMAN PERIPHERAL BLOOD

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Objectives: Natural killer (NK) cells are lymphocytes, which show cytotoxicity against virus-infected cells and tumor cells. We have investigated the effect of aerobic walking exercises and anaerobic exercises by treadmill on NK cells in healthy adult human peripheral blood. Methods: Peripheral blood lymphocytes were obtained from four healthy adult females before and after aerobic walking exercises, or from two healthy adult males before and after anaerobic transient maximum exercises by BRUCE treadmill protocol, and analyzed by two-color flow cytometric analysis. NK activities against K562 cells were measured by europium release assay. Maximum oxygen uptake (MOU) and ventilation threshold (VT) were analyzed by exercise loading data collecting system and breathing metabolic analyzer. Results: MOU was 35, 39, 31, 33 ml/kg/mim in females, and MOU was 43, 43 ml/kg/mim, and VT was 31, 23 ml/kg/mim in males, respectively. The absolute numbers of large granular lymphocytes (LGL) after the exercises were increased: 451/mm3 to 1308/mm3, 494/mm3 to 606/mm3, 204/ mm3 to 266/mm3 and 338/mm3 to 444/mm3 in the aerobic exercises, 140/mm3 to 1441/mm3 and 423/ mm3 to 1368/mm3 in anaerobic exercises, respectively. The absolute numbers of CD3-CD16+56+NK cells after the exercises were increased: 343/mm3 to 615/mm3, 448/mm3

to 635/mm3, 91/mm3 to 138/mm3 and 151/ mm3 to 251/mm3 in the aerobic exercises, 100/mm3 to 1280/mm3 and 730/mm3 to 2080/mm3 in anaerobic exercises, respectively. NK activities after the exercises calculated by lytic units/107cells were generally increased: 32 to 40 and 63 to 52 in the aerobic exercises, and 77 to 217 and 111 to 132 in the anaerobic exercises, respectively. Serum concentrations of three types of catecholamines (epinephrine, norepinephrine and dopamine) and lactate in peripheral blood were increased after the anaerobic exercises. Conclusions: NK activities after the aerobic and anaerobic exercises were generally increased via the increase of the absolute numbers of LGL and CD3-CD16+56+NK cells in healthy adult human peripheral blood.

Abstract: 784 Poster: 691

ANGIOTENSIN-CONVERTING ENZYME (ACE CD143) IN LEUKEMIC DENDRITIC CELLS (DC) IN ACUTE MYELOID LEUKEMIA (AML) PATIENTS

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Background. DC play a key role in the induction of adoptive immune response because they are efficient in antigen presentation and costimulation of naive lymphocytes. Leukemic DC (LDC) and DC from monocytes healthy donors are characterized by high levels of co-stimulatory molecules expression. The difference between LDC and DC from healthy donors are in the expression of surface ACE, as it is reported to be a high on the monocyte-derived DC in contrast to DC derived from leukemic blasts. Aim. We supposed that the absence of surface ACE expression reflects the alteration in the differentiation of LDC resulting in the block of transportation of ACE on the cell`s membrane. In order to confirm this hypothesis we investigated intracellular production of ACE. Methods. Blood samples were collected from 8 AML patients at diagnosis before induction chemotherapy. Mononucler cells were isolated using gradient centrifugation with Ficoll-Paque, leukemic cells has been cultured in the presence of 180 ng/ml calcium ionophore for 4 days. Two healthy donors constituted the control group (nonadherent cells were removed before culturing). DC were stained for surface and intracellular ACE and ACE expression was detected by flow cytometry. Two clones of antibodies were used (1D8 for nonactivated and 9B9 for activated forms of ACE). Statistical data were computed by program "Statistics for Windows 5.5". Results. DC derived from AML blasts have shown large amount of intracellular ACE: 70±12% (clone 1D8), 79 ±12% (clone 9B9). Surface ACE was detected in 2 ±2% (clone 9B9) and 0.8±0.5% (clone 1D8) cells. In contrast, DC derived from normal monocytes had intracellular ACE in 0.8±0.1% (clone1D8), 2.3±0.6% (clone 9B9) cells, surface ACE positive cells were 60.6 ±9.2% (clone 9B9) and 5.6±0.8% (clone1D8). The percentages of intracellular ACE producing LDC significantly differed from normal DC ($p=0,0001$and $p<0,0001$ for clones 1D8 and 9B9 respectively). The percentages of surface ACE positive normal DC cells exceeded such counts in AML patients ($p<0,0001$ for both clones). Conclusion. The data confirm the block transport of ACE on the membrane of LDC and alter of their differentiation.

Abstract: 785 Poster: 692

AUTOLOGOUS MESENCHIMAL STEM CELL TRANSPLANTATION IN AMYOTROPHIC LATERAL SCLEROSIS

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Introduction: Amyotrophic lateral sclerosis (ALS) is a highly morbid neurodegenarative second motor neu-ron disease of which hardly any kind of conventional therapy is effective. It has two clinical forms which are described as rapidly progressive and slowly progressive. Especially, the rapidly progressive form results in death with respiratory failure in three to five years. Therefore new therapeutic options are essential for ALS. Recently, mesenchimal stem cells have opened a new window for regenerative medicine in a number of diseases and the research is continuing extensively. These cells have the potential to differentiate to neurons in in vitro and animal experiments. Clinical studies have begun and the

first report is from Mazzini group, Italy. Aim: To evaluate the safety and efficiency of autologous mesenchimal stem cell transplantation to rapidly progressive ALS patients unresponsive to conventional therapy. Patients: After the ethical committee approval, three patients were enrolled. All of them were rapidly progressive ALS with a short expectance of survival. TU 63 years old male: Diagnosed at 2001, paralysis in both upper and lower extremities, progressive difficulty in speaking and swallowing. IG 44 years old male diagnosed at June 2000 and BT 29 years old male diagnosed at January 2002 also showed similar clinical status. EMG revealed general denervation and polyphasic motor unit potentials in all patients. Cells: After obtaining informed consent from patients, bone marrow aspiration was performed and mesenchimal stem cells were cultured and expanded in vitro in approximately 21-35 days. Results: TU: Laminectomy and intraspinal stem cell transplantion was applied to involved areas at Februaury 2004. Died at 48 hours with probable myocardial infarction. IG: 15 periodic intrathecal stem cell transplantions were applied. Clinical disease progression stopped but no change in EMG. BT: Laminectomy and intraspinal stem cell transplantion was applied to involved areas at September 2003 and periodic intrathecal 19 injections followed. Clinical disease progression stopped. New reinnervation potentials were detected in EMG. Conclusion: Autologous mesenchimal stem cell transplantation is a new and thrilling therapy procedure in ALS, further experience is awaited to reach conclusion.

Abstract: 786 Poster: 693

MESENCHIMAL STEM CELLS IN IATROGENIC FACIAL NERVE PARALYSIS: A POSSIBLE ROLE IN THE FUTURE

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A twenty-year old female patient with chronic otitis media suffered injury to intratemporal facial nerve during mastoidectomy. The facial nerve was completely destroyed in its mastoid segment leaving a gap of 8-10 millimeter between the nerve endings. Immediate transfer of a nerve cable graft from the great auricular nerve in the vicinity was performed. A temporary tarsoraphy was performed. In the follow-up, EMG on the 35th day showed denervation and axonal damage with no motor unit potentials. The patient was clinically graded as Grade VI facial nerve paralysis. The bone marrow cells of the patient were obtained and transformed to mesenchimal stem cells in vitro accordingly. The cell suspension was injected into the anastomotic sites on the 42 nd day after the initial surgical trauma with nerve grafting. The daily clinical monitorization showed progression of House-Brackmann Grade VI to V on the fifth day and to IV th Grade on the seventh day. The EMG obtained showed some rare regeneration motor unit potentials. Five months after the procedure, the patient has no asymmetry at rest, complete eye closure is possible, moderate asymmetry in the mouth movements. EMG in the fifth month shows increased and dense reinnervation potentials in the facial muscles. The patient is expected to further improve. The patient was graded as Grade III House -Brackmann at the fifth month post-treatment. This result is the best healing known compared with surgery alone according to data up till now. This case represents the first mesenchimal stem cell application in a peripheral nerve, namely the facial nerve.

Abstract: 787 Poster: 694

KILLED BUT METABOLICALLY ACTIVE (KBMA) MICROBES: A NEW VACCINE PARADIGM FOR ELICITING EFFECTOR T CELL RESPONSES AND PROTECTIVE IMMUNITY

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Vaccines based on live-attenuated organisms are desirable for their immunologic potency, but the risk of disease precludes their use in many instances. To address this dilemma, we have developed a new class of vaccines based on killed but metabolically active (KBMA) bacteria, which simultaneously takes advantage of the potency of live and the safety of killed vaccines. We removed genes required for nucleotide excision repair (uvrAB), rendering microbial-based vaccines exquisitely sensitive to inactivation by photochemi-

cal treatment combining psoralen and long wave ultraviolet light. Replication and colony formation of the nucleotide excision repair mutants was blocked by infrequent, randomly distributed psoralen crosslinks, but the resulting bacterial population was able to express its genes, synthesize and secrete proteins. Using the intracellular pathogen Listeria monocytogenes (Lm) as a model platform, recombinant psoralen inactivated Lm (uvrAB deleted) vaccines induced potent CD4+ and CD8+ T cell responses and protected mice against virus challenge in an infectious disease model and provided therapeutic benefit in a murine cancer model. Microbial KBMA vaccines used alternatively as a recombinant vaccine platform or a modified form of the pathogen itself may have broad use for the treatment of infectious disease and cancer.

Abstract: 788 Poster: 695

EFFECT OF BOOSTER DOSE IN CONTROL OF IMMUNITY FOR HEPATITIS B VIRUS IN MULTI-TRANSFUSED PATIENTS

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Introduction: Transfusion Transmitted Infections is one of the most important side effects of blood transfusion for multi-transfused patients and one of them is Hepatitis B Virus. Hepatitis B vaccine is obligatory for beta thalassemia patients, but the immune response to vaccination is less than healthy individuals. We studied the prevalence of HBV in our thalassemic patients for finding out; the frequency of these infections and compare to our previous data to detect the possibility of increasing rate. In addition, we studied the immune status of our patients for Hepatitis B Virus (HBV) in Adult Thalassemia Clinic in Tehran, which covers Thalassemia Major (TM), Intermedia (TI), Sickle Thalassemia (ST) and Hb H disease patients. Material & Method: For Hepatitis B viruse, we checked Hepatitis B surface antigen (HBsAg) Hepatitis B surface antibody (HBsAb), Hepatitis B core antibody (HBcAb) which was done by ELISA method. We classified the Immune status of patients to four category; 1/Immune to HBV via the vaccination (positive vaccinal) If HBs Ag: negative, HBsAb: positive, HBc Ab: negative; 2/ Immune to HBV via the natural disease (past infection) If HBs: negative, HbsAb and HBcAb: both positive; 3/ Non immune to HBV (negative) If all three parameters were negative; 4/ Carrier of HBV (carrier state) If HBs Ag was positive and HBs Ab and HBc Ab: both negative. We had grading of immunity to the HBV vaccine by antibody (HBs Ab) titration as below: Positive; if antibody level was more than 100 IU/mL; Negative if antibody level was less than 10 IU/mL and weakly positive if antibody level was 10-100 IU. Results: We studied 416 patients who were 303 (72.6 %) TM, 104 (25.2 %) TI, 7 (1.4 %) ST, and 3 (0.72 %) Hb H disease. We had 247 (58.2 %) male and 169 (40 %) female mean age was 25.6 years.256 patients (62.2%) were splenectomized (169 TM, 83 TI, 3 ST, 1 Hb H). According to our classification 300 (70.3%) were positive vaccinal; 66 (15.5 %) were immune to HBV from past infection; 40 (9.4 %) were negative and 3 (0.7 %) were carrier state of HBV (None of them had not active disease HBe Ag: negative). In grading of immunity to HBV vaccination, we had 236 (76.4%) HBsAb level more than 100 IU/mL (positive) 62 (20.1 %) between 10-100 IU/mL (weakly positive) and 11 (3.6 %) less than 10 IU/mL (negative). There was not correlation between the level of HBs Ab and spelenetomy or type of thalassemia. Discussion: We compared the results with our previous data.According to this comparison, we had increasing rate in positive vicinal patients [48.6% (of previous data) versus 70.3%], which was because of use of booster dose for such high-risk patients. Response rate with vaccination is more than 95% after complete course (three doses) in healthy individuals but failure to vaccination coverage seems a problem in chronically transfused patients. In European study, 22% of multitransfused thalassemic patients had not response to HBV vaccination, and in Cypriot study, only 45% of their patients was immunized by vaccination. There is not any recommendation of booster dose for healthy individuals but for thalassemic patients TIF advice to check the antibody level and administration of booster dose for patients with levels less than 10 IU/mL. Similar decision must be done for weakly positive (HbsAb level 10-100) patients or serial follow up needs for possibility of the booster dose, must be considered for this group of patients.

Abstract: 789 Poster: 696

IMMUNOMODULATORY EFFECT OF MSCS ON DC DERIVED FROM UCB

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Background: The Mesenchymal Stem Cells (MSCs), are cells that have ability to differentiate into multiline-age cell types. The mechanisms of immunomodulatory of MSCs on immune cells are unclear now and many ongoing investigations are involving with. Aims: To study immunomodulatory effect of MSCs on differentiation of monocyte into Denderitic Cells (DCs). Methods: Umbilical Cord Blood (UCB) was collected and MonoNuclear Cells (MNCs) separated by density centrifugation.Also,the human MSCs obtained from UCB After second passage of adherent cells in DMEM with 15% FBS.then, MNCs from UCB co-cul-tured on MSCs in IMDM with 10% FBS supplemented with cytokines that promotes DC differentiation. After 7 days, differentiated cells were harvested for flowcytometry analysis. Results: Flowcytometry analysis showed that percentage of DCs generated in co-culture with MSCs significantly lower than those that only cultured in present of cytokines. Also, proliferation of total cells in co-culture on MSCs was very high.this result may be indicate that MSCs can inhibit differentiation of monocyte into DCs and enhance expansion of primary population. Summary/ Conclusion: In conclusion, results indicate that MSCs have immunosuppresion effect on DC differentiation. These results are very useful in application of MSCs in Immunotherapy. Future investigations can be necessary to identify agents that involve in this process.

Abstract: 790 Poster: 697

EXTERNAL QUALITY ASSESSMENT SCHEME BY PRIVATE LABORATORIES IN TURKEY

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External Quality Assessment Schemes (EQAS) together with "Internal Quality Controls (IQC)" are indispensable to get more accurate laboratory results. We have organized an EQAS to assess analytical inadequacy and increase comparability among different private laboratories in Turkey. In 2002 we began to perform a program for hematology and chemistry, covering the measurement of uncertanity related bias and imprecision for analytical evaluation and interpretive comments against the reference interval as postanalytical evaluation. Our aim was to reduce the %CV values and increase the precision of the participant laboratories. Therefore all the laboratories in the programme were asked to use calibrator or control samples rutinely supplied by the reagent providers and assess critical performance characteristics such as limit of detection and limit of quantification. From the begining, we have sent 28 samples in 14 batches (2 levels/batch), 4 surveys annually. The number of participants only from private laboratories have reached to 110 from all over Turkey. Fresh samples which were taken from previously controlled human donors were diluted or concentrated by adding or discarding some of the plasma fraction and distributed among the participants by over night-delivery service in temparature controlled special shipping boxes. Sample preparation and shipping are done by Duzen Lab-oratories Group and periodically controlled by TURKAK (Turkish Accreditation Agency). Five parameters of CBC tests (Hb, Hct, RBC, WBC and platelet) were included to evaluation. We advice the participants to perform the CBC test in 24 hours. After performing the tests, all of the participants send their results via internet from our special web site (www.duzen.com.tr/qcr). The data is evaluated by a specifically designed computer program and controlled by one of our specialists and announced to the participants in less than 3 days. Preliminary results are always submitted to TURKAK as well as the Turkish Hematology Society. The participants can see their results from our web site by using a password. Participants also receive printed reports in 3 different format. Format 1 has information about the brief summary of the last 8 results of the participants. Result, mean, SD, SDI, participant number and CLIA 88 comparison are all shown in the same format together with Levey-Jenings graphics. In format 2, we show two different levels of analytes in Youden graphics. Format 3 is related with group evaluation and in this format the kits or groups are evaluated separetely. The CV values that we obtain from our participants are always in CLIA 88 limits since the beginning for all parameters but our aim is to reduce them by time. We think that this can be possible by using certified analyzers and calibrators by the laboratories. This requires enforcement of regulatory organizations and buyers of health services.

Abstract: 791 Poster: 698

CLINICAL ASPECTS OF SCLERODERMOID TYPE GRAFT VERSUS HOST DISEASE AFTER ALLOGENEIC HAEMATOPOIETIC CELL TRANSPLANTATION

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Background: Dermatological complications in chronic graft versus host disease (GVHD) are well known and affecting many allogeneic transplant recipients. One of the major dermatologic complications of chronic GVHD is sclerodermoid changes. AIM: Our purpose was to analyze the clinical features of sclerodermoid chronic graft versus host disease (GVHD) after allogeneic hematopoietic cell transplantation (AHCT) from 1986 through 2005. Method: We assessed age, sex, pre-transplant diagnosis, conditioning regimen, GVHD prophylaxis, preceding acute GVHD and chronic lichenoid and chronic systemic GVHD, clinical properties of sclerodermoid GVHD. Results: Sclerotic skin lesions developed in 15 allogeneic bone marrow (alloBM) and in 7 allogeneic peripheral blood (alloPB) patients. Thirteen patients were male and 9 were female with a mean age of 32.7±8.0 years. Underlying malignancies in patients undergoing AHCT included AML (n=10), CML (n=7), ALL (n=1), MDS (n=1) and MM (n=1). As conditioning regimen 18 patients received Bu+Cy and for GVHD prophylaxis 18 patients received short term methotrexate and cyclosporine and 4 patients received mycophenolate mophetil and cyclosporine. Acute GVHD appeared in 17 patients with hepatic involvement in 2, with gastrointestinal tract in 2 and skin involvement in 13 of these patients. Extensive chronic GVHD (liver, pulmonary, skin and oral mucosa) developed in 14 patients Sclerotic lesions developed after a mean of 681 ±411 days. Sclerosis was generalized in 19 patients (86.4%) and localized in 3 patients (13.6%). Leopard skin eruption appeared in 8 (36.4%) of the 19 patients with generalized sclerodermoid changes. In most of the cases sclerotic lesions appeared in the trunk and distal parts of the extremities spared. Joint retractions and dysfagia developed in 2 (9%) of the 22 cases. Eleven patients presented with oral mucosal involvement. One patient presented with lichen sclerosis et atroficus and one with septal panniculitis. Other associated lesions were poikiloderma (n=3), pyogenic granuloma-like lesion (n=1), bullous lesions and erosions (n=1), ulcers (n=2), ecrine hydrocystoma (n=1), acquired ichtyosis (n=2), scatricial alopecia (n=3), vitiligo (n=2), SICCA syndrome (n=2) and salivary abnormalities (n=5). Eight patients (36.4%) progressed from lichenoid to sclerodermoid lesions, 2 (9.1%) with lichenoid and sclerodermoid phases together and 12 (55.5%) with de novo sclerodermoid lesions. None of the patients had Raynoud phenomenon. Four patients were lost because of late transplant related complications. Conclusions: Sclerodermoid GVHD has a late onset and maybe quite disabling. Unlike scleroderma, acral involvement is rarely seen and most cases are presented with trunk involvement resembling leopard skin eruption. Extensive chronic GVHD precedes generalized sclerodermoid involvement in most patients. Although most lesions do not disappear in the course of the disease most patients have a good prognosis.

Abstract: 792 Poster: 699

MUTATION OF THE P53 GENE IS ASSOCIATED WITH BLASTIC TRANSFORMATION IN CHRONIC MYELOID LEUKEIMA

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ABSTRACT Chronic myelogenous leukemia (CML) is a clonal disorder of multipotential hematopoietic stem cells characterized by excessive proliferation of immature and mature myeloid cells. Molecular mechanisms in blastic crisis remains largely unknown. However loss of functions of tumor suppresser genes such as P53 might be involved in disease progression. This work was planned to investigate P53 protein expression and gene mutation in chronic myeloid leukemia and to evaluate its role in blastic transformation. Mutant P53 protein expression by flow cytometry and P53 gene mutation by polymerase chain reaction - single strand conformational polymorphism (PCR-SCCP) and sequencing technique were assessed in 26 patients with newly diagnosed CML, 11 patients at blastic crisis as well as 10 apparenlty healthy individuals selected

to act as a conrol group. In this study mutant P53 protein expression detected by flow cytometry was found in 3.8% of patients at chronic phase and in 27.7% of patients at blastic crisis opposite to 0 % of the control group. One patient had P53 mutant gene- as detected by PCR-SSCP sequencing technique in chronic phase in the form of transition point mutation (thymine ›cytosine) at codon 273 of exon 8. Three patients at blastic crisis had P53 mutant geen, one had similar pattern of sequencing as that in chronic phase while in the other 2 patients had denovo P53 gene mutations. There is framshift mutation where there is insertion of cytosine at codon 250 of exon 7 in one patient and transversion point mutation (guanine ›thymine) at codon 154 of exon 5 in the other patient. From this study we can conclude expression of mutant P53 as a result of P53 gene muta-tion may be important in the genesis of blastic crisis of chronic myeloid leukemia.

Abstract: 793 Poster: 700

CLINICO-HEMATOLOGIC AND PATHOLOGIC PROFILE OF ADULT FILIPINO PANCYTOPENIC PATIENTS

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BACKGROUND: Pancytopenia may be found in various disorders which primarily or secondarily affect the hematopoietic function of the bone marrow. The International Agranulocytosis and Aplastic anemia study showed aplastic anemia as the commonest cause of pancytopenia. Studies from other countries in Asia showed megaloblastic and aplastic anemias as the leading causes. There has been no systematic study on the clinical spectrum of pancytopenia in the Philippines so far. AIMS: This study is mainly aimed at determining the common causes of pancytopenia among adult Filipinos. It is also our objective to determine the demographic, clinical, hematologic and pathologic profile of adult Filipino pancytopenics. METHODS: This is a 10-month prospective observational (descriptive) study conducted simultaneously in three tertiary medical centers in the Philippines. Inclusion criteria are: (1) age at least 19 years, (2) hemoglobin (hgb) <110mg/dl for premenopausal females or <120 mg/dl for males and postmenopausal females, leukocytes <5,000/ul, and platelets <150,000/ul, (3) of Filipino citizenship and nationality, and (4) written consent. Patients were excluded if pancytopenia has already been previously worked up with diagnosis known. Peripheral blood smears, bone biopsy and marrow aspiration were performed and processed uniformly. Peripheral blood smears were examined by a single hematologist while bone biopsy and marrow aspirates were examined by a single hematopathologist. RESULTS: Twenty-two patients qualified and completed the study. Four of the patients were initially admitted for symptoms attributed to pneumonia while the rest of the patients had an initial impression of aplastic anemia. Results showed that pancytopenia occurs at any age group (mean 48.8 years) with no sex preponderance. There was no occupational association noted. Body weakness was present in all cases and was likewise the most common presenting complaint. Other common symptoms were bleeding and fever. Symptoms were noted for less than a month in the majority (45%). Pallor was a universal finding. Mean values for the blood cell components are: hgb 61mg/dl, platelets 64,545/ul and leukocytes 3,280/ul. Hypcohromia was seen in all peripheral blood smears. More than half had bone marrow hypocellularity largely associated with predominance of fat vacuoles with relative lymphocytosis (54.5%) while 23% had marrow hypercellularity with varying associated features. Histopathologic and clinical correlation revealed aplastic anemia (54%) as the most common cause of pancytopenia. Other causes are acute myelogenous leukemia (AML) 9%, immune thrombocytopenic purpura (ITP) 9%, myelodysplastic syndrome (MDS) 9%, acute lymphocytic leukemia, malaria, drug-induced pancytopenia and megaloblastic anemia (4.75% each) as the underlying cause of pancytopenia. CONCLUSION: Pancytopenia is a feature common to many illnesses and the distinction is more difficult in certain hematologic disorders. Aplastic anemia is the main cause of pancytopenia among adult Filipinos. Other leading causes are AML, ITP and MDS. Peripheral pancytopenia warrants careful and systematic investigation. In most cases, bone marrow aspiration as well as bone biopsy must be done with the results correlated clinically to make an accurate diagnosis.

Abstract: 794 Poster: 701

DOES THE XPD LYS751GLN POLYMORPHISM EFFECT THE LEVEL OF DNA DAMAGE IN HUMAN PERIPHERAL LYMPHOCYTES EXPOSED TO 17 BETA-OESTRADIOL-INDUCED OXIDATIVE STRESS?

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Some epidemiological and experimental studies showed that there is a relation oestrogen and development of some cancers and this relation can be originated from genotoxical effect related with the oxidative stress of hormone. It was suggested that lys751gln polymorphism of XPD protein known playing a role in repair of DNA damage has also a role in the development of some cancers related with oestradiol. In this study, we aimed to investigate the relation with 17 beta-oestra-diol (E2)-induced oxidative stress and how this relation was effected by XPD lys751gln polymorphism. For this aim, peripheral lymphocytes collected from healthy adult males were cultured with high concentration E2 (36 mikroM) for 48 hours. Oxidative stress and damage were investigated with changes in malondialdehyde and chemiluminescence levels. Evaluation of DNA damage was investigated with Comet assay. In our findings, it was observed that oxidative stress and damage in cell cultures incubated with E2 were increased, but no increase was observed in DNA damage. At the same time individual differences were observed in cell proliferation against E2. Our results suggested that polymorphism has no effect in these differences and damage but still needed further studies in order to evaluate XPD lys751gln polymorphism as a risk factor for possible oestradiol genotoxicity.

Abstract: 795 Poster: 702

DISTRIBUTION OF ABO BLOOD GROUPS IN PATIENTS WITH ACUTE AND CHRONIC LEUKEMIA, LYMPHOMA AND MULTIPLE MYELOMA IN TURKISH POPULATION

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Backgrounds: The relationshp between ABO blood groups and hematological malignancies was defined in some studies.Aim: We aimed to investigate the distribution of ABO blood groups in patients with acute myel-ogenous leukemia (AML), acute lymphocytic leukemia (ALL), Hodgkin`s disease (HL), non-Hodgkin`s lymphoma (NHL) and multiple myeloma (MM) in children and adults in Turkish population. Methods: This data were collected retrospectively from clinic records which were available between January 1996 and December 2004. Population distribution of blood groups was derived from the records of our hospital`s blood bank belonging to 1999. Results: In 1999, ABO blood group distribution of 12.207 donors was group A 43.2%, group B 15.3%, group AB 9.3% and group O 32.2%. We evaluated 184 AML(34.5%), 166 ALL(31.1%), 48 CML(9.0%), 48 MM(9.0%), 34 NHL(6.4%), 28 CLL(5.2%), 26 HL(4.9%) patients in this study. We compared the blood group distribution of the patients with the population sample. Blood group distributions of the patients was found to be correlated with the population sample except CML and NHL. In CML patients, blood group A was 19.3% more frequent and blood group O 19.7% less frequent than the population. In NHL patients, blood group B 22.9% was more frequent, and blood group O was 23.4% less frequent than the population. This is the first study in Turkish population. Conclusions: New studies with more cases might highlight the relationship between blood groups and hematologic malignancies.

Abstract: 796 Poster: 703

CA 15-3 CONCENTRATIONS IN BLOOD IN PATIENTS WITH SICKLE CELL DISEASE

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It is known that the CA 15-3 molecule is a mucin, being a product of the MUC1 gene. CA 15-3 is currently the most widely used circulating marker

for breast cancer. As with all biochemical cancer markers in current use, elevated CA 15-3 concentrations are not organ-specific. It was reported that patients with benign diseases (hepatitis, inflammatory disorders, benign breast disease, etc) had higher marker concentrations than those with healthy controls. However, to our knowledge, there is no information about serum levels of CA 15-3 associated with sickle cell disease (SCD) in literature. In this study, we aimed to define serum CA 15-3 levels in patients with SCD, which is characterized by chronic inflammation and ischemia-reperfusion injury. We prospectively measured serum CA 15-3 concentrations in patients with SCD (34 in steady state, 17 in painful crisis) (n=51), breast cancer (n=15), and normal healthy controls (n=20). Twenty-eight patients (79.4%) with SCD in steady state had CA 15-3 values > 30 U/mL while 13 (76.5%) in patients with SCD in painful crisis. Serum CA 15-3 concentrations were measured by a micro particle immunoassay without knowledge of the clinical diagnosis. Serum CA 15-3 concentrations were elevated in patients with SCD (53.39±23.25 U/mL in steady state, 45.77±21.19 u/mL in painful crisis) comparing healthy controls (13.81±8.43 U/mL) (P=0.00 for sickle cell in steady state, and P=0.01 for sickle cell in painful crisis). However, the difference between sickle cell steady state group and sickle cell painful crisis group was not statistically significant (P > 0.05, for both). When compared with the SCD group (SCD in steady state and SCD in painful crisis), serum CA 15-3 concentrations were found to be significantly elevated in patients with breast cancer (268.15±296 U/mL) (P=0.00 for both, respectively). These data suggest that the serum CA 15-3 concentration can elevate in SCD, and further investigation is necessary to evaluate for possible prognostic value in ischemia-reperfusion injury.

Abstract: 797 Poster: 704

DERMATOYOSITIS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION AS SOLE MANIFESTATION OF ACUTE GRAFT VERSUS HOST DISEASE

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Background: The idiopathic inflammatory myopathies (IIMs) comprise a heterogeneous group of diseases of unknown etiology characterized by chronic inflammation of the skeletal muscles. On the basis of unique clinical, histopathological, immunological, and demographic features, they can be differentiated into three major and distinct subsets: dermatomyositis, polymyositis, and inclusion-body myositis. Polymyositis and dermatomyositis usually occurred along with other manifestations of chronic graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (HSCT) had been reported. However, only few cases have been reported with IIMs as sole manifestation of GVHD. Case: 20-year-old woman received allogeneic HSCT in March 2005 with diagnosis of acute lymphoblastic leukemia from her HLA-identical sister. Preparative therapy included cyclophosphamide plus intravenous (IV) busulfan, and prophylaxis for acute GVHD consisted of cyclosporin A (CsA) and methotrexate. Two months later, the patient developed fever up to 39°C, along with muscle pain and weakness over the proximal lower extremities. Examination on admission revealed the presence of a heliotrope rash, Gottron`s papules, and severe proximal muscle weakness in the lower extremities. There was no peripheral edema, and her blood pressure values and chest and cardiac examinations were normal. The level of serum creatine phosphokinase (CPK) was markedly elevated (3022 U/L, normal range, 40 197 U/L). Antinuclear antibody was positive with a titer of 1: 320, but other autoantibodies, including rheumatoid factor and anti-Jo, were negative. There was no skin rash, jaundice, diarrhea, or other signs of acute or chronic GVHD, and no evidence of leukemia relapse or active viral, bacterial, or fungal infection. The electromyogram of lower extremities showed small-amplitude, short-duration and polyphasic action potentials, which were compatible with inflammatory myopathy. Treatment with high-dose steroids (60 mg/day) was maintained and IVIG therapy at a dose of 0.4 gm/day for 4 consecutive days was instituted. The patient responded well, with a reduction of CPK levels, and a progressive increase in muscle strength and disappearance of the skin lesions. Conclusion: To our knowledge, this is the first reported case of dermatomyositis as sole manifestation of acute GVHD that was successfully treated with IV steroid and IVIG therapy.

Abstract: 798 Poster: 705

RICKETS WITH DORFMAN-CHANARIN SYNDROME: A CASE REPORT

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Background: Dorfman-Chanarin syndrome (DCS) is a rare, autosomal recessive inherited lipid storage disease and charecterized by non bullous congenital ichthyosiform erytroderma, leucocyte vacuoles and variable. DCS comprimises variable involvement of liver, muscles, and central nervous system (CNS) due to abnormal metabolism of triglycerides. Examination of the peripheral smear for the presence of the charecteristic pathognomonic lipid inclusions in the leukocytes (Jordans anomaly) is crucial for establishing the diagnosis of DCS. The non membrane bound cytoplasmic inclusions primarily consist of neutral triglycerides. Aims: Upto date, only 32 cases of of this syndrome the DCS have been described worldwide. Therefore, we presented a DCS male with rickets. Case Report/Methods: A four years old male child of Turkish origin was born from nonconsanguineous marriage after an uncomplicated perinatal period. His sister and one of his cousins have similar generalized ichthyosis and ectropion. On physical examination, the patient had failure to thrive, diffuse erythroderma and ichthyosis with fine desquamation. The abdominal examination revealed a 5 cm hepatomegaly. Rachitic rosaries could be palpated on the chest and the wrist was enlarged. There were clinical features suggesting rickets. He was dull (IQ,70) and had mildly delayed motor function, adjustıng two years of age. Routine all hematological parameters and coagulation profile were normal. Light microscopic examination of peripheral smear revealed vacuolated in leucocytes typicals of DCS (Fig 1). Alanine/aspartate amino transferase activities were elevated (150/120 IU/L). There was low calcium (5.5 mg/dl), mild elevation of serum phoshorus (5.5 mg/dl), elevated alkaline phosphatase (1181 IU/dl) and parathyroid hormone (281 IU/L). Lipid analysis showed an increase in tryglicerides (235 mg/dl, normal: 30-86 mg/dl), and very low density lipoprotein (44.8 mg/dl, normal: 1-24 mg/dl) and a decrease high density lipoproteins (26 mg/dl, normal: 35-84 mg/dl) with normal total cholesterol. Radiography of the wrist showed cupping and fraying of distal ends of radius and ulna. His abdominal ultrasonography showed mild to moderate hepatomegaly with increased echo-genety, and abnormal electromyography was normal. Pathological electroencephalography findings originating from cerebral subcortex reported. Summary/Conclusions: Informations about this rarely seen syndrome is limited. Clinical progression in these patients changes from mild to fatal. We believe that patients with icthyosis should be evaluated in point of DCS and by increasing the reported DCS cases, pathogenesis and progression of the disease should be more clear. Leucocytes cytoplasm (neutrophil, eosinophyl, monocyte) contains optically clear vacuoles.

Abstract: 799 Poster: 706

THE EFFECTS OF BONE MARROW ASPIRATION AND BIOPSY PROCEDURES ON QTC INTERVAL AND QT INTERVAL DISPERSION IN A PATIENT WITH HEMATOLOGIC DISORDER

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Electrocardiographically, QT interval reflects the ventricular repolarisation time. Meanwhile, QT dispersion shows the instability of cardiac repolarisation. Prolongation of corrected QT (QTc) interval and the QT dispersion may cause arrhythmia and sudden death. During bone marrow aspiration and biopsy procedure, which is a frequently applied diagnostic procedure, rarely cardiovascular complications are defined. However, the literature knowledge about the sudden deaths in relation to malign arrhythmia is limited. This study aims to search the effects of bone marrow aspiration and biopsy procedures on the variables of QTc and QT dispersion. The study group included 23 patients who underwent sternal aspiration, 6 posterior spinal iliac aspiration, and 19 posterior spinal iliac biopsy procedures. Electocardiographic records (by the 12-lead ECG) were taken before and during bone marrow aspiration and biopsy procedures. There was no effect on QTc interval and QT interval dispersion during sternal aspiration, posterior spinal iliac aspiration, and posterior spinal iliac biopsy procedure

modes. This study is the first to assess the QTc interval in patients undergoing bone marrow aspiration and biopsy procedures in patients with hematologic disorder. Data obtained have supported the theory that bone marrow aspiration and biopsy procedures have no negative effects on ventricular repolarization time, and routine monitoring is unnecessary except for special circumstances (arrhythmia, pregnancy, vasoactive drug use, etc).

Abstract: 800 Poster: 707

SONOGRAPHIC EVALUATION OF SPLEEN SIZE AND PREVALENCE OF ACCESSORY SPLEEN IN HEALTHY MEN

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OBJECTIVE: It is known that the measurement of splenic length in routine clinical practice is a very good indicator of actual splenic size. Knowledge of the normal range of spleen size in the population being examined is a prerequisite. Racial differences in splenic length could result in incorrect interpretation of splenic measurment The purpose of this study was to establish the range of spleen length and to determine the prevalence of accessory spleens in healthy men. SUBJECTS AND METHODS: Healthy men 17-42 years old 2179 volunteers from the annual army Reserve Officer Training Corps training camp at Manisa were included in the study. Sonographic measurements of spleen length were performed on 2179 militarry persons. Presence of accesory spleen were obtained. In addition, the height, weight, and age of each volunteer were recorded. Using linear regression analysis relation of spleen length and body height, weight and body mass index (BMI) was evaluated. Additionally the prevalence of accessory spleen by detected on ultrasound was calculated RESULTS. The mean body height for men was 173.12 cm ± (SD) 6.56 cm, mean body weight for men was 69.08 kg ± (SD) 9.76 kg, mean BMI for men was 22.62± (SD) 2.87. Mean spleen length was 107.65 cm ± (SD) 18.44 cm. Statistically significant correlation ($p < 0.01$) between spleen lenght and body height, weight and body mass index (BMI) was not found. The prevelance of accessory spleen was determined 2.3% on ultrasound screening. CONCLUSION. Ultrasonography because of diagnostic efficiency is suggested the method of choice in diagnosis and monitoring of splenomegaly. Standards of normal spleen sizes have been developed for different area. But ultrasonography does not allow complete detection of accessory spleens

Abstract: 801 Poster: 708

PRIMARY MEDIASTINAL LARGE CELL LYMPHOMA

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Primary mediastinal B-cell lymphoma (PMBL) is a distinct lymphoma subtype among Diffuse large B-cell Lymphoma, which according to WHO classification belongs to aggressive lymphomas. PMBL is defined as a diffuse proliferation of large neoplastic lymphoid cells with primary involvement of the mediasinum and has putative thymic origin, with distinct clinical, morphologic, phenotypic and genetic features. Our case is male, 38y, at presentation with temperature (B), sweating (B), malaise, dyspnea, and symptomps and signs of superior vena cava syndrome. SR 94/110, Hb 110 g/l, Le 15,9 x 10&8313;/l, Plt 530 x 10&8313;/l. LDH 1156 mmol/l. No periferal lymphadenopathy. Initial chest X-ray showed mediastinal tumor with massive lung involvement and pleural effusion (Figure 1). Abdominal ultrasound revealed no lymphadenopathy. Bone marrow involvement was negative. According to Ann Arbor staging system it is stage IV B. Diagnostic open lung surgery was performed. Pathohystological finding was PMBL. Immunophenotype: CD 45, CD 19, CD 20, CD 79a,CD 5-,CD 23,CD 10-,CD 30(weak). According to IPI score our patient is in the group of high intermediate risk. He received R-CHOP regimen. After 8 cycles there was no big difference, so we decided to give him adjuvant radiotherapy to the tumor masses - 41.4 Gy. Reevaluation: the parameters followed were better, but a difficult task is to asses complete response when a residual mediastinal mass is present on imaging after completion of therapy. Since we have neither Gallium SPECT nor PET-FDG-Scan, we decided to give him a maintenance therapy with Rituximab 375mg in 3 months intervals (with Ig support). Follow up on a monthly basis revealed that patient is in a good general condition with respiratory failure, normal parameters, except slightly increased LDH. Evacuation of 2 l pleural effusion / intra-tumor mass liquid was performed. No malignant cells found. Patient

should be monitored very carefully. When persistent mass increases at any time, he should receive the same treatment as those in relapse, with salvage chemotherapy followed by intensification with ASCT. Figure 1. CT scan

Abstract: 802 Poster: 709

THROMBOMODULIN AND D-DIMERS IN PREECLAMPSIA AND HYPERTENSION OF PREGNANCY

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Background: Thrombomodulin is a protein secreted from the endothelial cells and is involved in cell adhesion and cell activation. Its levels are increased in cases where endothelial activation is observed. Eclampsia and pre-eclampsia is a condition where endothelial cell activation is observed during pregnancy of unknown mechanism and may be life threatening for the mother and the fetus. Aim: Early markers for the beginning and prognosis of eclampsia would be of particular importance in these cases. Methods: We studied 13 women with preeclampsia (group 1), 17 with hypertension of pregnancy (group 2), and 9 normal pregnant women (group 3). We measured Thrombomodulin and D-dimers` levels in the plasma of the above cases, in order to investigate whether these proteins would be of prognostic significance. We used ELISA (DIACLONE Reaserch) for thrombomodulin measurement and nephelometry for d-dimers` detection (VIDAS-Biomerieux). Results: The levels of thrombomodulin in group 1 were 1.70 ng/ml, 1.46ng/ml in group 2 and 6.2 ng/ml in group 3. The levels of d-dimers were 2896 ng/ml in group 1, 2164 in group 2, and 2025 in group 3. We found non-significant difference between the levels of thrombomodulin and d-dimers between the 3 groups (p=0.3 and 0.7 respectively). There was positive correlation between the levels of thrombomodulin and d-dimers in the studied population (r=0.3642). Conclusions: There were increased levels of d-dimers and decreased levels of thrombomodulin in the pregnant women compared to nonpregnant. There was no significant difference between the three groups of pregnant women. Furthermore, there was positive correlation between thrombomodulin and d-dimers. Further investigation is needed to see the significance of these findings.

Abstract: 803 Poster: 710

EVALUATION OF CELL CULTURE EXPERIMENTS IN DETERMINATION OF MUSTARD GAS\`S MECHANISM AND ITS ANTIDOTES

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Sulfur Mustard (SM) causes systemic and local damages and can eventually lead to death. Many studies are being done to define mustard gas toxicity mechanism and to find an efficient way to decrease its side effects. Most of these studies are now being done in cell cultures. Therefore, choosing a suitable culture is necessary to get correct results. New theories about Mustard gas mechanism of action such as poly ADP ribose polymerase, thiol-calcium and lipid peroxidation theories are common in the fact that sulfur mustard increases oxidants agents and generates free radicals. Therefore, antioxidants are the most used antidotes against mustard gas. One important point to consider is the effects of exogenous agents. Their positive or negative effects cause problems in the evaluation of results. RPMI 1640, a cell culture medium, contains antioxidants such as glutathione, systemic and niacinamide, so it makes problems in the evaluation of SM toxicity mechanism and its antidotes. Furthermore, gentamicine,a cell culture antibiotic, generates ORS and has effects on musfard gas mechanism, so it is not recommended. Since HBSS is free of interfering agents, it is a suitable medium to preserve living cells like lymphocytes.

Abstract: 804 Poster: 711

THE USE OF SUBJECTIVE GLOBAL ASSESSMENT IN DETERMINING THE NUTRITIONAL STATUS OF HEMATOLOGIC MALIGNANCIES

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Background and Aims: The degree of malnutrition is one of the most important criteria in patients with hematological malignancies that effect both survival and the quality of life. Whether during the process of diagnosis or after initiation of treatment, hospitalized patients become deprived of good nutrition for a various number of reasons. As a result their nutritional status fail to keep up with the already increased catabolic rate, causing severe results such as progressive fatigue, electrolyte imbalances, poor wound-healing and immune suppression. Determining which patients are under nutritional risk could gain importance especially in hematological malignancies in which diagnosis and treatment should be planned dynamically. For this purpose the use of Subjective Global Assessment (SGA) could be convenient, a method that refers to the overall evaluation of a patient by an experienced dietician that correlates the subjective and objective aspects of the patient`s medical history and physical examination. Methods: We used the SGA method to determine the nutritional status and malnutrition risk of 70 patients randomly selected among all hematological malignancies admitted to Ibn-i Sina Hospital Hematology Service during the period April 2003 - June 2005. Patient demographics are shown in Table1. Review of the patients` history by the Nutrition Committee included an assessment of weight and weight change, dietary intake, gastrointestinal symptoms, disease state, physical activity and the presence of fever and stress. The patients were classified as well nourished (A), mild-to-moderately malnourished (B), or severely malnourished (C). The C-reactive protein (CRP), prealbumine and transferrine levels at the time of the evaluation were also recorded. Results: After evaluation 30 (50.8%) patients were distinguished as A, 22 (37.3%) as B and 7 (11.9%) as C. When status A patients were compared to status B+C according to their diagnosis, stage of disease and whether they were in relapse or remission, no significant difference was found. The prealbumine levels were found to be significantly different between the two groups, while CRP and transferrine levels remained insignificant. Conclusions: The relationship between the type and stage of the hematological malignancy and the patient`s SGA score thus his malnutrition risk could be better understood by increasing the number of cases and prolonging the follow-up of the study. This study showed us how we could be informed of our patients` nutritional status by following the laboratory parameters closely.

Abstract: 805 Poster: 712

SUBCUTANEOUS INFILTRATION AND MESENTERIC PANNICULITIS IN THE COURSE OF ERDHEIM CHESTER DISEASE

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Erdheim-Chester disease is a unique pathologic and radiographic entity characterized by bilateral symmetric sclerosis of the diametaphyseal regions of long bones and infiltration of foamy lipid-laden histiocytes in involved organ and tissues. It is a rare non-Langerhans Cell histiocytic disease of unknown etiology that is characterized pathologically by xanthogranulomatous infiltrates of multiple organs. It has benign course unless there is organ infiltration. We hereby present a patient in her early sixties with bilateral mild knee and leg pain. Radiological examinations showed typical bilateral symmetric medullary sclerosis at the diametaphyseal portions of long bones of the lower extremity. The diagnosis was confirmed by a bone biopsy, and bisphosphonate (alendronate) was started as first line treatment. Pain on the involved sites was palliated by this treatment, but the patient was admitted due to abdominal pain and subcutaneous nodular lesions on pretibial region in both sides. Abdominal CT revealed the diagnosis of mesenteric panniculitis. Biopsy was performed for subcutaneous nodules and the diagnosis was confirmed as Erdheim Chester disease in soft tissue. Radiotherapy was planned directed to bone lesions. Patient will be evaluated for further treatment options including systemic chemotherapy according to clinical course of the disease. Although, Erdheim Chester disease is clinically benign disorder, involvement of visceral organs and progressive disease should be carefully evaluated for aggressive treatment modalities. And also, further studies with long-term follow-up and ultrastructural evaluation are needed.

Abstract: 806 Poster: 713

FACTOR VIII,VON WILLEBRAND FACTOR IN ISCHAEMIC HEART

DISEASE,CORRELATION WITH LIFESTYLE

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Alteration in the coagulation system and in platelet aggregability are important considerations in the development of atherosclerotic cardiovascular disease. The aim of the study is to detect levels of von Willebrand factor antigen (vWF Ag) and coagulation factor VIII (FVIII) in patients with IHD and their role in the pathogenesis. Patients and methods: The study included fourty (40) patients with IHD and twenty (20) healthy subjects served as a control group. The patients were divided into two groups: Group I: twenty (20) patients with acute myocardial infarction (AMI) and Group II: twenty (20) patients with angina (eleven with unstable angina and nine stable angina. Patients and controls were subjected to thorough clinical examination, electrocardiogram, CBC, CPK, aPTT, PT, PC, FVIII, vWF, fibrinogen,platelet aggregation and lipogram. The relation between FVIII, vWF, fibrinogen and platelet aggregation with lifestyle factors, including body mass index(BMI),smoking and type of work had been studied. Results: vWF Ag levels showed significantly higher levels in patients with IHD and AMI than in controls ($p<0.001$ and $p<0.01$, respectively). Platelet aggregation was significantly increased in patients with AMI ($P < 0.001$) and patients with angina ($p <0.02$) when compared to that in control group. Fibrinogen levels showed higher levels in 27.5% of the total number of patients, the mean value of vWF Ag, FVIII and platelet aggregation showed higher levels with the increase in BMI, number of cigarettes smoked/day and female gender. Although vWF Ag and FVIII levels were higher in patients who were not using prescribed medicine than those who were, yet it did not rise to statistical significance. Conclusion: the higher levels of vWFAg, FVIII and platelet aggregation suggested their role in the pathogenesis and can be used as markers for occurrence of IHD.Lifestyle factors in patients with IHD causing changes in haemostatic variables could be considered risk predictors for cardiovascular events. Lifestyle modification may decrease thrombotic tendency and increase ability of blood to flow.

Abstract: 807 Poster: 714

PAPILLARY THYROID CARCINOMA

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Thyroid cancers are quite rare, accounting for only 1.5% of all cancers in adults and less than 5% of all cancers in children. The annual incidence of thyroid cancer varies worldwide/ from 0.5 to 10 per 100,000 population. Of all thyroid cancers, 74-80% of cases are papillary cancer. History of exposure of the head and neck to x-ray beams, especially during childhood, has been recognized as an important contributing factor for the development of thyroid cancer. In contrast to other cancers, thyroid cancer almost always is curable. Mean survival rate after 10 years is greater than 90% and is 100% in very young patients with minimal non-metastatic disease. No prospective clinical trials have clearly determined the "best treatment" of patients with papillary cancer. Still, the treatment is controversial especially in children. This paper is a case presentation of a 5 years old girl had papillary Thyroid carcinoma and literature review.

Abstract: 808 Poster: 715

EFFECT OF FLUVASTATIN ON SERUM MYELOPEROXIDASE LEVEL IN PATIENTS WITH DYSLIPIDEMIA

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Background: Statins exert favorable effects on cholesterol metabolism but may also possess antioxidant and anti-inflammatory effects. Myeloperoxidase (MPO) and its oxidant products have been shown to be related with endothelial dysfunction and increased risk of coronary events. Thus, we investigate whether statins have an effect on serum MPO. Methods: 85 patients were enrolled who had an indication of statin therapy according to the National Cholesterol Education Program, Adult Treatment Panel III guideline. Patients were put on fluvastatin XL 80 mg/gün p.o. therapy. Baseline and 3rd month`s MPO levels were determined by ELISA. Results: Patients

mean age was 53 years and 42% were males. Although serum MPO levels were reduced in 47 (55%) patients at 3rd month, mean MPO levels were not different from baseline (p>0.05). Conclusions: These findings suggest that the antioxidant effect of fluvastatin XL may not be related with myeloperoxidase.

Abstract: 809 Poster: 716

CLINICO-HEMATOLOGIC AND PATHOLOGIC PROFILE OF ADULT FILIPINO PANCYTOPENIC PATIENTS

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BACKGROUND: Pancytopenia may be found in various disorders which primarily or secondarily affect the hematopoietic function of the bone marrow. The International Agranulocytosis and Aplastic anemia study showed aplastic anemia as the commonest cause of pancytopenia. Studies from other countries in Asia showed megaloblastic and aplastic anemias as the leading causes. There has been no systematic study on the clinical spectrum of pancytopenia in the Philippines so far. AIMS: This study is mainly aimed at determining the common causes of pancytopenia among adult Filipinos. It is also our objective to determine the demographic, clinical, hematologic and pathologic profile of adult Filipino pancytopenics. METHODS: This is a 10-month prospective observational (descriptive) study conducted simultaneously in three tertiary medical centers in the Philippines. Inclusion criteria are: (1) age at least 19 years, (2) hemoglobin (hgb) <110mg/dl for premenopausal females or <120 mg/dl for males and postmenopausal females, leukocytes <5,000/ul, and platelets <150,000/ul, (3) of Filipino citizenship and nationality, and (4) written consent. Patients were excluded if pancytopenia has already been previously worked up with diagnosis known. Peripheral blood smears, bone biopsy and marrow aspiration were performed and processed uniformly. Peripheral blood smears were examined by a single hematologist while bone biopsy and marrow aspirates were examined by a single hematopathologist. RESULTS: Twenty-two patients qualified and completed the study. Four of the patients were initially admitted for symptoms attributed to pneumonia while the rest of the patients had an initial impression of aplastic anemia. Results showed that pancytopenia occurs at any age group (mean 48.8 years) with no sex preponderance. There was no occupational association noted. Body weakness was present in all cases and was likewise the most common presenting complaint. Other common symptoms were bleeding and fever. Symptoms were noted for less than a month in the majority (45%). Pallor was a universal finding. Mean values for the blood cell components are: hgb 61mg/dl, platelets 64,545/ul and leukocytes 3,280/ul. Hypcohromia was seen in all peripheral blood smears. More than half had bone marrow hypocellularity largely associated with predominance of fat vacuoles with relative lymphocytosis (54.5%) while 23% had marrow hypercellularity with varying associated features. Histopathologic and clinical correlation revealed aplastic anemia (54%) as the most common cause of pancytopenia. Other causes are acute myelogenous leukemia (AML) 9%, immune thrombocytopenic purpura (ITP) 9%, myelodysplastic syndrome (MDS) 9%, acute lymphocytic leukemia, malaria, drug-induced pancytopenia and megaloblastic anemia (4.75% each) as the underlying cause of pancytopenia. CONCLUSION: Pancytopenia is a feature common to many illnesses and the distinction is more difficult in certain hematologic disorders. Aplastic anemia is the main cause of pancytopenia among adult Filipinos. Other leading causes are AML, ITP and MDS. Peripheral pancytopenia warrants careful and systematic investigation. In most cases, bone marrow aspiration as well as bone biopsy must be done with the results correlated clinically to make an accurate diagnosis.

Abstract: 810 Poster: 717

RISING NUMBERS OF ACUTE LEUKAEMIA AND CHRONIC MYELOID LEUKAEMIA SEEN IN ACCRA, GHANA

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Background: A previous study in the year 2000 had shown a gradual increase in acute leukemia over a period of 4 years. The data showed an increase from 25 cases in the year 1996 to 39 in the year 1999. Chronic leukemia was not examined. Information on age especially was incomplete with over a third of the cases having no age stated. An attempt was made to improve docu-

mentation and since 2003 almost all the cases have been properly documented. The apparent increase in the number of cases seen at clinics at the Korle-Bu Teaching Hospital, the main referral centre in Ghana, continued and hence this study. Aim: To document the numbers age and sex characteristics of leukemia seen at the KBTH between 1st January 2003 and 30th April 2005, and to confirm any apparent increases. Methods: Records of bone marrow reports were examined. All new cases with diagnosis of leukemia made by the hematologist were included. Marrows done to assess remission status were excluded. Name, sex, age and diagnosis were recorded. The data was analyzed by tallying into year of diagnosis age group and sex. Results: Over the 28 month period, there were a total of 220 cases in the following order of frequency; Acute Lymphoblastic Leukemia (ALL) 74, Chronic myeloid leukemia (CML) 55, Chronic lymphoid leukemia (CLL) 51, and Acute Myeloid leukemia (AML) 40. Using the yearly numbers for 2003, 2004 and projected figures for 2005, the rise in numbers was most consistent with ALL 25 to 34 to 45, steepest with AML 15 to 16 to 27, and CML 18 to 25 to 36 and nonexistent with CLL 18 to 25 to 21 respectively. The chances of developing acute leukemia were more than 3 times higher in those aged 34 and below as compared to older subjects. ALL showed a cluster below 20 years, whilst AML was uniformly spread. There was a preponderance of females in CLL, CML and AML which did not achieve statistical significance ($p>0.05$). ALL was significantly commoner in males ($p<0.05$). There was no case of CLL below the age of 35 years. Summary: The reportage of leukemia is on the increase in the main referral centre in Ghana. The reasons for this may be in environmental degradation and an increase in the indiscriminate use of potentially carcinogenic substances in the agriculture, food and other industry. Awareness may also be a factor. A more comprehensive study looking also at potential leukemogenic enhancing agents is recommended, in order to curb the rise.

Abstract: 811 Poster: 718

THE EFFECTS OF CHRONIC CADMIUM TOXICITY ON HEMOSTATIC SYSTEM

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Cadmium (Cd), a highly toxic heavy metal, is distributed widely in the general environment. The characteristic clinical manifestations of chronic Cd intoxication include renal proximal tubular dysfunction, osteomalacia, and anemia. Accumulating evidence suggests the cadmium toxicity may also affect various organs such as liver, lung, testis, and hematopoietic system. The aim of this study was to determine the effect of chronic cadmium exposure to the anticoagulant system in rats. Forty five adult Wistar albino rats were randomly allocated into two groups. In the cadmium group; the animals were treated for 4 weeks with 15 ppm CdCl2. Prothrombin time, activated partial thromboplastin time, plasma protein C and antithrombin III levels were determined in the rats. Protein C and antithrombin III decreased to statistically significantly lower levels in rats plasma after cadmium exposure than were found in the control group. Results also show that cadmium exposure shortened prothrombin time and activated partial thromboplastin time in rats. We conclude that exposure to low levels of cadmium is associated with an increased risk of thrombosis.

Abstract: 812 Poster: 719

TWO CASES OF CHLOROMA THAT PRESENTED WITH NEUROLOGICAL SIGNS WITHOUT BONE MARROW INVOLVEMENT: INITIALLY THOUGHT TO BE LYMPHOMA

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Granulocytic sarcomas (chloroma) are extramedullary tumours composed of myeloid precursors. They occur most commonly in the context of AML, myeloproliferative disorders;CML or myelodysplastic disorders, and rarely unaccompanied by other haematological disorders. The first case is a 43-year-old lady who presented with small bowel obstruction for which she underwent a small bowel resection. Initial histopathology revealed NHL for which she received CHOP with no response. Further review of the histopathology revealed that the specimen was strongly positive for CD15, CD34, CD43, CD45, CD68 and lysozyme but CD20 negative, suggestive of chloroma. Bone marrow examination was normal. This patient re-presented with right 3rd cranial

nerve palsy. MRI brain scan revealed bilateral intra-cisternal rd cranial nerve masses. Cytospin and immunophenotyping of CSF fluid confirmed myeloid blasts. Bone marrow examination, once again, revealed no leukaemic involvement. She received six courses of intrathecal hydrocortisone and cytarabine followed by two courses of mitoxantrone, amsacrine and etoposide. MRI brain scan then revealed complete resolution of the bilateral rd nerve chloromas. The second case was a 62-year-old female who presented with right leg stiffness and swelling. Examination revealed a large right groin firm mass, decreased power and reflexes in the right leg. Histology report showed sheets and nests of regular large cells, no clefts, no giant cells, provisionally thought to be NHL. Further immunostains were positive for CD34, CD43, CD45, CD68 and lysozyme but CD20 negative, suggestive of chloroma. Bone marrow examination was normal except for cytogenetics which revealed (9,22)q34q11 indicating CML transformed locally to a chloroma. This patient was treated with clofarabine and daunorubicin which has lead to complete resolution of the mass, as well as imitinab. The diagnosis of chloromas is not infrequently misdiagnosed histopathologically as NHL. Primary granulocytic sarcoma is rare, and poses a diagnostic pitfall for both pathologists and haematologists. We will review the literature, and discuss recent insights into the basic biological properties of these rare tumours as well as treatment options.

Abstract: 813 Poster: 720

Â-THALASSEMIA MAJOR AND ABNORMAL GLUCOSE METABOLISM

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SUMMARY: Aim: The life expectancy in patients with Â-thalassemia major has extended considerably after the introduction of hypertransfusion protocols. However, this resulted in an increase of endocrine complications such as glucose intolerance and insulin dependent diabetes. The aim of the study was to evaluate the incidence of insulin dependent diabetes mellitus (IDDM), impaired glucose tolerance (IGT) and associated factors in transfusion dependent Â-thalassemia major patients who had been observed in our hospital. Methods: 33 patients with thalassemia major were chosen for this evalution. Mean age was 10,8±3,2. control group consisted of 15 healthy children with mean age 0,8±2,8. Oral glucose tolerance test was Canpolat ve ark. applied both for the study group and healthy controls. Blood samples were taken at 0, 60 and 120 minutes and the results were interpreted according to the criteria published by World Health Organisation. The glucose values of thalassemia group and healthy controls were evaluated with Student-t statistical analysis. Patient with normal and abnormal glucose metabolism were compared in terms of age, ferritin, ALT, the number of total transfusion with Mann-Whitney U test. Results: The percentage of IDDM and IGT was determined as 6,06% and 12,12%, respectively. The mean age, number of total transfusion, maximum feritin level and ALT levels of the patients with abnormal glucose metabolism was 12,8±3,9, 222±86 U, 4583±1116 mg/dl and 55±84 U/L, respectively. ALT and maximum ferritin levels were found significantly high in thalassemic patients with abnormal glucose metabolism. HbsAg was found positive in all of the patients with one HBV DNA seropositivity. Conclusion: Thalassemic patients should be followed up closely for abnormal glucose metabolism. It is recommended that glucose metabolism should be checked earlier in uncompliant patients and patients with HBV infection.

Abstract: 814 Poster: 721

ADVANCES IN MOLECULAR HEMATOLOGY

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Not so long ago,meny of blood diseases were almost always deadly. Today improvements in diagnosis and treatment have dramatically increased survival rats for these diseases. The laboratory plays a crucial role in diagnosis and therapy, and new molecular technologies have greatly improved patient care. Molecular diagnostic techniques the may be employed include;southern blot analysis and the polymerase chain reaction(PCR),for the analysis of DNA, and reverse transcriptase PCR(RT-PCR) for the investigation of RNA. Peripheral blood cells are used for molecular genetic analysis with three main aims. Firstly, to show clonality(and, by implication, neoplasia) by demonstration of clonal rearrang-

ment of T-cell receptor or immunoglobin genes. Secondly, to demonstrate the presence of various oncogene rearrengments that are strongly associated with specific hematological neoplasms. Thirdly, to demostrate inherited abnormalities of genes, e.g. a and B globin genes, that cause hematological abnormalities.This article provides a brief summary of the role of new molecular technologies in use for diagnosis, Prognosis, and therapeutic of blood diseases. Because of its high sensivity,PCR has become useful for identifying small numbers of residual leukemia or lymphoma cells at times when blood and bone marrow appear histological normal. PCR can detect the presence of one abnormal cell among a background of 1000 to 1000,000 normal cells.

Abstract: 815 Poster: 722

DIAGNOSTIC AND THERAPEUTIC ADVANCES IN ACUTE LEUKEMIAS

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Until recent years, acute leukemias;acute lymphoblastic leulemia (ALL),acute myeloid leukemia(AML), acute biphenotypic leukemia, were almost always deadly. Today improvements in diagnosis and treatment have dramatically increased survival rates for these diseases. Dispit the increased incidence of acute leukemias in some countries due to atomic explusion), mortality rates for these diseases have remained relatively constant as the result of improvements in therapy. The laboratory plays a crucial role in diagnosis and therapy, and new molecular technologies have greatly improved patient care. Currently, diagnosis of leukemias and lymphomas is based on a combination of methos; clinical feature, microscopic examination of blood, bone marrow,, cytochemical and immunohistochemical staining of specimens, immunophenotyping by flow cytometry, cytogenetics, and molecular analysis, ultrastructural examination fluorescent in situ hybridization (FISH). The combination of all of these methods allows the identification and subclassification of leukemias. Such subclassification is important because the specific-dignosis guides clinicians in the selection of optimal therapy and provides prognostic information. In recent years important advences have been achived in the treatment of patients with acute myeloid leukemia. However, most of these advences have applied to young AML patients, while elderly AML patients continue to face a dismal outcome.Several studies have attempted to explain the worse prognosis in elderly AML patients on biological grounds. Treatment in children with ALL by current therapies is one of greast achivements of modern oncology. Complete remission (CR) rates in adults with ALL are 63%-86%.

Abstract: 816 Poster: 723

DNA SEQUENCING OF B-THALASSAEMIA MUTATIONS IN EGYPT

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ß-Thalassaemia refers to a group of inherited disorders characterized by a reduced of ß-globin chains, affecting around 7 % of the world`s population being prevalent in tropical and subtropical regions including the Mediterranean, Southeast Asia and Southern China. The aim of this study was to characterize ß-thalassae-mia mutations, both common as well as rare among Egyptian ß-thalassaemia children. Incorporation of DNA sequencing in Egypt for the first time enable the characterization of mutations not detected by mutation specific detection procedures was a prime concern of this work. An attempt to understand the ß-thalassaemia spectrum in Egypt to be the base of carrier screening and prenatal diagnosis programs is an important goal of this study. Ninety five subjects were studied, gene mutations by allele specific priming (PCR-ARMS). Uncharacterized samples were subjected to automated fluorescent direct DNA sequencing of PCR products.The commonest ß-thalassaemia mutation among studied cases was IVSI-6 mutation accounting for 36.6% followed by the IVSI-110 mutation which accounted for 25.8%,then the IVSI-1 mutation 19%.Less common mutation detected were -87accounting for 3.2%, the IVSII-745 accounting for 6.4%, the Hb Knossos(CD27) mutations each accounting for 3.2%, IVSII-848 was 1.6%.The least common mutations were CD5, CD39,CD37 each accounting for 1% and the very rare mutation CD15 accounting for 0.5%,two sickle/ß-thalassaemia (1%).In conclusion the use of PCR amplification and direct sequencing have permitted the accurate characterization for unidentified alleles and successfully solved 100% of the examined samples.

Abstract: 817 Poster: 724

BONE MARROW ANGIOGENESIS IN CML: ITS CORRELATION WITH PROGRESSION OF THE DISEASE

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Bone marrow angiogenesis has been reported to be increased in several haematological malignancies. Although the clinical significance of this phenomenon in most haematologic malignancies is presently an unresolved issue, there is indisputable evidence indirectly implicating bone marrow angiogenesis in the pathophysiology and course of some of them. The present study was designed to explore the possible role of angiogenesis in the evolution of aggressive phase in chronic myeloid leukaemia (CML). We studied the changes of Micro Vessel Density (MVD) in 55 patients of CML in different phases of the disease (chronic - 15, accelerated - 15, blastic - 15, remission - 10). In addition 5 control cases from subjects with no evidence of any marrow disease were evaluated. Bone marrow trephine biopsy sections were immunostained with CD 34 and developed by indirect immuno peroxidase method. Overall, the group of chronic phase CML had higher MVD and more branching micro vessels than controls. Blastic phase was characterized with increased number of micro vessels with rounder shape and smaller caliber than in chronic phase. However, there was no increase in MVD or any change in vascular pattern in cases of CML in accelerated phase. Ten cases of CML in remission had comparable MVD and vascular pattern as in CML in chronic phase.

Abstract: 818 Poster: 725

METHOTREXATE SERUM AND CEREBROSPINAL FLUID CONCENTRATIONS AFTER DIFFERENT HIGHDOSES OF METHOTREXATE INFUSIONS

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Background: Adequate dose intensity is of major importance for prevention of central nervous system (CNS) involvement in acute lymphoblastic leukemia (ALL). Minimum cytotoxically effective concentrations of methotrexate (MTX) are defined as 16µmol/L in serum and 0.5-1µmol/L in cerebrospinal fluid (CSF). Whereas administration of the dose of MTX to provide these cytotoxic levels especially in CSF has not been well established and it has been used in 1-5 g/m2 doses in variable chemotherapy schedules in ALL. Purpose: We aimed to find out the most cytotoxically effective dose to provide adequate concentrations in the serum and CSF. Material Method: We measured steady state concentrations of MTX in serum and in CSF in three group of patients in whom MTX was administered 2g/m2, 3g/m2 and 5g/m2 as 24 hour infusion. There were 15 patients in each group and they have been receiving high dose MTX over 24 hours as a part of their therapy schedules. Blood and CSF samples were collected from all the patients at the end of the 24 hour infusion of MTX, prior to the triple intrathecal treatment. Methotrexate concentrations were determined by the fluorescence polarization immunuassay. Results: Cytotoxically effective MTX concentrations in serum (over 16µmol/L) were achived in 93.4% of patients in each group whereas cytotoxic CSF concentrations (over 1µmol/L) could be achieved in 40.3%, in 43.6% and in 87% of the patients in the first, second and third groups respectively after the administration of MTX over 24 hour. Conclusion: Administration of MTX as a dose of minimum 5g/m2 seems to be inevitable in the patients with ALL for prevention of CNS involvement.

Abstract: 819 Poster: 726

CAN MYCOPLASMA-MEDIATED ONCOGENESIS BE RESPONSIBLE FOR FORMATION OF MULTIPLE MYELOMA AND ACUTE LYMPHOBLASTIC LEUKEMIA?

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Objectives: To investigate the association between Mycoplasma sp. infection and different hematological malignancies. Methods: DNAs isolated from paraffin embedded blocks. Acute lymphoblastic leukemia (ALL)(29), multiple myeloma (MM)(42), Hodgkin lymphoma (HL)(17), non-Hodgkin lymphoma (NHL)(25) and acute myelogenous leukemia (AML)(31) bone marrow biopsy or tumor tissue samples from 144 patients with different hematological malignancies and 40 healthy controls were studied. Molecular DNA analysis was done after nested polymerase chain reaction performed in two steps with seven primers (four outer and three inner) that can recognize at least 15 different Mycoplasma sp. Results: Mycoplasma sp. DNA was detected with the ratios of 28% (8/29) in ALL, 40% (17/42) in MM, 0% (0/17) in HL(0/17), 16% (4/25) in NHL, 6% (2/31) in AML and 5% (2/40) in healthy control group with molecular analysis. These results were compared with the clinical parameters of the patients. Beta-2 microglobulin levels which is an important prognostic factor for MM patients, were significantly higher in the patients who had mycoplasma DNA compared to the patients who didn`t have (p=0.039).The frequency of Mycoplasma sp. DNA existence in ALL and MM groups were significantly higher compared to the control group (p=0.009 and 0.000 respectively). Conclusions. The relationship between mycoplasma infection and MM and ALL has been investigated for the first time, and a significantly high existence of Mycoplasma sp. DNA was found in the tissues of patients with ALL and MM compared with that found in a healthy control group. This suggests that mycoplasma-mediated multistage carcinogenesis may play a role in the development of ALL and MM. Confirmation of our results by other investigators may help to high-light the role of mycoplasma in the development of cancer. These results should not be exaggerated, but the presence of Mycoplasma sp. infection should be investigated further in patients with MM and ALL. This work supported by the Turkish Scientific and Technical Research Council (TUBITAK) Research Fund No: SBAG-AYD-409.

Abstract: 820 Poster: 727

EVALUATION OF NURSE CARE IN ORAL LESSIONS IN CANCER PATIENTS

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Introduction: Oral lessions are among the most frequent and troublesome complications in cancer treatment which effects quality of life. Oral care is very important in preventing oral lesions in cancer patients. This is a descriptive survey conducted in hematological cancer patients to evaluate the nurse care in oral lesions. Methods: This survey is conducted in Ankara University Medical School Ibn-i Sina Hospital Department of Hematology. 32 patients received the questionarre designed by the investigators. Percentages and Chi-square test was used for evaluation.Results: 40.6% of the patients graduated from primary schooland 9.4% graduated from university. 87.5% was married and the diagnoses were 37.5% AML, 15.6%ALL 12.5% MM and 9.4% Aplastic anemia. They received differents therapies according to their underlying dieases. 40.6% developed oral lesions and 93.8% had education related to oral care. 96.9% received daily oral care and follow-up. Among those patients, 34.5% had pain related to oral lesions and 40.6% could not receive oral food. Development of oral lesions, inability to feed orally and pain was compared according to their level of education and receiving information about oral care. No difference could be found among the groups($p>0.05$). All patients were satisified with the oral care and follow-up by the nurses.

Abstract: 821 Poster: 728

THE RELATIONSHIP BETWEEN THE TREATMENT AND MUCOSITIS IN HEMATOLOGY PATIENTS

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Introduction: Mucositis is the damage of mucosal membranes related mainly to chemo or radiotherapy in hematological patients. Methods: This study is conducted in Ankara University Medical School, Ibn-i Sina Hospital inpatient and stem cell transplantation units between Jan 2004- Dec 2004. 48 patients are observed with a query form and percentages, chi square test and Mann-Whitney tests are used for evaluation. Results: Patient group consisted of 51.2% women and 48.8% men.

The diagnoses were 47.9% AML, 16.7% ALL.14.5% were followed in the stem cell transplantation unit. 97.9% of the patients were using mouth washes , 64.6% were teethbrushing, 37.5% were receiving G-CSF/ GM-CSF, 43.8% received consolidation and 33.3% received induciton therapies. Mean age was 38 years. There were 80% mucositis in women and 65.2% mocositis in men.

Abstract: 822 Poster: 729

THE THERAPEUTIC REACTIVATION OF FETAL HEMOGLOBIN BY HYDROXUREA IN PATIENTS WITH ß-THA-LASSEMIA/HBE DISEASE

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Background: Patients with severe inherited disorders of ß-globin chain structure or synthesis, in particular sickle cell disease (SCD) and ß-thalassemia, may have milder illness if they produce unusually high levels of fetal hemoglobin (HbF)1. Hydroxyurea (HU) is one of several agents that has been shown to enhance HbF levels in patients with SCD2 and may be useful as a therapy for ß-thalassemia. However, limited information exists on the effects of HU in patients with thalassemia. The aim of this study was to analyze the effect of HU on the hematological profile and clinical manifestations in ß-thalassemia patients. Methods. HU was administered to 10 patients with ß-thalassemia/HbE, including 5 patients who has been splenectomized. These patients were treated with escalating doses (final range, 15 to 20 mg/kg/d) for 2 years. HU was started at a dose of 500 mg daily, and if there was no toxicity, the dose was increased to a maximal total dose of 2 g daily and continued for 24 months. The HbF, total Hb, MCV, MCH, serum ferritin, and serum lac-tate dehydrogenase (LDH) levels were evaluated before and during treatment. Results. Almost all patients responded with an increase of 15 to 18% in HbF levels, from a median (range) of 14.2% (2.5 - 61.3) to 33.8% (3.4 - 80.3), 42.5% (34.2 - 72.3) and 39.8% (39.4 - 51.4; $p < 0.05$) at 6 months, 18 months and 24 months post-HU, respectively. The increment in total Hb level began one month post-HU, peaked at 6 months and thereafter started to progressively decline to the baseline level (increment in total Hb; 1.1 g/dL [0.5 - 4.5], 1.2 g/dL [0 - 2.8; $p < 0.05$], 0.6 g/dL [0.1 - 0.8] at 1, 6, and 24 months, respectively). MCV and MCH started to increase in the first month post-HU with a maximum increase at 3 to 6 months of HU therapy ($p < 0.05$). Response to HU was also shown by a reduction in serum ferritin, serum LDH and splenomegaly. Apart from mild leukopenia and oral ulcers that resolved upon dose reduction of HU, no significant toxicity was noted. Conclusion. We conclude that increased HbF production in ß-thalassemia/HbE patients, with an improvement in erythropoiesis, can be achieved using HU with minimal toxicity. This beneficial effect of HU in this population would need to be confirmed in larger clinical trials.

Abstract: 823 Poster: 730

THE PREVALENCE OF CYTOPENIA IN MEGALOBLASTIC ANEMIA

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Megaloblastic anemia presents itself with various clinical features. Although acute pancytopenia cases with megaloblastic changes occurring due to co-trimoxazole or arsenic were reported before, severe trombocytopenia may be detected especially in intensive care unit patients with acute folic acid deficiency. The case of pancytopenia caused by folic acid and vitamin B12 deficiency in a pregnant woman has also been reported. Retrospectively, we observed the patients in our clinic who had been diagnosed with megaloblastic anemia the presence of cytopenia is significant. We studied 44 megaloblastic anemia diagnosed patients without a history of pregnancy, co-trimoxazol treatment or arsenic and anesthetic ingestion between May1998-May 2005. We performed esophagogastroduedoscopy to all patients and we studied anti parietal /anti IF/anti intrinsic Ab in blood samples and found atrophic gastritis in 72%. and anti parietal Ab 89 %. The age characteristics were shown in the table below (Table 1). 52.3 % patients were male, 47.7 % were female, mean age was 58.54 ± 13,38 (range 24-75) . 30 % of patients were in 60-69 age range. Upon admittance 56,8 % of the patients had leukopenia and 65,9 % had thrombocytopenia. There has not been a relation between leukopenia (Ki-Kare: 6,980, p: 0,222) and thrombocytopenia (Ki-Kare: 5,5 026, p: 0, 358) when the patients ages are considered. Admitting leukocyte and thrombocyte levels of

the patients reached their normal values in an average of three weeks with vitamin B12 therapy. Such a case of high prevalence of cytopenia in megaloblastic anemia has not been reported before in the studies. The high cytopenia levels that we have found may be caused due to late admittance to the hospital or it may as well be a local situation in our country.

Abstract: 824 Poster: 731

HIGH DOSE METHYLPREDNISOLONE THERAPY BEFORE SPLENECTOMY IN IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Splenectomy is the only curative therapy for most chronic ITP cases. Corticosteroids have been used as a standard therapy for the past 50 years, but refractory or relapsed cases are common and remission is often temporary. In most cases, splenectomy is endicated for relapsed or refractory ITP. In order to prepaire for the splenectomy, safe platelet count is important and must be elevated before the operation to avoid bleeding disorders. Intravenous immunoglobulins may be added, yet it is not an affordable therapy. We have reported 35 ITP cases in which a high dose corticosteroid therapy have been applied and endicated for splenectomy between May 1999-January 2003.Clinical features, the beginning and the final platelet counts and side effects of the therapy are shown in the tables.T test and multivariate test chi-square were applied for the parameters and it has been found statistically of value. In most of the cases the platelet counts were above 30.000/mm3 in the third, 60.000/mm3 in the fifth, 90.000/mm3 in the seventh and 100.000/mm3 in the tenth day. Consequently, we have reported that high-dose methylprednisolone therapy increases the platelet counts rapidly and has less side effects.

Abstract: 825 Poster: 732

INCIDENCE OF HEPATITIS C AND HEPATITIS B VIRUS IN HAEMATOLOGIC MALIGNENCIES

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Cancerogenesis is a multisystem case that contains genetical, environmental and infectious causes. Especially in B cell lymphoproliferative disorders Hepatit C Virus has been found significantly overrepresented, it is considered that a viral cause may alter the proliferation of B cells. Therefore HCV and HBV markers have been investigated in recently diagnosed hematologic malignencies admitted to our clinic between the years 1999-2004. A total sum of 118 patients were included. The mean age was 53.73 ± 14.44 (range 15-80 years) and 58.5 % of the patients were male whereas 41.5 % were female. Disorders n % NHL 55 46.6 CLL 21 17.8 HL 17 14.4 CML 15 12.7 AML 5 4.2 MDS (RAEB) 2 1.7 Multipl Myeloma 2 1.7 Hairy Cell L. 1 .8 Total 118 100.0 NHL: Non - Hodgkin Lymphoma. CLL: Chronic Lymphoid Leukemia. HL: Hodgkin lymphoma. CML: Chronic Myelogenous Leukemia. AML: Acute Myelogenous Leukemia. MDS: Myelodysplastic Syndromes (Refractory anemia with excess blasts) All markers (HepB) Any marker pozitive Disorders negative (%) (HepB) (%) Total (%) AML 2 (40,0) 3 (60,0) 5 (100,0) CLL 10 (47,6) 11 (52,4) 21 (100,0) MDS (RAEB) 1 (50,0) 1 (50,0) 2 (100,0) Multiplmyeloma 1 (50,0) 1 (50,0) 2 (100,0) NHL 29 (64,4) 16 (35,6) 45 (100,0) HL 13 (76,5) 4 (23,5) 17 (100,0) CML 12 (80,0) 3 (20,0) 15 (100,0) Hairy Cell L. 1 (100,0) 1 (100,0) Total 69 (63,9) 39 (36,1) 108 (100,0) When any of the HepatitB markers which were found to be positive in the disorders shown above are taken into account, it is seen that the incidence of such a case in AML is 60%, in CLL 52.4 %, in MDS (RAEB) and Multiplmyeloma 50%. Not a single significant correlation has been observed between the malignancies and any of the positive HepatitB markers (Ki-Kare: 7.406, p: 0.388). CLL 2 66,7 CML 1 33,3 Total 3 100,0 The distribution of the patients according to their disorders whose HepatitC markers are positive is shown in the table above. It is found that any of the HCV markers is positive in an incidence of 66,7 % in CLL, 33.3% in CML. Marker positive n % HepB 39 92,8 HepC 3 7,2 Total 42 100,0 It has been reported that HBV constitutes 92,8 % of all the positivity in the Hepatit markers. As a result, neither HBV nor HCV can be considered as a factor in the etiology of these hemotologic malignancies.
