activity and mitogenic lymphocyte transformation were investigated. It was found increased plasma levels of MDA and decreased protein thiol groups in patients with beta thalassemia major. Also, the plasma free iron concentration was higher in patients. At the beginning, it was found that decreased NK activity in patients with thalassemia major in comparison with healthy volunteers. Selenium (10-7 M) and vitamin C (200 mg/ml) significantly increased NK activity whereas vitamin E significantly decreased NK activity of both thalassemia patients and healhty volunteers in different doses. No difference was found between patients with thalassemia major and healthy volunteers in mitogenic lymphocyte transformation. But vitamin C (200 mg/ml) decreased mitogenic lymphocyte transformation against PHA. This findings indicate that there were increased oxidative stress and impaired NK activity in thalassemia patients and vitamin C and selenium may modulate NK activity. However, between NK activity and mitogenic lymphocyte transformation may become reverse relation. This study was supported by İstanbul University Research Fund. (Project number: T-907/061100)

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AN ATYPICAL RH HEMOLYTIC DISEASE CASE WITH HEMOPHAGOCYTOSIS AND SEVERE IRON OVERLOAD DUE TO TRANSFUSIONS

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The frequency and complications of neonatal Rh hemolytic disease decreased currently by anti-D administration; but in some cases, the preventive administration of anti-D is still insufficient and physicians should be aware about different clinical presentations and complications. In this case report we present a hydrops fetalis case due to Rh hemolytic disease who had hemophagocytosis and severe iron overload secondary to transfusisons and treated successfully with intravenous desferrioxamine. The patient was a girl born from Rh(+) father and Rh(-) mother from the sixth pregnancy as the fifth live born child. Her mother did not receive any anti-D administrations after her deliveries. During the follow-up of her last pregnancy, indirect Coombs test was found to be 3+ and there were findings compatible with hydrops fetalis on fetal ultrasonography. The fetus received intrauterine O Rh(-) red cell concentrate transfusions twice. She was delivered with cesarean section on the 34th gestational week because of uterine contractions. Cord blood hemoglobin was 9.3 g/dL, total bilirubin 4 mg/dL and conjugated bilirubin 2.5 mg/dL. She had normoblastemia but no reticulocytosis. Her blood group test result was O Rh(-) and direct Coombs test was negative. Because of the rapid rise of total and conjugated bilirubin, exchange transfusions were performed on postnatal 19th and 62th hours. On postnatal 2nd day, hepatosplenomegaly, leukopenia, and thrombocytopenia developed and bone marrow aspirate examination showed erythroid cell hemophagocytosis. Intravenous immunoglobulin treatment was started for Rh hemolytic disease and secondary hemophagocytic lymphohistiocytosis. The tests for final and differential diagnosis of secondary hemophagocytic lymphohistiocytosis and conjugated hyperbilirubinemia were done in order to determine underlying pathology. Serum ferritin level was found 5527 ng/mL and liver biopsy showed severe iron overload and cholestasis without hemochromatosis and fibrosis. To protect the liver from further damage, intravenous desferrioxamine was started five times/week. Five weeks later, serum ferritin level declined to 1385 ng/mL and chelation therapy was stopped. On follow-up, the bilirubin levels were normalized and she was discharged from hospital in good clinical condition. Her blood group test result was AB Rh(+) when she was 4 months old. The case is presented to emphasize the importance of iron overload in transfused neonates and to draw attention to occurrance of hemophagocytic syndrome in Rh hemolytic disease as a rare finding.

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CHRONIC IDIOPATHIC URTICARIA AND REFRACTORY DERMATITIS IN A CASE OF VITAMIN B12 DEFICIENCY

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Allergic contact dermatitis is an itchy skin condition caused by an allergic reaction to material in contact with the skin. It arises some hours after contact with the responsible material, and settles

down over some days providing the skin is no longer in contact with it. Allergic contact dermatitis is distinct from irritant contact dermatitis, in which a similar skin condition is caused by excessive contact with irritants. Irritants include water, soaps, detergents, solvents, acids, alkalis, and friction. Irritant contact dermatitis may affect anyone, providing they have had enough exposure to the irritant, but those with atopic dermatitis are particularly sensitive. Most cases of hand dermatitis are due to contact with irritants. The dermatitis is generally confined to the site of contact with the allergen, although severe cases may extend outside the contact area or it may become generalized. Sometimes the allergen is transmitted from the fingers so unexpected sites can be affected for example the eyelids and genitals. Dermatitis is unlikely to be due to a specific allergen if the area of skin most in contact with that allergen is unaffected. The affected skin may be red, swollen and blistered or dry and bumpy. Cobalt is a metal found naturally in soil, dust, and seawater. It is usually found in association with nickel. Cobalt and its salts have many uses. Reactions to contact with cobalt in an allergic individual include allergic contact dermatitis and irritant dermatitis. Vitamin B12 injections administered to allergic individuals may produce a red, tender and itchy area around the site of the injection. Oral ingestion of vitamin B12 is known to cause intractable hand eczema is some patients. "Nickel" which is the most common cause of allergic contact dermatitis, is not associated with worsening of dermatitis following administration of Vitamin B12 and this feature is in contrast with cobalt allergy. In this article, a 21 year girl with nickel dermatitis will be presented who were refractory to usual treatments held for contact dermatitis. Following diagnosis of macrocytic anemia and treatment with Vitamin B12 injections, significant improvement in signs and symptoms occurred with no further recurrence

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EVALUATION OF TREATMENT RESPONSE TO THE FIRST DOSE PARENTERAL VITAMIN B12 IN PATIENTS WITH B12 VITAMIN DEFICIENCY BY THE NEW AUTOMATED RETICULOCYTE PARAMETERS

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Aim: It is known that in the patients with B12 vitamin (VB12) deficiency, there is a reticulocyte crisis that reaches to a maximum point in the fifth and eighth day of the therapy. In this study, it was aimed to determine the changes in the new automated reticulocyte parameters after the first dose parenteral (PE) VB12. It was also aimed to evaluate whether the early response to the treatment is determined with the use of this parameter or not. Method: Before the treatment of 14 patient with B12 vitamin deficiency and after first dose PE B12 in the 2nd and 7th day, absolute reticulocyte number (ARN), %Reticulocyte (%R), mean corpuscular volume reticulocyte (MCVr), content hemoglobin reticulocyte (CHr), mean hemoglobin concentration of reticulocytes (CHCMr) parameters were studied with Advia 120 (Bayer Diagnostics, Tarrytown, NY) autoanalyzer. The rate between these erythrocyte and reticulocyte parameters are compared with the treatment. In addition, the patients` serum iron, iron binding capacity and ferritin were studied and the non- iron deficient patients were included in this study. Post-therapy values were compared with 34 healthy control, also. Results: After the treatment, in the 7th day, an increase in the %R and MRS (p=0.05), MCVr, CHr and a decrease in CHCMr was found (p=0.01, p=0.01, p=0.04, respectively) without any significant statistical changes in the 2nd and 7th day in the Hb and MCV. In the 7th day, MCVr decreased but still was beyond the normal and CHr was reached to the normal level, on the other hand CHCMr was observed to be much lower than the pretreatment level (as follows 105.51±7.35, 28.25±2.60, 26.92±2.60). However, in the 2nd day of the treatment, a significant statistical change in these parameters was not found. According to the control group, although the rate of MCVr/MCV was much higher before the treatment, this rate decreased in the 7th day of the treatment (1.27±0.15, 1.15±0.13, respectively) and it reached to the same rate with the control group. It was detected that the rate of CHr/CH significantly decreased in the 7th day (day0:0.97, day7:0.86, p=0.03), on the other hand CHCMr/CHCM was decreased in the 7th day, but this difference was insignificant. Conclusion: The increase of the number and the rate of the reticulocyte and the decrease of MCVr, CHr, CHCMr, MCVr/MCV and CHr/CH parameters can be used in following treatment response. The results revealed that these parameters particularly changed between the second and the seventh days.

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LIVER INVOLVEMENT IN SICKLE CELL DISEASE

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Background/aims: Liver involvement in sickle cell disease (SCD) may take place due to primary disease itself or secondary conditions such as iron overload, viral hepatitis and cholelithiasis. In the present study we have tried to evaluate the frequency of hepatic dysfunction and etiological factors in 48 patients with SCD. Methods: Clinical and laboratory investigation including liver function tests, serological tests for viral hepatitis, abdominal ultrasonography were performed in all of the patients. Additionally from 13 patients liver biopsies were taken. Results: Intrasinusoidal sickling and Kuppfer cell hyperplasia were consistently seen in all of the biopsy specimens. There were hepatomegaly in all patients, whereas liver function test abnormalities were seen in 27% of them. The prevalence of cholelithiasis was found as 35%. The most significant contributory finding was the presence of hemosiderosis in histological examination of liver specimens. Conclusion: Our data suggest that chronic liver injury in patients with SCD seems to be a multifactorial phenomenon depending mostly on overlapping factors such as iron overload and viral damage rather than primary disease itself.

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INSULIN AND C-PEPTID LEVELS IN PATIENTS WITH B-THALASSEMIA MAJOR

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SUMMARY Previous studies has demostrated that patients with .-thalassemia major have altered glucose metabolism. The aim of this study was to provide further evidence and investigate factors associated with it. 33 patient with .-thalassemia major and 15 age matched controls underwent 2 hour glucose tolerance test and insulin and c-peptid levels were measured at 0, 60 and 120 minutes. Insulin index and c-peptid index were calculated. Patients with .-thalassemia major had significantly higher glucose levels at 0, 60 and 120 minutes and fasting insulin levels were lower compared to controls. Although there was no difference in c-peptide and c-peptide index; significantly lower insulin index was found in patients with .-thalassemia major. Although fasting hipoinsulinemi was detected in patients with .-thalassemia there was no difference c-peptid and stimulated c-peptid and stimulated insulin levels. This results shows that beta cell function was preserved. Significantly lower insulin index contrast to sufficient insulin secretion shows that insulin resistance in patients with .-thalassemia major.

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THE PERCENTAGE OF FRAGMENTOCYTES IN DIABETES MELLITUS

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Diabetic nephropathy is one of diabetes mellitus complication which will caused progressive decreased of renal function. Currently. most of clinicians used proteinuria as one of the criteria for diabetic nephropathy. However, this parameter is not an early sign of renal damage, because its positivity showed late stage of renal damage. Microalbuminuria also has it advantage, because it is very sensitive. Previous study showed that one of the microangiopathy result`s is fragmentocyte, where the erythrocyte will cut as they flow through the damage vessels. The aim of this study is to compare the percentage of fragmentocytes in diabetic nephropathy, in diabetic without nephropathy, and in normal individuals. And we also like to find whether there is any correlation between the length of time suffered from diabetes mellitus, systolic and diastolic blood pressure, and the percentage of fragmentocytes in each group. Ninety-nine subjects were recruited for this study, consists of 66 diabetic patients, who came to the Endocrinology Clinic of Dr Hasan Sadikin Hospital in Bandung Indonesia (33 diabetics nephropathy, 33 diabetics without nephropathy), and 33 subjects who came to that hospi-

tal for medical check up and considered normal. Subjects who had lower urinary tract infection, Kimmelstiel-Wilson syndrome, malignant hypertension, and blood disease such as thalassemia, were excluded. Data were analyzed with one-way anova, multiple comparisons Dunnett, coefficient point multi serial correlation, and Pearson`s test. The average fragmentocytes in diabetic nephropathy were 5.10% (95% CI 4.20-6.20); in diabetes without nephropathy were 2.20% (95% CI 1.80-2.60) and in healthy subjects were 0.1% (95% CI 0.04-0.14). By one-way anova, we found F = 57.694 and p value = 0.00. The coefficient of point multi serial correlation was 0.739530, which means that the percentage of fragmentocytes in those three groups have a close correlation. We can conclude that fragmentocyte could become the marker of microangiopathy in diabetes mellitus. This study also reveals that there were a correlation between the percentage of fragmentocytes and length of time suffered from diabetes, systolic and diastolic blood pressure, in diabetic subjects, while in normal individuals no correlation were found.

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COMPARISON OF MATERNAL AND CORD BLOOD HEMATOLOGICAL PARAMETERS

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Background: Anemia is one of the most common problems during pregnancy in both industrialized and developing countries. According to the report of World Health Organization, 35-75% of pregnant women in developing countries and 18% of women in industrialized countries have anemia. The most common cause of anemia in pregnancy is iron deficiency. Hemodilution, previous insufficiency in the iron pool and inadequate intake of iron are its principal causes. United Nations Survey reported that the prevalence of IDA in pregnant woman is 18-38% in developing countries and nearly 5060% in Turkey. Megaloblastic anemia is also observed in pregnancy. Folate deficiency is the most common cause of megaloblastic anemia during pregnancy and occurs in 1-50% of pregnant women.The other cause of megaloblastic anemia during pregnancy is vitamin B12 deficiency. Vitamin B12 levels start to decrease from the first trimester. Vitamin B12 status in the neonatal period is strongly associated with maternal vitamin B12 status. Aim: The aim of this study was to investigate the effect of maternal iron, folate and vitamin B12 levels on the same hematological parameters of her newborn baby in a Turkish pregnant women group. Methods: Complete blood count, ferritin, folate and vitamin B12 levels were obtained from 15 preterm and 109 term newborns and their mothers. Results. In this study, there were no significant differences between age, parity, education, iron supplementation and socioeconomic status of the mothers in preterm and term groups. The study revealed that 26.7% of pregnant women in the preterm group and 16.5% of those in the term group have anemia. The incidences of iron deficiency anemia (IDA) in the mothers of preterm and term groups were 53.3% and 66.1%. The anemia was detected in 6.7% of preterm babies and 4.6% of term babies. Cord blood ferritin levels between preterm and term babies were not different. There was no correlation between mother and cord blood ferritin levels. Serum folate levels were low in 8.1% of the mothers in the preterm group; however, folate levels of all mothers in the term group were normal. Neither the preterm nor the term babies had low folate levels. There was positive correlation between maternal and cord blood folate levels. Besides, maternal vitamin B12 levels were low in 20% of the preterm group and 31% of the term group; cord blood vitamin B12 levels were low in 6.7% of preterm babies and 3.7% of term babies. There was positive correlation between maternal and cord blood vitamin B12 levels. Summary. In our study, iron and vitamin B12 deficiencies were commonly observed in pregnant women. Recent studies have reported that newborns whose mothers have vitamin B12 or iron deficiency during pregnancy period are more likely to have vitamin B12 or iron deficiency during infancy period. Thus, it is very important to diagnose, prevent and treat anemia during pregnancy for both maternal and neonatal health.

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ANTIBODY DEFICIENCY DISORDERS IN PATIENTS PRESENTING WITH CYTOPENIAS

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Here we present 4 adult patients admitted with various hematological cytopenias and finally diagnosed to have an antibody deficiency disorder. None of them had a family history. One patient was a 38-year-old male who had recurrent jaundice episodes beginning from 17 years-old. Coombs + hemolytic anemia was detected. The second patient was a 23 year old female referred to our department because of unexplained pancytopenia. She had recurrent pulmonary infections. The third patient was a 48 year old female admitted to the hospital with intestinal obstruction and consulted to our department because of leukopenia and anemia. She had chronic otitis media and hepatosplenomegaly and bone marrow aspiration disclosed myeloid maturation arrest. All three patients had panhypogammaglobulinemia. Another patient, a 31-year-old woman also presented with unexplained pancytopenia with macrocytosis. She also had recurrent sinopulmonary infections. Partial IgA deficiency was detected in this case. So in conditions with unexplained cytopenias antibody deficiency disorders should be considered and serum immunoglobulin levels should be measured.

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ACUTE PAINFUL CRISES OF SICKLE CELL DISEASE IN EGYPTIAN CHILDREN: PREDICTORS OF SEVERITY FOR PREVENTIVE STRATEGY

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Background:Acute painful crises is the most common presenting symptom in sickle cell disease (SCD). Because of the wide range of clinical severity despite of the same single genetic defect, many studies were searching for the risk factors of SCD severity. Objective: the aim of this work is to identify infants and young children with SCD who are likely to have recurrent or severe painful crises to suggest accurate prognostication and proper therapy plan. Subjects and methods: in a mixed hospital-com-munity-based population(76 cases), demographic data, preliminary diagnostic parameters for SCD (sicklingtest, Hb electrophoresis) as well as basal blood counts were collected and correlated to two dependant variables as indices of SCD severity. The 1st is pain rate (average number of days of painful episods per year of follow up), the 2nd is the occurence of serious life threatening complication. Data were merged and analysed blind to these two variables of severity. T-test, one way ANOVA and Pearson correlation were done for detection of association to pain rate. Forecasting the clinical severity was done by discriminate analysis using the relevant risk factors for pain rate as independant predictors. Results: Pain rate is significantly high in Hb SS patients especially those having early onset of dactylitis.A statistically significant negative correlation between pain rate and basal Hb, Hct values, but with positive with basal Hb F.Arterial o2 saturation is negatively correlatedto pain rate,moreover, o2 desaturation is considered as a strong predictor of recurrence especially if <80%. Three statistically significant parametres were found to be the best predictors for disease severity; SCD genotype, basal Hb level and early onset of dactylitis (F1 coefficient were 2.74,0.737 and -0.420 respectively). Conclusion: We can conclude that SCD infants with genotypes SS and low basal Hb presented around age of 6 month should be closely monitored even before the development of dactylitis with special attention to their ventilation and oxygen status. Recommendations:A powerful therapeutic plan should be formulated for these cases; in the form of effective pain killers, community-based educational treatment to improve the spiritual well-being and self efficacy of manipulating their pains, leading to mitigation of SCD morbidity and mortality.

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BRAINSTEM AUDITORY EVOKED POTENTIALS IN CHILDREN WITH BETA-THALASSEMIA MINOR

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Beta-thalassemia minor is one of the most frequent monogenic disorders that is characterized by microcytosis and hypochromia. The prevalence of beta-thalassemia minor is 2-3% in Turkey and this rate greatly shows regional differences. Although there are some controversies, iron deficiency anemia (IDA), the most common hypochromic microcytic anemia in the world, has

been shown to impair brainstem auditory evoked potentials (BAEPs). The thalassemia syndromes, the most common form of hypochromic microcytic anemias after IDA, are among the major public health problems in many parts of the world. Of these, beta-thalassemia minor constitutes the majority. In this study, we investigated BAEPs of the patients with beta-thalassemia minor to see if hypochromic microcytic red cells might lead to impairment on BAEPs. Forty patients (23 female, 17 male) and 33 healthy controls (15 female, 18 male) enrolled into the study. The demographic characteristics and the results of laboratory tests are shown in Table 1. Mann Whitney U test was utilized for the statistical analysis. The data revealed the prolongation of waves I, III, V, IPL I-III, IPL III-V, and IPL I-V as compared with the controls and the differences were statistically significant. These findings show BAEP abnormalities recorded from distal part of acoustic nerve to the lateral lemniscus that suggest an auditory dysfunction in children with thalassemia minor. The most devastating consequence of IDA is neurocognitive deficits that may be irreversible, which affect children of all ages. Thus, the development of IDA in a child with beta thalassemia minor may augment the undesirable effects of these diseases on BAEPs in children that may affect cognitive achievements adversely. Therefore, the infants and children with thalassemia minor should undergo BAEP evaluation as early as possible since the infants and toddlers are vulnerable to IDA. Investigation of BAEPs on adult patients with thalassemia minor may be fruitful.

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INVESTIGATION OF PERIODONTIC PROBLEMS IN CASES WITH THALASSEMIA MAJOR

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Although treatment of thalassemia major (TM) patients with blood transfusions and chelating agents prolonged lifetime, various complications damaged the quality of life. In thalassemia, various tissues and cells such as liver, heart, endocrine tissues and bone are affected due to chronic iron accumulation and chronic anemia. We have found no study investigating periodontological problems. Therefore we have investigated gum diseases aud accessories accumulated on gum. For this purpose, totally 76 patients aged between 5-18 years and admitted to Antalya State Hospital and SDU Hospital of Medical Faculty. Control cases were composed of 20 cases aged between 5-18 years to extract a tooth. Plaque index (PI), gingival index (GI) and periodontal tooth depth (PTD) were measured to evaluate the hygiene status of tooth, inflammation of the gum and the distance from periodental pocket floor to gum floor, respectively. Thalassemic patients were clinically examined and periodontal prablems were evaluated using GI, PI and PTD scores. The findings were compared with those of controls. Mean values of GI, PI, PTD scores of patients were significantly different (p=0,003) from those of controls. On the other hand, correlations between GI, PI, and PTD and serum ferritin and some parameters of histopathological findings of gum were calculated. As a result, periodontological and gingival problems of the patients were significantly higher than those of controls. No significant correlation was found between serum ferritin levels and GI, PI and PTD scores of the patients.A significantly important correlation was found between GI, PI, and PTD and iron content of inflammed area and gingivitis, iron content of inflammed area and collagen type-I, collagen type-I and fibrosis of gum in the patients and controls.

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EVALUATION OF CARDIAC FUNCTIONS AND INVESTIGATION OF ENALAPRIL TREATMENT ON THOSE FUNCTIONS IN THALASSEMIA MAJOR PATIENTS

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Purpose: In this study, cardiac functions of thalassemia major patients living in Denizli, Turkey

were evaluated by echocardiography. Effect of enalapril treatment on thalassemic patients who are asymptomatic even diastolic dysfunction was observed. Materials and Methods: 40 (23 male, 17 female) thalassemia major (mean age 13,1±4,5 years) and 40 healthy subjects (mean age 13,5±4,3 years) were included in this study. 24 thalassemia major patients (13 male, 11 female) who were diagnosed to have diastolic dysfunction by echocardiography were put on 0.1-0.5 mg/kg/day (max 5 mg) enalapril treatment. On the sixth and twelfth months of the treatment echocardiographic examinations were repeated. Results: Mean hemoglobin and serum ferritin values were 9.3 gr/dL (6-12) and 4358 ng/dL (999-8588) respectively before transfusions. All of the patients demonstrated normal systolic function whereas 26 (67%) of them had diastolic dysfunction. Left ventricular MPI values were above normal in all patients and right ventricular MPI values were above normal in 97% of the patients. When compared to control group right ventricular wall thickness, left ventricle mass index, cardiac index, mitral deceleration time, mitral E/A ratio, isovolumic relaxation time, tricuspid deceleration time, right and left ventricle MPI values were increased, however left ventricular Vp values, mitral and tricuspid A wave amplitudes were decreased ($p<0.05$). Between Vp values and serum ferritin levels significant negative correlation was observed. After 12 months of enalapril treatment, there was no statistically significant difference between patient and control groups in regards of left and right ventricular diastolic function parameters such as deceleration time, E wave, A wave, E/A ratio and isovolumic relaxation time besides MPI which reflects global function of the heart. Vp values were dramatically improved by enalapril treatment.

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PANCYTOPENIA AND HEMOPHAGOCYTIC SYNDROME IN A PATIENT WITH FEVER OF UNKNOWN ORIGIN: ADULT ONSET STILL`S DISEASE

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Hemophagocytic syndrome (HPS) is a clinicopathologic entity characterized by systemic proliferation of benign hemophagocytic cells of the monocyte-macrophage-his-tiocyte lineage, associated with fever, cytopenias, hepatosplenomegaly, lymphadenopathy, and coagulopathy. Adult onset Still`s disease (AOSD) is a systemic inflammatory disease of unknown etiology and pathogenesis that is charaterized by polyarthritis, intermittent high fever and typical skin eruptions. AOSD rarely manifests as HPS or fulminant hepatitis. A 23- year- old male patient who was presented with fatigue, and high fever rising especially at nights for 15 days. During the evaluation of his symptoms, pancytopenia and hepatosplenomegaly were detected. His WBC was 3200/mm3, hemoglobin was 11gr/dl and platelet was 85000/mm3. Routine laboratory examination was normal. During the follow up period hepatic transaminases rised, hypoproteinemia and hypoalbuminemia were detected. Athralgia developed. Liver biopsy was performed and active hepatitis, submassive necrosis were detected and histological activity index was 18/18, fibrosis was 1/4. Hepatic viral serology, other infection and malign tumour tests were negative. ANA and RF were negative. Pancytopenia got worse than the first examination. Hypersplenism was thought, splenectomy was decided and performed successfully. Multiple biopsies were taken in diagnostic laparotomy. Pathological evaluation showed splenic ischemic hemorrhagic necrosis, diffuse erythrophagocytosis, fibrin thrombi in vascular lumen. Diffuse submassive hemorrhagic necrosis and diffuse erythrophagocytosis were detected in hepatic specimen. Finally, the patient was diagnosed to have AOSD according to Yamaguchi`s criteria. Methotrexate 15 mg/week, azothiopyrine 50 mg/day were started. Intravenous immunoglobulin 1gr/kg/day was used for seven days. His fever and hepatic transaminases dropped to normal levels and ascites vanished. Twenty days later, his general well being and laboratory tests got worse during the preparation procedures for hepatic transplantation. The patient died due to probable hepatic failure or septic shock. We conclude that it should be kept in mind which HPS may be secondary to malignancy, infection or autoimmune disease such as AOSD.

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IMMUNOSUPPRESSIVE THERAPY IN SEVERE APLASTIC ANEMIA

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Treatment strategy in severe aplastic anemia (SAA) depends on the age of the patients and availability of an identical sibling donor. Allogeneic bone marrow transplantation is indicated in patients under 40 years of age if such a donor is available. In the absence of a donor and in older patients the treatment of choice is immunosuppression. Between 1999-2004, 6 patients with SAA were treated with immunosuppressive therapy in our department. The age of the patients varied between 22-70 years. The diagnosis was established by peripheral blood smear and bone marrow biopsy examination. In all cases SAA was idiopathic. The treatment consisted of antilymphocytic/antithymocytic globuline (ALG/ATG) + corticosteroids + cyclosporine + G-CSF in all 6 patients. In 5 patients (83.3%) response was achieved, in 3 of them (60%), complete response. The other 2 patients with partial responses, with various degrees of pancytopenia, are still under treatment with cyclosporine (1-2 years). One patient died due to haemorrhagic complications. All 5 patients are still alive, 1-5 years after treatment, transfusion independent. None of the patient displayed clonal evolution towards paroxysmal nocturnal haemoglobinuria, myelodysplastic syndrome or acute leukemia.

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SEASONAL FLUCTUATIONS ON THE INCIDENCE OF HOSPITAL ADMISSION FOR PAINFUL CRISES IN ADULT SICKLE CELL PATIENTS

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Sickle cell disease (SCD) is characterized by the recurrent, painful episodes and organ damage resulting from microvaascular occlusion. Conflicting results have been reported concerning the correlation between climatological changes and frequency of painful episodes in patients with sickle cell disease (SCD). However, there is only little information about seasonal variation of vasoocclusive crisis in adult sickle cell patients. The aim of this study was to examine seasonal fluctuations in hospital admission of patients with SCD due to the vasoocclusive crises. The number of vasoocclusive episodes was extracted from the Hematology Register in Başkent University Hospital, Adana, Turkey (located in Meditteranean Region). Monthly avarage of the hospital admission for the last three years was examined. In 2003-2005 period, the highest incidence of episode frequency had occured in January, May and July. Possible precipitating seasonal factors of painful episodes were discussed. This study suggest that climatization may contribute to the occurence of the painful crises particularly in Meditteratean Region in Turkey. Hot weather may lead to dehydratation while cold weather results with vasoconstruction. Simple preventive measures related to the regional enviromental factors can decrease the painful episodes in patients with SCD.

Abstract: 294 Poster: 201

THE FREQUENCY, ETIOLOGY AND CLINICAL IMPACT OF ANEMIA IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Familial Mediterranean Fever (FMF) is an inflammatory disorder characterized by recurrent episodes of fever and serosal inflammation. The disease primarily begins in the childhood period and is frequent in individuals of Mediterranean countries. Recently, the existence of chronic inflammation was reported to be in 25-65% of FMF patients. Chronic inflammatory disorders are associated with an increased risk of patients developing anemia. However, there is no data about the frequency of anemia and anemia of chronic disease (ACD) in FMF patients both in childhood and adulthood. The aims of this study were to investigate the frequency, etiology, the existence of different demografic, clinical, laboratory and genotypic features of the patients with anemia as compared to the patients without anemia and the responses to therapy. Sixty-four FMF patients who were on colchicine therapy with a median age of 13 years were evaluated retrospectively. Of these, 30 (46.9%) were girls and 34 (53.1%) were boys. The mean follow-up duration of patients were 5.2 years. The frequency of anemia was in-

vestigated cross-sectionally and the etiologies were searched. As a result the frequency of anemia was 28.1% and it was hypochromic and microcytic in all patients. ACD (9.4%), iron deficiency anemia (19%) and beta thalassemia trait (3.1%) were the causes of anemia. The frequency of articular disease during the attacks which is associated with severe disease and amyloidosis, poor response to the colchicine therapy and increased requirement of other antiinflammatory drugs was found higher in the patients with anemia. The incidence of splenomegaly and evident acute phase response during the attack-free periods was found higher and there was no response to the iron therapy in the ACD group. In conclusion, this is the first report about the frequency of anemia and ACD in FMF.The ACD occurred in 9.4% of our patients as an evidence of chronic inflammation. It is important to keep in mind the presence of ACD when treating an FMF patient with anemia because it will direct to the right choice of treatment and improve the quality of life of patients.

Abstract: 295 Poster: 202

SURVIVAL AND EFFECTIVE FACTOR IN ACQUIRED APLASTIC ANEMIA IN CHILDREN

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Introduction: Aplastic anemia is a clinical syndrome in which there is peripheral blood pancytopenia due to reduced or absent production of blood cells without evidence of another marrow disorder. The disorder may be acquired or inherited like Fanconi anemia. Method: In this study, survival and prognostic factors in acquired aplastic anemia is determined.This analytic cross- sectional study was done on 224 patients who referred to Ali Asghar Children`s Hospital from 1977 to 2000.Data of patients was collected retrospectively in census methods. Data was analyzed by Kaplan - Meier survival curves and life tables. In order to determine the factors influencing survival log rank test and cox regression analysis in SPss soft ware were used. Result: 5 and 10 year survival of acquired aplastic anemia were 55%, 41.6% respectively. In bivariate analysis, absolute neutron phil count less than 100/ulit (P=0.00) and ESR more than 60 mm /h (P=0.04) were negatively associated with survival and improved survival was associated with pallor at time of diagnosis (P= 0.04).In multivariate analysis just association between absolute neutrophil couht (EXP(B)=5.18) and pallor (EXP(B)= 0.41) with survival were proved. Conclution: In study,survival of patients with acquired aplastic anemia in comparison with othor countries was in the lowest range of survivals.

Abstract: 296 Poster: 203

POST-GASTRECTOMY ANEMIA: EVALUATION OF 72 CASES WITH POST-GASTRECTOMY ANEMIA

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Anemia is frequently seen in patients following gastrectomy. The purpose of this study is to document causes of anemias developing in post-gastrectomy period, and to determine the importances of sex, type of gastrectomy, the interval following gastrectomy and complete blood count parameters on type of anemia. A total of 72 patients (23 women and 49 men) who have a gastrectomy operation in their medical history and admitted for the evaluation of anemia were enrolled in study. Patients previously evaluated and treated for anemia or have well-known causes of anemia other than gastrectomy were excluded from study. Iron deficiency anemia was present in 68 (94,4%) of 72 gastrectomized patients with anemia. Deficiencies and vitamin B12 and folate were present in 57 (79,2%) and in 3 patients, respectively. The most common cause of anemia was the combination of iron and vitamin B12 deficiencies. Iron deficiency was present in the majority of patients followed by vitamin B12 deficiency in frequency. There was no difference between the groups that had post-gastrectomy period >5 and <=5 years according to the distribution of causes of anemia. In all cases with iron deficiency, MCV and MCH values were either normal or below normal limits. All of the cases with low leukocyte counts had vitamin B12 deficiency. Leukocyte and platelet counts were in normal range in majority of patients. In conclusion, the gastrectomized patients should be followed for anemia, and treated appropiately based on the cause of anemia.

Abstract: 297 Poster: 204

VITAMIN B12 DEFICIENCY PRESENTING WITH SPLENOMEGALY: A CASE REPORT

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A 34-year old female patient presented to the emergency room with complaints of chest and abdominal pain that had been present for at least a week. Four years ago the patient had been diagnosed with anemia but no specific treatment was given at that time. The patient had been feeling relatively well until two months ago when she began experiencing fatigue, loss of appetite, nasuea, palpitations and swelling of the legs. On initial examination, her blood pressure was 130/80 mmHg, pulse rate was 120/min, temperature was 38.2 C. She had pallor of the skin, conjuctiva and mucous membranes and scattered petechia. On cardiac auscultation she had a pansystolic murmor in all areas. There was marked tenderness over the sternum and epigastrium on palpation. Liver was 3 cm and spleen was 5 cm palpable below the right and left costal margin, respectively. The laboratory examination showed pancytopenia with hemoglobin=2.7g/dL, MCV=115.5 fL, hematocrit= %8.2, WBC=2080/mm3, thrombocytes=81000/mm3. Peripheric blood smear showed macro-ovalocytes, aniso-poikilocytosis, hyper-segmentation of the neuthrophils and 3-4 thrombocytes per hpf. Initial reticulocyte count was 1,5%. She had indirect hyperbilirubinemia and increased LDH. She also had increased cardiothoracic ratio on chest-x-ray and sinus tachycardia on electrocardiogram. Other blood test results were as follows: Vitamin B12=79(211-911)pg / mL, folate = 9.9(1.1-20)ng/mL, ferritin=56(10-291) µgr/L (Table 1). Abdominal USG showed an enlarged spleen. Bone marrow aspiration showed megaloblastic changes and dysmorphism in the erythroid lineage. The patient was transfused to a hemoglobin count of 5.5gr/dL and was put on parenteral vitamin B12 as soon as vitamin B12 results were obtained. Upon intiation of treatment the patient reported feeling better and her chest and abdominal pain regressed over days. Her reticulocyte count was 11% on 4th day of treatment. After the 5th day, oral iron and folate was added to her treatment. Her spleen disappeared during the course of 12-day hospital stay. This was confirmed with an ultrasound finding of a normal sized spleen on 2nd month of treatmet. Her blood test results also showed improvement during her hospital stay (table). Her upper GI endoscopy revealed antral gastritis and urease positivity. She was treated for H. Pylori and was recommended to continue monthly vitamin B12 injections for the rest of her life. Vitamin B12 deficiency can occur at a relatively young age with atypical manifestations. The case illustrates a rare entity where spelonomegaly accompanies B12 deficiency with pancytopenia that is reversible upon treatment with vitamin B12.

Abstract: 298 Poster: 205

COMPLETE BLOOD COUNT AND FETAL HEMOGLOBIN VALUES IN FANCONI ANEMIA HETEROZYGOTES

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Background and Aims: Fanconi anemia (FA) is a recessively inherited disorder characterized by multiple congenital malformations, progression to aplastic anemia, and increased predisposition to malignancy, particularly acute myelogenous leukemia. Parental heterozygotes of FA patients are normal in appearance and lack overt laboratory abnormalities. The aim of the study was to determine if any of the parameters of complete blood count and fetal hemoglobin (Hb F) was abnormal in FA heterozygotes. Material-Method and Results: This study involved 57 parents of children with Fanconi anemia who referred to Hacettepe University Faculty of Medicine, Pediatric Hematology Unit between January 2004 and June 2005. Healthy parents with proper age and gender distribution (n=40) comprised the control group. Complete blood count and Hb F levels were studied in all of the subjects and the results of the study group and the control group were compared. The mean age of 57 parents (34 males and 23 females) comprising the study group was 37.84±5.35 years (range: 23-47 years), while the mean age of 40 parents (20 males and 20 females) comprising the control group was 37.0±4.84 years (range: 24-44 years). There were no statistically significant gender and age differences between the groups ($p>0.05$). No significant difference was detected between the Hb, Htc, RBC, MCV, RDW, WBC, and platelet counts of the study and control

groups (Table). In other words, the mean values of these parameters do not seem to show great variance between the groups. However, HbF values were significantly higher in FA heterozygotes than the subjects in the control group ($p<0.001$) (Table). MCV values of the FA heterozygotes (86.7±7.13 fl) also seems to be high than that of the control goup (84.38±6.24 fl), whereas the difference was not statistically significant. Conclusion: These results suggest that FA heterozygotes show minor hematological abnormalities. It may be resulted from partial expression of the Fanconi gene in the hetereozygotes. Therefore, comprehensive studies investigating the hematological and constitutional abnormalities of FA heterozygotes are needed.

Abstract: 299 Poster: 206

THE RELATION OF IMMATURE RETICULOCYTE FRACTION TO PLATELET PARAMETERS IN IRON DEFICIENCY ANEMIA

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Background: Immature reticulocyte fraction (IRF) quantitation which is normally less than 5 % of normal reticulocytes is a useful tool in monitoring erythropoietic activity. It has been suggested that evaluation of reticulocyte maturity could help estimating the qualitative impairment of erythropoiesis, diagnosis and treatment of anemias. In iron deficiency anemia (IDA), platelet counts are usually increased but its relation to erythropoietic activity is not clear. This study was conducted to investigate the relation between the platelet counts and IRF in patients with IDA. Methods: Fifty three patients with IDA (26 boys, 27 girls) between 5 months -17 years (median 30 months) of age were studied. Patients were divided into two groups as group I (43 children, 81 %) with normal platelet counts and group II (10 children, 19 %) with increased platelet counts (> 450X109/L). IRF, platelet counts, mean platelet volume (MPV), platelet distribution width (PDW) were studied in CELL-DYNE 4000 (Abbott, USA) autoanalyser before, at the first month and at the end of iron therapy) (Table 1). Friedman test was used for statistical analysis. Results: The median pretreatment IRF value was lower in group I as compared to group II but the difference was not statistically significant. There was also no significant diffference between two groups in terms of platelet parameters. In both groups; IRF was found to be decreased during the treatment ($p < 0.005$). Although MPV was found to be slightly increased in group I and there was a decrease in group II during the treatment, these differences were not statistically significant ($p > 0.005$). There were also no difference in platelet counts, and PDW during the treatment ($p > 0.05$). No correlation was found between platelet parameters and IRF within the treatment phases. Conclusion: In conclusion, no significant correlation was observed between IRF and platelet parameters suggesting that elevation of platelet counts is independent of erythropoietic activity.

Abstract: 300 Poster: 207

CHILDHOOD ACQUIRED APLASTIC ANEMIA

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Thirty-eight children admitted to Cerrahpaşa Medical School, Pediatric Hematology-Oncology Department between 1990-2005 with the diagnosis of acquired aplastic anemia were reviewed retrospectively 14 of the patients were females and 24 were males aged between 6 months-14 years (average 8 years) with a median age of 6 years. Aplastic anemia was associated with infection (one hepatitis A, one CMV, one EBV, one parvovirus, one chicken pox infection) in 5 patients. It was drug induced in 2 patients (one exposure to topicaly used gunpowder for gale treatment and one exposure to chloromphenicol) and unknown etiology in the others. Hemoglobin values were 2.3-8.9 gr /dl (mean value 5.9), leucocytes were 200-6600/mm3 (mean value 3200), platelets 1000-53000/mm3 (mean value 23000) and reticulocyt counts were O% and 1.8% (mean count 0.39%). Bone marrow aspiration was performed to all of the patients and all were found hypocelluler.Eleven patients received ATG treatment in combination with cyclosporin-A and G-CSF. Two patients developed fever and rash; one patient

experienced an anaphylactic reaction during courses of treatment with ATG. Three of the patients treated with ATG responded 6 to 8 months after treatment Three patients received a second course of ATG 6 months after the first one,but still were unresponders. One case secondary to CMV infection was in remission at 12 months after treatment with G-CSF and Cylosporin-A.;and another one developed spontaneous remission at 8 months after diagnosis.

Abstract: 301 Poster: 208

IRON CHELATION THERAPY AND SERUM FERRITIN LEVELS IN PATIENTS WITH THALASSAEMIA

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Background: Every unit of blood contains about one fifth of a gram of iron, so a thalassaemic person who receives 20 units of blood a year, also receives about 4 grams of iron a year. There is no natural way of getting rid of this iron, so it has to be stored. Desferal`s only function is to prevent problems due to iron overload. The best guide to our iron overload and our need for Desferal is the serum ferritin level. Ferritin is the substance that hold iron in the stores in the liver and other tissues. Aims: The aim of the study was to evaluate the effect of Des-feral therapy, according to ferritin level in patients with thalassaemia in our Thalassaemic Unit in Sofia folowing five years of treatment. Methods: 35 patients (16 males and 19 females), mean age 22 years old participated in this study. The patients received regular transfusions of red cells every 3 to 4 weeks to maintain hemoglobin concentration above 9 g/l. Patients underwent regular Desferal therapy five days a week. We assessed efficacy of the Desferal treatment by periodic measurement of serum ferritin concentration. Serum ferritin was determined by immunoradioimetric assay. Results: The serum ferritin levels in patients with thalassaemia were hihger than in a normal person. The best balance was reached when the ferritin level was about 1000 to 1500 ng/ml. The initial mean serum ferritin level was 2600 ng/ml which dropped to 1400 ng/ml at the end of the study. A serum ferritin level lower than 1000 ng/ml was achieved in 5,8 % of the patients. There was a statistically significant decrease in the values of ferritin levels after chelation treatment compared to values of ferritin prior the initiation of the therapy. In 2 patients advanced cardiac siderosis resulted in heart failure and life-threatening arrhythmia. Conclusions: The results showed the effectiveness of Desferal in reducing or stabilizing the body iron load, as assessed by serum ferritin levels in our thalassaemic patients. The strongest direct evidence supporting the beneficial effect of Desferal and low ferritin level in haemosiderotic heart disease was the reversal of myocardiopathy in these cases.

Abstract: 302 Poster: 209

GENOTYPIC CHARACTERISTICS OF PATIENTS WITH BETA THALASSEMIA

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Thalassemia is an autosomal recessive inherited hemolytic anemia characterized by defective synthesis of globin chains. It is classified into two main groups as alpha and beta thalassemia according to which of the two globin chains are defective. The prevalence of beta thalassemia gene in the world population is approximately 3%. The prevalence in our country is 2%. Mutational analysis of 50 patients with beta thalassemia, who have been followed-up in Hematology-Oncology department of our clinic, is carried out by Beta Globin Strip Assay method. 44 (88%) of our patients were diagnosed as thalassemia major and 6 (12%) as thalassemia intermedia. There was consanguinity between the parents in 19 (28%) of the patients. When birth places of the parents were assessed, we found out that, Marmara Region covered the highest percentage with 14 patients (28%). 60% of the patients were homozygous while 17 (34%) were mixed heterozygous. In two patients whose mutations could not be determined, DNA sequence analysis was performed and homozygous mutation was identified in codon 15 (TGG› TGA) (Portuguese type). IVS-I-110 mutation was the most frequent mutation in homozygous patients (30%) while IVS I-110 and FSC 8 coexistence was identified in mixed heterozygous patients (8%). IVS I-110 mutation was most commonly encountered in the Marmara region, when the birth places of parents were taken into consideration. In conclusion, it is emphasized that the genetic heterogeneity in terms of thalassemia mutations and prevalent consan-

guinal marriages in İstanbul increase the incidence of the disease.

Abstract: 303 Poster: 210

EVALUATION OF IRON DEFICIENCY IN CHRONIC RENAL FAILURE: THE ROLE OF RETICULOCYTE HEMOGLOBIN CONTENT (CHR)

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Background: Iron deficiency leads the hyporesponsiveness to erythropoietin in hemodialysis patients and results in renal anemia. So, the early detection of iron deficiency is of value for the successful treatment of renal anemia. At present, serum ferritin and transferrin saturation (TS) are recommended for assessing iron deficiency. However, they have a limitation in estimating iron status because the lack of accuracy and precision in dialysis patients. Aim: The reticulocyte hemoglobin content (CHr) has been proposed as a useful tool in iron status assessment. We investigated the accuracy of CHr in comparison to the conventional test. Methods: We selected 130 hemodialysis patients (76 female and 54 male, mean age 55.5¡3/413.6). We measured Hb, reticulocyte, CHr levels (using ADVIA120 autoanalyzer, Bayer Medical, USA), iron parameters (iron, TIBC, ferritin), blood urea nitrogen (BUN) and creatinine. Iron deficiency in this study was defined as a serum ferritin ¡Â 100§¶/L or a TS ¡Â 20. Most patients were in the state of taking oral iron supplements. Results: The mean patient characteristics included Hb 10.0¡3/41.1 g/dL and CHr 33.1¡3/42.0 pg. In 80 patients with normal ferritin and normal TS, CHr was normally distributed with mean 33.7¡3/41.6 pg. Sixteen patients with low ferritin and low TS showed CHr level of mean 31.0¡3/41.7 pg. Eight patients was classified as low ferritin and normal TS (Group 1) and 26 patients as normal ferritin and low TS (Group 2). Group 1 and group 2 showed mean CHr 32.5¡3/42.0 pg and 31.5¡3/41.6 pg. CHr level was more related to TS than serum ferritin. There was no correlation between CHr and BUN or creatinine level. 55 patients (Hb<10) received EPO therapy, and increment of Hb is larger in patients with high CHr than in patients with low CHr. Conclusion: CHr is available in measuring iron status in dialysis patients, especially in patients in iron deficiency with normal ferritin. It is considered that the CHr cut-off value 32 pg is appropriate for the assessment of iron deficiency. Also, CHr might be useful to select an adequate treatment policy in renal anemia and to predict the degree of increase in Hb.

Abstract: 304 Poster: 211

OCULAR ELECTROPHYSIOLOGIC CHANGES IN PATIENTS WITH BETA-THALASSEMIA MINOR

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Background: Anemia is one of the precipitating factors for optic nerve and retinal ischemia. Purpose: To determine the electro-oculography (EOG), electroretinography (ERG) and pattern visual evoked potential (pVEP) responses in patients with beta-thalassemia minor. Methods: Beta-thalassemia minor patients were divided into 2 groups. Group 1 comprised 20 patients with anemia, and group 2 comprised 19 patients without anemia. EOG, ERG and VEP were performed in 39 patients with beta-thalassemia minor. One eye of the patients was included in the study. Results: The mean age of group 1 and 2 were 26.8±7.6 and 25.6±4.5 years, respectively (p=0.91). In ERG, there weren`t any delay in maximal rod-cone responses (p>0.05). Mean scotopic b-wave amplitudes of groups were 96.3±24.8 µV and 81.8±18.1 µV, respectively (p<0.05). Mean photopic b-wave amplitudes of groups were 93.9±16.5 µV and 85.5±18.2 µV, respectively (p<0.05). Flicker cone response amplitude was also reduced in anemia group (p<0.05). The difference between groups for pVEP responses were insignificant (p>0.05). There was no significant difference between groups in the arden index of EOG (p=0.91). Conclusion: Although there is no statistically significant difference in the EOG and VEP responses of beta-thalassemia minor patiens with and without anemia, ERG responses of beta-thalassemia minor patiens with anemia had better results. Further clinical trials on the photoreceptor metabolism and anemia may highlight the role of anemia on the retinal cells of beta-thalassemia minor patients.

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PULMONARY FUNCTIONS IN PATIENTS WITH BETATHALASSEMIA MAJOR

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Objective: To reserch the respiratory functions and the relation to the level of ferritin in patients with beta thalassemia major to whom hipertransfusion and iron chelation was applied. Method: 39 patients with beta thalassemia major were seperated into two groups; A (severe) and O (mild) according to their ages and ferritin levels. K (control) group had 20 healthy children in the same ages. Ferritin levels of both control and patient groups were measured and respiratory functions were investigated with spirometry. The parameters of FVC, FEV1, FEV1/FVC, PEF, FEF25-75 were observed. The type lung disease (obstructive or restrictive) was determined according to these parameters. The ferritin levels and respiratory functions of each groups were compared. Results: the ferritin levels of the three groups were significantly different. When FEV1 values were compared, only A and K groups were significantly different from each other. The parameter of FVC, there was a significantly negative correlation between ferritin and FVC, FEV1, FEV1/FVC, PEF and FEF25-75 parameters were similar in each three groups. Conclucion: The abnormality of respiratory function tests in patients with beta thalassemia major was secondary to hemosiderosis which was a type of restrictive lung disease. This situation was strongly related to their ferritin levels.

Abstract: 306 Poster: 213

EVALUATION OF COGNITIVE FUNCTION IN PATIENTS WITH BETA-THALASSEMIA MINOR

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Background: Beta-thalassemia minor is a common, congenital, and mostly symptomless disease. Deficient synthesis of beta globin subunit of the hemoglobin is responsible for the laboratory findings. As the automatic blood counters are more frequently used in general clinical practice, the number of the diagnosed cases increased. Aim: Previous studies have shown cognitive disorders and their healing at early stages by treatment in especially iron deficiency anemia. We aimed to evaluate the cognitive function in patients with beta-thalassemia minor by means of latency and amplitude of P-300 potentials. Methods: P-300 potentials, age, gender, education status of 39 beta thalassemia minor patients (8 Female, 31 Male) with 24 healthy controls was compared (Table 1). Nutritional etiology was ruled out in patients with anemia. Results: No statistical difference was noted in patients and controls and patients with and without anemia regards to P-300 latency and amplitude. Conclusion: Cognitive dysfunction was not noted in patients with beta-thalassemia minor.

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GENOMIC AND PROTEOMIC CHARACTERISTICS OF A CASE WHO HAVE GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

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In this case study, a female individual and her broth-er`s Glucose-6-Phosphate Dehydrogenase (G6PD) activities and genetic mutations were investigated. According to enzyme analyses complete deficiency of G6PD activity determined on both of the cases. When mutation analyses performed it is found that they are carrying Gd-Medi-terranean mutation at homozygous and hemizygous state female and male respectively. To investigate proteomic properties of enzymes of both cases, the enzymes were partially purified by means of ion-exchange chromatography. After purification, only brother`s enzyme activity were observed and the enzyme kinetics were analysed on this subject. When the findings examined, the KmNADP were found to be different compared to kinetic properties of Gd-Mediterranean. In addition to above investigations the erythrocyte mem-

brane proteins of both cases were studied. The Anykrin and Band 4.1 membrane proteins of female and Anykrin membrane protein of male subjects were observed to be deficient. Although, erythrocyte membrane proteins and G6PD activities have been found to be deficient on both cases, no any hematological abnormality were observed.

Abstract: 308 Poster: 215

THORACIC SPINAL CORD COMPRESSION SECONDARY TO EXTRAMEDULLARY HAEMATOPOIESIS IN THALASSAEMIA INTERMEDIA SUCCESSFULLY TREATED BY LOCAL RADIOTHERAPY AND HYDROXYUREA

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Hydroxyurea (HU) therapy has been proven as an active agent in the treatment of sickle cell disease but its beneficial effects were less and inconstantly manifested in .-thalassaemia. We report a case of splenectomized thalassaemia intermedia (TI) patient of 44-years-old with intrathoracic mass of extramedullary haematopoiesis (EMH) invading the epidural space, diagnosed by magnetic resonance imaging and successfully treated with local radiotherapy and continuous therapy with HU. The treatment with HU in the reported patient induced the disappearance of the ectopic masses and the independence from regular transfusion therapy, without further extraosseous expansion of the haematopoietic tissue and signs of toxicity for at least 2 years. However, until accepted guides for the use of HU in thalassaemia patients will be established, this treatment will be restricted to patients with severe clinical problems such as extended and symptomatic EMH, severe osteoporosis or transfusion-requiring therapy complicated by alloimmunization. Radiation therapy was useful as emergency treatment until HU became effective, was well-tolerated and could be considered as first line therapeutic method in symptomatic EMH from thalassaemia. A screening by imagistic methods of paraosseous localization of EMH should be performed in TI patients with severe impairment of the skeleton, splenectomy, more severe anaemia or in the presence of suggestive modifications of peripheral blood, as the progressive increase of the erythroblasts, reticulocytes and indirect bilirubin, in conditions of a not suitable decrease of the Hb level. The patient presented an association with an indolent, non-progressive lymphoproliferation with T-large granular lymphocytes (LGL) which has been considered as coincidental but important from the diagnostic point of view.

Abstract: 309 Poster: 216

A COLD AGGLUTININ PATIENT WHO HAS MANAGEMENT DIFFUCULTIES

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Cold hemagglutinin disease is a cold autoimmune hemolytic anemia (cAIHA) caused by an autoantibody, such as IgM, directed against the I-antigen present on the surface of erythrocytes. Affected patients show varying clinical presentation ranging from mild to serious hemolytic anemia, episodic hemoglobinuria, acrocyanosis, or other peripheral vaso-occlusive events which are all occasioned by cold exposure. In mild chronic cold agglutinin disease preventing cold exposure usually suffices to avoid disease exacerbation. However, treatment of severe disease is difficult. Splenectomy or glucocorticoids are generally disappointing, but exceptions have been reported. Treatment with alkylating agents, as for example chlorambucil or cyclophosphamide, may be effective in some patients. We argued the investigation and treatmentent approaches related to the treatment procedures of severe cAIHA case that is the refracter of prednisolon, ritixumab and plasmapheresis which this case was evaluated by many different medical centers. A 68 years old male patient was evaluated because of deep pale, coombs positive hemolytic anemia and acrocyanosis. In the laboratory investigation, the protein electrophoresis revealed that the hipogamaglobulinemia, qantitative IgG ve IgM values were under the normal interval, and at the serum immunofixation an uncertain cappa band was seen. At the flow-cytometric analyses of the agranular cells in the periferik blood, 20.6 % lymphocytes was seen, the distribution of the lymphocytes were 65.9 % CD3, 29.2 % CD56, 0.1 % CD19, and at the bone marrow analyses 15.3 % lymphocytes was seen, the distribution of the lymphocytes were 91.7 %

CD3, 0.6 % CD19. Direct coombs, test IgG: 4+, C3d: 4+, Indrect coombs test: pozitive, cold agglutinin was positive at 1/512 titration. Bone marrow aspiration revealed: Hypercellular bone marrow, which shows an eritroid hyperactivity and malign infiltration, wasn`t found. A series of laboratory studies were made on the disease pathophyisology. The T cell domination at the patients` peripheral blood and bone marrow, the nonexistance of B cells, the fact that the serum factor is a reason for the aglutination at the eritrocytes eventhough it was inactivated at the 56 C showed that an another mechanism besides the intervention of hemolysis, Ig and compleman functions. Generally, primery cold agglutinin disease is known as a low-grade lymphoproliferative disease. However our findings make us think that the pathophyisology may be different and, other alternatives should be evaluated except the treatments directed towards the B cells.

Abstract: 310 Poster: 217

EPOETIN ALFA IS A SUITABLE TREATMENT OF ANEMIA ASSOCIATED WITH DIFFERENT HEMATOLOGICAL DISORDERS

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Background: Anemia is a common associated symptom of numerous hematological disorders. Over the last decade, administration of recombinant erythropoietin (epoetin alfa or beta) has become a modern option in its management, however, in clinical practice there still predominates transfusion therapy despite its numerous, persistent risks. Nevertheless, numerous clinical trials have already demonstrated that in patient population suffering from hematological malignancies, epoetin alfa administration results in significant increase of hemoglobin level and improvement of their life quality, or at least in decrease of erythrocytal products consumption. Aims: This communication summarizes the results of post-marketing surveillance of Janssen-Cilag aimed to ascertain the efficacy of treatment with epoetin alfa in patients with different hematological disorders and at the same time to evaluate the impact of this treatment on the quality of their lifes. Methods: Treatment efficacy in separate patients of the population monitored has been evaluated not only according to hemoglobin level increase, but also according to its effect on erythrocytal products consumption needed to control anemic syndrome. Results: Overall, 98 patients were included in this evaluation, average age was 64.76 +- 2.80 years (median 65). Majority representation (overall 72.5%) had patients with different lymphoproliferations-30x chronic lymphocytic leukemia (CLL), 28x multiple myeloma (MM), 8x non-Hodgkin´s lymphoma (NHL) and 5x Waldenström`s macroglobulinemia (WM). Full-extend monitoring, i.e. at least 3-month treatment with epoetin alfa, was passed by 83 (84.7%) patients. Favourable effect of epoetin alfa administration was most often reported in patients with MM (85.7%), WM (80%) and CLL (76.7%). Approximately 3/4 of the patient population monitored showed quality of life improvement, in some cases even without dependence on therapeutic effect achieved. Conclusions: Administration of epoetin alfa within treatment of underlying anemia in numerous hematological disorders represents a suitable alternative to the substitution therapy via erythrocyte transfusions. In the patient population monitored we verified suitability of trial of this therapeutic approach, particularly in patients with different lymphoproliferations, mainly in MM, WM and CLL. Anemia control in such patients often results in quality of life improvement irrespective of results of their underlying disorder treatment.

Abstract: 311 Poster: 218

A PATIENT WITH HEREDITARY SPHEROCYTOSIS DIAGNOSED WITH 58 YEARS OLD: A CASE REPORT

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Hereditary spherocytosis (HS) is a heterogen disorders regarding clinical severity, protein defect, mode of inheritance. Since there is usually a family history, and typical clinical and laboratory picture, the diagnosis is often easily made without additional laboratory tests. We describe here a 58-year-old male patient of HS appyling with fatigue complaint. He was informed that his anemia was caused by vitamin deficiency, and he was given blood transfusion. After the patient admitted to our department, The results of laboratory tests were determined hemoglobin level of 5.2 g/dl, hematocrit level of 19.1 %, WBC count of 5200

/mm3, platelet count of 318 000 / mm3, MCV level of 94 fl, MCH level of 28.1pg, MCHC level of 32.7 g/dl, reticulocyte level of 14.1 (corrected), Total biluribin/ direct biluribin level of 2.64/0.48 mg/dl, LDH level of 328 U/L. On physical examination, he had splenomegaly 15 cm in size. In peripheral smear was seen anisocytosis, poikilocytosis, polychromasia and spherocytes (30 percent). On bone marrow examination was seen hyperactivity of erytroid cell. Direct coombs test was negative and osmotic fragility was increased. Hemoglobin electroforesis was normal. With this finding, the patient diagnosed HS is given to operation of splenectomy. After the splenectomy, the patient is followed without problem. Hemoglobin increased to 8.2 g/dl level. Hereditary spherocytosis is easy to diagnose in childhood but we discuss our case because it won`t be able to diagnose late ages.

Abstract: 312 Poster: 219

THE EFFECT OF THE BETA-THALASSEMIA MINOR ON THE OPTIC NERVE HEAD ANALYSIS

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Background: A variety of ophthalmologic findings have been reported in patients with anemia. Aim: To determine the effect of beta-thalassemia minor on the optic nerve head topographic analysis. Methods: A total of 39 beta-thalassemia minor patients were divided into 2 groups. Patients with iron, folic acid, or vitamin B12 deficiency were ruled out. Group 1 comprised 20 patients with anemia, and group 2 comprised 19 patients without anemia. One eye of each patient was included in the study. All subjects underwent complete ocular examination. Optic nerve head topographic analysis was performed by using a confocal scanning laser ophthalmoscope type Heidelberg retina tomograph (HRT). The following stereometric parameters were evaluated: disc area, area and volume of cup, area and volume of neuroretinal rim, cup shape measure, and mean retinal nerve fiber layer thickness. Results: The mean age of group 1 and 2 were 26.8±7.6 and 25.6±4.5 years, respectively (P=0.91). Their mean disc areas were 2.01±0.3 mm2 and 2.53±0.6 mm2, respectively (P =0.009). The differences between groups for area and volume of cup, area and volume of neuroretinal rim, cup shape measure, and mean retinal nerve fiber layer thickness were insignificant (p>0.05). There was no significant difference between mean intraocular pressure of both groups (p=0.93). Conclusion: In beta-thalassemia minor patients with anemia, optic disc area showed a statistically significant reduction compared to the patients without anemia.

Abstract: 313 Poster: 220

CHEWING GUM PICA IN AN IRON DEFICIENT PATIENT

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Pica, the compulsive eating of non-nutritive substances, has been recorded in every region of the world. A strong association between the pica objects and their complications in the individuals with pica was found in some studies conducted in Turkey. Geophagia (soil eating) is known to be the most frequent use of pica object. However, unusual materials consumed by individuals with pica have been recorded in literature as sporadic case reports. Here in, we report a case of intense and prolonged eating of chewing gum (chewing gum pica) which is a daily consume of about 30 chewing gum per day for 15 years. The patient also had an iron deficiency anemia. A rapid regression of prolonged chewing gum consumption was observed after treatment of iron deficiency. To our knowledge, this is the first case of chewing gum pica associated with iron deficiency anemia

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Abstract: 314 Poster: 221

AUTOIMMUNE HEMOLYTIC ANEMIAS- CERRAHPAŞA EXPERIENCE

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Aim: to describe clinical and laboratory features and treatment responses of cases with autoimmune hemolytic anemias (AIHA) followed in Cerrahpaşa Medical Faculty. Material - Method: 28 cases with AIHA (12 males and 16 girls)) were diagnosed in the period from january 1985 to December 2004. Median age at diagnosis was 18,5

months for males and 66 months for girls. Patients were treated with steroids, IVIG and/or splenectomy. Folic acid supplementation was given to all patients. Results: Paleness was noted in 19 cases and icterus in 18. Splenomegaly and hepatomegaly were palpable in 20 cases. Mean Hb value was 6 gr/dl (Range: 2,2-12 gr/dl.). Mean reticulocyte count was 10,3% with a corrected reticulocyte count of 2%. Mean MCV was 90 fl. Plateled counts were normal except for 3 cases with Evans syndrome. Mean WBC count was 15500/mm3 (Range: 2600-31800/ mm3). Direct Coombs test was found to be possitive in 18 cases. Haptoglobulin levels of 25 cases were decreased. Iron, iron binding capacity, ferritine levels were normal or high in all but 3 cases. Eleven patients had a viral infection in the weeks preceeding anemia. Steroid and IVIG were given in 24 and 11 cases respectively. Splenectomy was performed in 4 cases. Treatment responses were permanent in 13 cases, transient in 2. Nine cases were steroid-dependent. All patients were steroid responsive. Conclusion: AIHA was more common and seen at higher ages in girls. Response to treatment was %50. Chronicity and relapse were frequent. Steroid is still the first choice of treatment.

Abstract: 315 Poster: 222

RENAL TUBULAR FUNCTION IN CHILDREN WITH BETA-THALASSEMIA MINOR

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Background: beta-Thalassemia minor is a common heterozygous hemoglobinopathy that is characterized by both microcytosis and hypochromia. It has been postulated that low-grade hemolysis, tubular iron deposition, and toxins derived from erythrocytes might cause renal tubular damage in adult patients with b-thalassemia minor. Aim: To investigate the renal tubular functions in children with beta-thalassemia minor and to determine its possible harmful effects. Method: The study was conducted on thirty-two children (14 female and 18 male) at the age of 5.8±3.1 years (range 2-14 years) with beta-tha-lassemia minor. The patients were classified as anemic [hemoglobin (Hb) <11 g/dl](Group 1, n=14) and non-anemic [Hb> 11 g/dl] (Group 2, n=18). A control group was formed with 18 healthy children whose ages and sexes match those in other groups (Group 3, n=18). Fractional excretion of sodium (FENa, %), fractional excretion of magnesium (FEMg, %), fractional excretion of uric acid (FEUA,%) and tubular phosphorus reabsorption (TPR, %) were calculated with standard formulas. Urinary calcium excretion (mg/kg/24 h), zinc (Zn) (µg/dl), glucosuria (mg/ dl), beta-2 microglobulin (mg/dl) and N-acetyl-beta-D-glycosaminidase (NAG, U/mmol creatinine) levels were measured through biochemical methods. Results: There was no statistically significant difference among the three groups in terms of the results of FENa (%), FEMg(%), FEUA(%), TPR(%), calciuria (mg/kg/24 h), NAG, urine Zn, glucosuria, urine beta- 2 microglobulin levels ($p>0.05$). Conclusion: We postulate that the children with beta-tha-lassemia minor should be followed to determine tubular dysfunction in the course of aging especially in those populations with high prevalence.

Abstract: 316 Poster: 223

IRON DEFICIENCY ANEMIA IN HOSPITAL PERSONNEL

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Background:Iron deficiency anemia is the most common form of anemia. Aims:In order to evaluate the iron status of our personnel we planned a trial. In iron deficient cases we evaluated the causes underlying it. Methods: Sixty personnel (39 females, 21 males) were enrolled in the study. The mean age of females was 33 years and males was 38 years. Results:The mean hemoglobin concentration was 13.3 g/dl. In females the mean hemoglobin concentration was 12.4g/dl whereas it was 14.25 g/dl in males. Although some of the cases had normal Hb concentrations they had low ferritin levels. When we investigated the underlying causes and sex most of them were females of reproductive age (19/21). Five of them were pregnant and two of them had just gave birth to a child. Four (3 males, 1 female) of them had positive stool occult blood tests and the cause was internal hemoroids detected by rectoscopy. And one chronic gastritis was detected by gastroduodenoscopy. Six personnel had menorrhagia defined by our obstetrics and gynecology department. Three had intrauterine devices. Others had no defined underlying cause for menorrhagia.

Amazingly only 8 of the 21 cases had manifest anemia. Conclusion: We conclude that 21/60 (35%) of our personnel had low ferritin levels. Iron deficiency anemia is an important problem even in hospital personnel that should not be ignored

Abstract: 317 Poster: 224

INVESTIGATION OF HELICOBACTER PYLORI INFECTION IN BETA-THALASSEMIA MAJOR PATIENTS WITH RECURRENT ABDOMINAL PAIN

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Background: Recurrent abdominal pain (RAP) suffers many children especially those affected by .-thalassemia major. The role of Helicobacter pylori is still unclear in children with RAP. Objectives: The aim of present study was the comparison of .-thalassemia major patients and normal controls with recurrent abdominal pain in H. pylori infection. The factors influencing H. pylori prevalence were also investigated. Patients and methods: A series of 50 .-thalassemia major cases (30 females, 20 males; aged 6 to 25 year) and 50 age- and sex- matched controls, both presenting with RAP, were recruited during a period of 18 months. The study participants were drawn through multi-stage random sampling method among those met Apley`s criteria. All the patients and controls were undergone diagnostic esophagogastroduodenoscopy with biopsy. H. pylori infection was confirmed by two histopathological examination on endoscopy sample and rapid urease test. Results: H. pylori infection in thalassemic patients was more common than controls (34/50 (68%) vs. 30/50 (60%)), but this higher frequency was not statistically significant. A clear relationship was found between the prevalence of H. pylori and age, duration of transfusion/chelation programs, pain duration and splenectomy. In contrast, it did not correlate with abdominal pain characteristics, blood group, serum ferritin level and pathology of upper gastrointestinal tract. The most frequent endoscopy abnormality was gastritis (72%). Nausea and heartburn were the leading associ-ated-symptoms. Conclusion: High prevalence of H. pylori infection suggests that H. pylori should be remembered as a likely cause of RAP in .-thalassemia major patients.

Abstract: 318 Poster: 225

BONE MINERAL DENSITY IN BETA-THALASSEMIA MAJOR AND INTERMEDIA

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Background: Thalassemia is a hereditary disease causing reduction in trabecular bone tissue even in well-treated subjects. Objectives: This study is established to assess bone mineral density (BMD) and bone mineral content (BMC) in patients with .-thalassemia major and intermedia, and to determine the biochemical and hematological profiles that may influence bone health. Patients and methods: 106 thalassemic patients (49 major and 57 intermedia) were scanned by daul energy x-ray absorptiometry technique for BMD and BMC. The effects of sex, transfusion/chelation program as well as haemoglobin, calcium, phosphorus, alkaline phosphatase and ferritin serum level on BMD and BMC, were evaluated. Results: The bone values in patients less than 20 y/o were compared with control group, while in patients older than 20 y/o T score was used to define the normal values. In patients younger than 20 yr, considering thalassemia major and intermedia together, BMD and BMC were decreased in lumbar region ($p < 0.05$). Bone values were the subjects to change in parallel with haemoglobin level only in major thalassemia. Conclusion: The results of present survey lead us to concern about the routine bone densitometry to evaluate and follow-up the thalassemic patients and about the appropriate preventative and therapeutic strategies.

Abstract: 319 Poster: 226

AN UNUSUAL CASE OF BARDET-BIEDL SYNDROME PRESENTING WITH PANCYTOPENIA

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Bardet-Biedl syndrome (BBS) is a heterogeneous autosomal recessive disorder characterized by obesity, pigmentary retinopathy, polydactyly, renal malformations, mental retardation, and hypogenitalism. A case of BBS with hematological manifestations is reported. The patient presented with pancytopenia and associated features of the disease including retinitis pigmentosa, polydactyly, slight mental retardation, obesity and hypogonadism. As the disease is usually undiagnosed, hematologists as well as other internal medicine specialists should be aware of this relatively rare syndrome which can involve the hematopoietic system.

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CASE REPORT OF A HOMOZYGOUS BETA THALASSEMIA PATIENT WITH HYPERSPLENISM EXPERIENCING FEBRILE NEUTROPENIC EPISODE

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Splenomegaly which actually has a great variety of causes, results in unsuitable hypersplenic sequestration. Leucocytes and thrombocytes which are sequestrated in the spleen may continue their normal life span and may join the blood stream slowly in infectious and traumatic conditions when necessary. Neutropenic fever due to hypersplenism in non malignant diseases is described in very rare conditions. Especially as in thalassemia major leading to hypersplenism/splenomegaly it is known to be a cause of leucopenia and susceptibility to infections but there is no report about a homozygous thalassemic/ hypersplenic patient experiencing febrile neutropenia without the interaction of any medication used. We present a 16 years old nonsplenectomised homozygous beta thalassemia patient having cytopenias for about one year, not related with any drug use. After a time that her ANC became 1.0 x 109/L, she experienced a FUO continuing 4 days, with all of her blood, urine and stool cultures negative, described as neutropenic fever. Therapy was started with sefepim and amicacin immediately together with G-CSF 30 mU/d. She became afebrile after 3 days, her condition improved and ANC raised to 3.2 x 109/L, so the therapy was modified to amoxicillin-clavulonic acid p.o. after 3 afebrile consecutive days. The patient was splenectomised after 3 months and cure was obtained for the cytopenias. Fever in non splenectomised thalassemia major patients should raise the suspicion of neutropenic fever for prompt treatment plan, as can be seen in this rare case report.

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MOLECULAR CHARACTERIZATION OF B-THALASSEM-IA GENES IN ROMANIAN POPULATION

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b-Thalassemia is a worldwide inherited disorder characterized by a reduction or complete absence of a b-globin expression. Comparing to Mediterranean countries, b-thalassemia in Romania are uncommon, but without an efficient diagnostic approach, especially prenatal diagnosis, in a few years b-thalassemia will be a serious health problem. By this reason we evolve this study based on efficient diagnostic strategy for obtaining fast results. Hematological data were collected with automated cell counters (Coulter). Quantitation of hemoglobin was done by cation exchange HPLC and by agarose gel electrophoresis. Analysis of b-thalassemia mutations was based on sequential PCR amplification of most of the b-globin gene and running on denaturing gradient gel electrophoresis of amplification products. Definitive characterization of mutations in samples identified with shifted DGGE patterns was performed ARMS-PCR and/or PCR-restriction enzyme analysis methods. Fifty patients with b-thalassemia were included: 43 cases with heterozygous b-thalassemia and 7 cases with homozygous b-thalassemia. The spectrum of b-thalassemia mutations in our population is very heterogenous. DNA anlysis of 57 b-thalassemic chromosomes revealed 10 different mutations (in frequency order): IVS I-110 (23chr), cd 39 (8chr),

IVS I-6 (7chr), IVS II-745 (6chr), IVS I-1 (5chr), -87 (2chr), cd 5 (2chr), cd 6 (2chr), cd 51 (1chr), polyA (1chr). The most frequent mutations were: IVS I-110 (G/A)[40,35%]. These results show that the origin of b-thalassemia in Romania is Mediterranean as we expected, except cd 51 discovered only in Hungarian population (3.13%). Prenatal diagnosis of thalassemias has given a new dimension to the prevention of these, but in order to implement this, a knowledge of the mutations and the incidence of these, is essential. This work was supported by grant 217 / 2003 VIASAN.

Abstract: 322 Poster: 229

IMPROVED SURVIVAL OF CONGENITAL DYSERYTHROPOIETIC ANEMIA TYPE-II

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We presented a case of congenital dyserytropoietic anemia diagnosed with hypersplenism symptoms. One year ago, a 74-year-old man was admitted to hospital because of weakness, jaundice and darkness of urine. Physical examination revealed jaundice and hepatosplenomegaly. Blood analysis showed pancytopenia (hemoglobin:5.3 g/dL, WBC count: 2800 cells/mm3 and platelet count: 67000 cells/mm3), hyperbilirubinemia, increased LDH and decresed haptoglobin levels. Direct and indirect Coombs` tests were negative. Abdominal ultrasonography confirmed hepatosplenomegaly. Bone marrow examination was revealed specific findings for congenital dyserytropoietic anemia type II (CDA-II) that increased early erythroblasts, erythroid hyperplasia, megaloblastoid changes, multinuclearity of mature erythroblasts. Patient was diagnosed CDA-II and hypersplenism. Splenectomy was performed. Anemia, leukopenia and thrombocytopenia improved. Although congenital dyserythropoietic anemia generally presents in infancy or adolescence, our patient diagnosed at 74-year-old and splenectomy spared from transfusion reqiurement.

Abstract: 323 Poster: 230

GROWTH FAILURE IN CHILDREN WITH THALASSEMIA MAJOR

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Growth failure in children with thalassemia major has been attributed to hypoxia, desferrioxamin toxicity, bone disorders, hyper transfusion, and high ferritin levels and also with endocrine disabilities like hypogonadisam, delayed sexual maturation, hypothyroidism, GH deficiency. We analyzed the height of 16 children with blood transfusion dependent homozygous beta-thalassemia. All the children receive transfusion at the level of hemoglobin between 80 and 85 g/l every month in amount approximately 25 - 30 ml/kg weight. Most of the children aged 7-8 years have a normal height; only one child has a height on the third percentile. The linear growth started to decrease from l0th year in the most of children and it falls bellow the third percentile after the age of 15 in children without spontaneous or induced puberty. The height of children with spontaneous or induced puberty is between 35 and 75 percentile. Conclusion: A significant percentage of children with thalassemia major show growth retardation as they progress toward puberty.

Abstract: 324 Poster: 231

PAINFUL CRISES IN ADULTS WITH SICKLE CELL SYNDROMES: EXPERIENCE OF THE INTERNAL MEDICINE DEPARTMENT OF A PROVINCIAL HOSPITAL

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INTRODUCTION The prevalence of homozygous sickle-cell anemia in Greece (HbSS) is estimated to be 27/100,000. Although the prevalence of HbS gene is <1% countrywide, in certain regions it can reach 15%. The prevalence of sickle-cell thalassemia (HbSâ-thal) is much higher, due to the highly prevalent â-thalassemia gene (~ 8%) throughout Greece. The prefecture of Viotia, northwest of Athens, where our hospital is located, is considered among the regions where HbS is highly prevalent GOALS To study the location and the intensity of pain, as well as the

factors precipitating acute painful crises of sickle-cell syndromes in adults MATERIALS AND METHODS During a 5yr period (June 2000 to May 2005), 34 patients with sickle-cell syndromes were seen in our Emergency Room, resulting in a total of 72 admissions. Of those, 28 cases were due to HbSS and 44 to HbSâ-thal RESULTS During pain crises, the most commonly involved sites were the back, legs, arms, chest and abdomen, typically with more than one site being involved. In order to evaluate the intensity of pain, a 3 level pain scale (mild-moder-ate-severe) was used, while pain management followed the 3-step "analgesic ladder" recommended by WHO. Of the 28 HbSS painful episodes, pain was mild in 12% and pain relief has been achieved by non-narcotic analgesics. In 59% pain was moderate and treated with weak opioids + NSAIDs, while in the remaining 29% of the crises pain was severe and required treatment with strong opioids + NSAIDs. Respectively, in pain crises of HbSâ-thal, mild pain occurred in 26%, moderate pain in 58% and severe pain in 16%. The median duration of hospitalization was 3.8 days. Precipitating factors were infections (37%), exposure to cold weather (27%), dehydration (12%), extreme physical exercise (7%), physical or psychological stress (6%), alcohol withdrawal (2%), hypoxia (2%), while the cause for the 7% remained unidentified. On a 5yr basis, during the 2-month period January-February, when temperatures reach lowest levels, the number of painful episodes admitted to our service increased by 112%. A less significant increase of 19% was seen cumulatively in July-August, reflecting the increased number of dehydration cases due to high temperatures. CONCLUSIONS It is well known that painful crises are the leading cause for hospitalization of patients with sickle-cell syndromes. Thus, it is important for health care providers handling such cases to be adequately trained in providing analgesia. Additionally, as frequency of acute pain episodes is strongly related to the exposure to precipitating factors, the health care providers must provide counseling on necessary precautions and protective measures, and recommend vaccinations against influenza and pneumococcus.

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SLEEP PATTERN IN PATIENTS WITH BETA-THA-LASSEMIA MINOR

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Background: Although chronic anemia causes many symptoms, patients with thalassemia minor are usually symptomless. In patients with chronic anemia sleep disturbance, anxiety and sadness are some of the most common symptoms. There is little knowledge about sleep structure in patients with chronic anemia such as thalassemia. The aim of this study is to investigate sleep structure in patients with beta-thalassemia minor. Methods: Sixteen drug-free subjects with beta-thalassemia minor and sixteen sex-and age-matched healthy subjects were enrolled in the study. None of the seventeen subjects suffered from any psychiatric or neurologic disorders. All subjects slept in the laboratory for two consecutive nights. The first night served as an adjustment night, the second night results were used for analysis. Their sleep patterns were compared with healty normal controls (Table 1). Results: The patients with beta-thalassemia minor showed increased total sleep time, sleep period time and increased percentage of REM sleep. The percentage of stage 4, REM latency and sleep efficiency are decreased. Conclusion: In patients with beta-thalassemia minor, the disturbances of sleep continuity was found as a prominent finding in this polysomnographic study.

Abstract: 326 Poster: 233

P-WAVE DISPERSION AND QTC DISPERSION IN IRON DEFICIENCY ANEMIA

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Background: Anemia is a known risk factor for ischemic heart disease. It has been reported that anemic condition accompanies electrocardiographic abnormalities. Prolonged P-wave and corrected QT dispersion (QTc) are known to predispose the heart to atrial and ventricular arrhythmias, respectively, they have not been enough examined in the patients with iron deficiency anemia. Methods and Results: We have performed electrocardiography on 30 patients

with iron deficiency anemia before and after iron therapy (2 male, 28 female; mean age, 40.1 ± 10.0 years). Maximum P-wave duration, minimum P-wave duration, maximum QT interval and minimum QT interval have been measured from 12-lead ECG at a paper speed of 25 mm/sec. P-wave dispersion is defined as difference between the maximum and the minimum P-wave duration. OT dispersion is defined as the difference between the longest and shortest QT intervals. QTc dispersion has been also calculated by using Bazett`s formula. After iron supplementation, the average hemoglobin level has increased from 9.30±1.5 g/dl to 13.4±1.2 g/dl (p>0.001). P-wave dispersion (36±13 msn v. 35±13 msn, p>0.05) and QTc dispersion (50±15 msn v. 48±13 msn, p>0.05) had no statistically significance different in the patients with iron deficiency anemia before and after iron therapy. Conclusion: The present results suggest that iron deficiency anemia has not caused the increase in P wave dispersion and QTc dispersion.

Abstract: 327 Poster: 234

SPLENOMEGALY AND SECONDARY HYPERSPLENISM IN A PATIENT WITH CHRONIC TORSION OF THE PEDICLE OF WANDERING SPLEEN

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If the spleen is not fixed within the left subphrenic space, it gradually passes into the lower abdomen, where is much more exposed to trauma. Torsion of the splenic pedicle could also takes place causing infarctus necessitating an emergency surgery. Venous stasis causes splenomegaly and sometimes secondary hypersplenism. The autors present 16,5 year old girl with torsion of the splenic pedicle of the wandering spleen for 7200, in spite of which the patient had neither splenic infarctus nor splenic vein thrombosis, possibly due to thrombocytopenia, but had splenomegaly and secondary hypersplenism with pancytopenia causing bleeding, sideropenic anaemia and mild jaundice. After treatment with iron the patient was submitted to splenectomy which resulted in almost immediate rise in the number of all blood cells, even in thrombocytosis.The autors suggest early surgical treatment of the wandering spleen, preferebly splenopexy, before serious complications take place when in a majority of patients splenectomy had to be performed. Accessory spleens, if present, should be also removed.

Abstract: 328 Poster: 235

DEVELOPMENT AND CONTROL OF PREGNANCY AND PUERPERIUM OF A WOMAN AFTER BEING DIAGNOSED MEDULLAR APLASIA

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The case of a twenty-eigth-year-old-woman was studied and diagnosed as congenital medullar aplasia, the patient was monitored from the start of pregnancy and every month until birth. After delivery she was monitored every fifteen days during forty five days, performing the following tests: red corpuscles count, white corpuscles count, blood platelets count, medium corpuscular volume (MCV), hemoglobin determination, leukocyte formula (under microscope) ad time Quick. The hematological numbers, which were totally altered at the start of gestation, were corrected by using ferrous fumarat and folic acid, which was helped with desmopresina acetate, not being necessary to prescribe neither corticoids nor replacement through blood transfusion. The hematological results had been corrected by the time of delivery consequently, there were not any physiological nor physchological complications in both mother and baby`s health.

Abstract: 329 Poster: 236

TRIMETHOPRIM-SULFAMETHOXAZOLE (TMP-SMZ) RELATED APLASTIC ANEMIA

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Aplastic anemia is a disorder that characterized by peripheral blood pancitopenia with bone marrow hipocellularity. Although, most cases of

aplastic anemia are idiopathic, there are many causes such as radiation,drugs and chemicals, infections, PNH etc, in etiology. Drug-induced aplastic anemia occur either a dose-dependent or idiosyncratic mechanism. We presented a case with aplastic anemia related TMP-SMX. 28 year-old-woman was admitted to hospital because of weakness and fatigue. CBC was established pansitopenia. Bone marrow aspiration and biopsy showed hiposellularity with predominance of fat cells. Aplastic anemia was diagnosed. Patient`s history had no chemicals, radiation exposure or preceding viral illness. Drug history was elicited and repeated use of TMP-SMX was observed. After treatment with Antithymocyte globulin (5 mg/kg per day) and cyclosporine (5 mg/kg per day - 4 days), hematologic and clinical recovery were obtained.

Abstract: 330 Poster: 237

FLOW CYTOMETRY CD 45-SSC GATE IN DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF MEGALOBLASTIC ANEMIA

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Flow cytometry CD 45-SSC gate is standartly used in the assessment of bone marrow and give information about cell distribution in the bone marrow. We use this gate routinely in patients who have the diagnosis of megaloblastic anemia and we observed a specific appearence when we examined them. Because of the specific appearence we observed in CD 45-SSC gate of patients with megaloblastic anemia we decided to assess if we can use this gate in diagnosis and differential diagnosis of megaloblastic anemia. We assessed the bone marrow of 23 patients with megaloblastic anemia with flow cytometry CD45-SSC gate added to aspiration and biopsy. All patients had cobalamin deficiency and folic acid was within normal ranges. FITC was used as a fluorochrome. All patients had this specific appearence in normoblasts. Normoblasts were seen upwards giving a shape like a shoe (Figure 1). We also examined the bone marrow of patients with anemia due to reasons other then cobalamin deficiency. Diagnosis in this group were 1 non Hodgkin lymphoma, 3 Hodgkin lymphoma, 2 aplastic anemia, 2 iron deficiency anemia and 1 acute non lymphoblastic leukemia in remission. None of them showed the appearence seen in megaloblastic anemia group. We also examined the bone marrow after at least 3 months therapy in 6 of patients with megaloblastic anemia and observed that the specific appearence seen before therapy disappeared. Figure 1. CD 45-SSC gate in a patient with megaloblastic anemia before and after therapy We think this specific appearence is due to excessive DNA in normoblasts of patients with megaloblastic anemia and can be confused with the plasma cells in multiple myeloma. As a result, flow cytometry CD 45-SSC gate may have a role in diagnosis and differential diagnosis of megaloblastic anemia.

Poster

COMPARISON OF NEUTROPHIL GENE EXPRESSION PROFILES IN PATIENTS WITH SICKLE CELL DISEASE TO NORMAL CONTROLS: EVIDENCE FOR INFLAMMATION AND METABOLIC ACTIVATION

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Although sickle cell disease (SCD) is a single gene disorder resulting from a Glu›Val substitution at residue 6 of the ß chain of human adult hemoglobin, it shows remarkable phenotypic heterogeneity with expression of the disease varying from very mild cases with survival into the 6th or 7th decade to a very severe course with frequent pain episodes and life threatening complications resulting in severe organ damage and early mortality. The frequency of painful episodes varies greatly among patients with similar genotypes. Chronic inflammation is a well-established feature of SCD even at steady state, and the degree of inflammation tends to correlate with disease severity. Elevated neutrophil count, as a reflection of the overall inflammatory state, has emerged as a poor prognostic indicator and has been associated with adverse outcomes including stroke and early mortality. To further delineate the role of neutrophils in the pathogenesis of various complications and in overall disease severity in SCD, we analyzed the gene expression profiles of neutrophils from 4

patients with "severe" disease (>3 vaso-occlusive episodes [VOE] per year), 8 patients with "mild" disease (<3 VOE/year) and compared these to each other and to the gene expression profiles of neutrophils from 5 age and sex matched, healthy, non-sickle cell, Afri-can-American individuals. Granulocytes were separated from freshly collected venous blood using Histopaque (Sigma diagnostic) density gradient separation. Total RNA was extracted immediately after cell separation by using Rneasy Mini Kit (Qiagen). Two micrograms of total RNA was converted to double stranded cDNA (ds-cDNA) by using SuperScript Choice System (Invitrogen). In vitro transcription was performed on the ds-cDNA using Enzo RNA transcript labeling kit. After the fragmentation, labeled RNA was hybridized to a set of oligonucleotide arrays (HG U133A, Affymetrix, Santa Clara, CA) and the data was analyzed with the Microarray suite 5.0 software (Affymetrix). In general, a larger number of genes were differentially expressed between mild patients vs controls compared to that of severes vs. mild patients. Out of the differentially expressed genes (314 genes for severe vs. control, 718 genes for mild vs control), those with greater than two fold expression were analyzed with the geneMAPP software for localization into biological pathways. Genes related to cellular proliferation, growth and maintenance, DNA repair, DNA replication, and cell cycle progression were expressed at significantly higher levels in SCD patients compared to controls. The most notable finding was the significantly higher expression of genes leading to NFkB activation and inhibition of apoptosis: IAP-1 (increased 6.7 fold and 4.7 fold in mild and severe patients respectively), IkB (decreased 0.14 fold and 0.3 fold), Apaf-1 (decreased 0.4 fold in mild), and c-jun (decreased 0.4 fold in severe); Traf-2 (TNF receptor associated factor-2; increased 3.5 fold and 2 fold); genes in the MAPK signaling pathway: ERK-2 (increased 3.5 fold and 2-fold), MAP2K3 (increased 3.5 fold and 2 fold). These data show that neutrophils in SCD patients are activated with higher expression of genes in the TNF, MAPK, and NFkB pathways consistent with an inflammatory state. Since neutrophil apoptosis is considered critical for the resolution of inflammation, delayed or inhibited apoptosis of neutrophils would further maintain this inflammatory state even during the so-called

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Abstract: 332 Poster: 239

TREATMENT OF RELAPSED IDIOPATHIC THROMBOCYTOPENIC PURPURA WITH THE ANTI-CD20 MONOCLONAL ANTIBODY RITUXIMAB

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BACKGROUND AND AIMS: Rituximab is a chimeric anti-CD20 monoclonal antibody active against normal and malignant B cells.Idiopathic thrombocytopenic purpura has antibody bind to platelet and causes platelet destruction in the reticuloendotelial system. METHODS: To investigate this, we treated 5 patients with rituximab 375 mg/m2 i.v. every 7 days for 4 times. All patients had active and symptomatic autoimmune thrombocytopenia that had relapsed or was refractory to standard therapies. RESULTS: Treatment was well tolerated and no acute or delayed toxic events were recorded. Response criteria were as follows. Complete remission (CR): normalization of thrombocyte count for at least 30 days. Partial remission (PR): an increase of thrombocytes to above 30.000/ mm3 for at least 30 days. Minor response (MR): any increase above 30.000/ mm3 for less than 30 days but more than 10 days. No response (NR): failure to achieve any of the above responses. Four patients achieved CR, one patients in PR. Four CR patients are ongoing; One patient in CR relapsed after 6 months.One patient died because of intracranial bleeding. SUMMARY/CONCLU-SIONS: Rituximab appears to be a promising immunotherapeutic agent for the treatment of autoimmune thrombocytopenias.

Abstract: 333 Poster: 240

INHERITED THROMBOPHILIA IN PATIENTS WITH HEMOPHILIA

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Background: Despite that a good correlation usually exists between the clinical severity of the disease and plasma clotting factor activities, a small proportion of patients with severe hemophilia exhibit a milder clinical presentation. The aim of this study was to assess the significance of prothrombotic risk factors in hemophilic patients. Methods: We have investigated the prevalence of the factor V G1691A (FV Leiden) mutation, factor

II G20210A variant, C677T and A1298C methylene tetrahydrofolate reductase (MTHFR) gene single nucleotide polymorphisms (SNPs) in Turkish patients with hemophilia. Results: Of 28 patients none of them were found to be a carrier of FV Leiden and prothrombin G20210A gene mutations. The allele frequency of MTHFR C677T and A1298C gene polymorphisms were found as 39.3% and 28.6% respectively. Three of the severe hemophilic patients, two with homozygote MTHFR C677T polymorphism and the other with double heterozygote MTHFR gene polymorphisms had a delayed onset of first symptomatic bleeding episode. Conclusion: Our results suggest that the milder bleeding diathesis is occasionally seen among Turkish hemophilic patients which may be explained by the low prevalence of concomitant expression of highly prevalent prothrombotic risk factors in the general population such as factor V G1691A and prothrombin G20210A mutations. However influence of MTHFR gene polymorphisms on clinical phenotype needs to be further investigated before definite conclusions are made.

Abstract: 334 Poster: 241

RECOMBINANT FACTOR VIIA FOR SEVERE GASTROINTESTINAL BLEEDING AFTER BONE MARROW TRANSPLANTATION IN A CHILD WITH CIRRHOSIS AND ACUTE LYMPHOBLASTIC LEUKEMIA

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Treatment of hemophilia with inhibitors has been of major concern and recombinant factor VIIa (rFVIIa) is an alternative for management of hemophiliac patients with inhibitors. Additionally, it has been used off-label for the treatment of massive life-threatening hemorrhage associated with various bleeding situations. Gastrointestinal bleeding is a potentially fatal complication of myeloablative chemotherapy presenting with massive life-threatening hemorrhage that progresses into hemorrhagic shock in bone marrow transplantation (BMT) recipients. The transfusions of blood products including platelet concentrates, packed cells, and fresh frozen plasma are the essential therapy in the management of hemorrhage. However, transfusions may be inadequate in the treatment of some patients with persistent bleeding. Herein, we describe a 7-year-old boy with acute lymphoblastic leukemia (ALL), cirrhosis, and severe intractable gastrointestinal bleeding after BMT and succesful treatment with rFVIIa. A 7-year-old boy with cirrrhosis, familial renal glucosuria and relapsed ALL underwent allo-sibling bone marrow transplantation. He developed grade II acute GVHD on day +7 and sinusoidal obstruction syndrome on day +9. On day +16, he experienced hematemesis, hematochesia, and melena. At this time, physical examination showed jaundice, ascites, hepatomegaly, purpurae, pallor, hypotension, and tachycardia. The results of laboratory investigation revealed Hb 6.1 g/ dl, WBC 2000/ml, Plt 23000/ml, and elevated liver transaminase levels. Prothrombin time (PT) 12.1 sec. (normal: 10-14 sec.), activated partial thromboplastin time (aPTT) 44 sec. (normal: 25-38 sec.), fibrinogen 206 mg/dl (200400 mg/dl). In order to treat GI bleeding, supportive therapy was administered including the infusions of fresh frozen plasma (30 ml/kg), apheresis platelets (8 units), and packed cells (36 ml/kg). Unfortunately, bleeding persisted. rFVIIa was administered at a dose of 90 mg/kg/ dose via intravenous route at hours 0 and 2. The bleeding was controlled by rFVIIa infusion. We observed no further bleeding despite he had still severe thrombocytopenia. No more blood product transfusions were required. No adverse event was seen after the use of rFVIIa. In order to control massive GI hemorrhage that observed in BMT setting, we experienced an excellent result with the use of rFVIIa in this child with ALL. Since it is functional at a key point in the clotting cascade, rFVIIa seems to be a novel therapeutic option for patients with massive bleeding conditions.

Abstract: 335 Poster: 242

VON WILLEBRAND DISEASE TYPE 2N (NORMANDY) IN TWO FAMILIES

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von Willebrand disease type 2N (Normandy) is due to a defect in the factor VIII binding site of

von Willebrand factor (vWF), which is transmitted in autosomal recessive fashion. Patients resemble those with mild hemophilia and have low levels of factor VIII. We report here two families with the diagnosis of vWD type 2N. In the first family, 3 siblings, two females and one male, were 59, 67 and 69 years of ages, respectively. They did not have a history of spontaneous bleeding episodes. All had only prolonged bleeding after dental extractions. The older female patient described prolonged post-partum bleeding. Their parents had consanguinity (first-degree cousins). There was no history of bleeding disorder in the family. Their hemostasis screen showed a normal bleeding time and a prolonged activated partial thromboplastin time (aPTT) at 55.4 s, 63.7 s, 50.7 s (normal range 28-40 s), respectively. Factor VIII levels were reduced at 14.73 %, 4%, and 10.72% (normal range 60150%) and ristocetin cofactor activities were at 134%, 75%, and 138% (normal range 50-150%), respectively. Platelet aggregation studies including ristocetin induced platelet aggregation were normal. In the second family one female patient, 50 years of age, was studied. She had posttraumatic hematoma and postpartum prolonged bleeding episodes as well as spontaneous bleedings such as epistaxis and metrorrhagia. Their parents had consanguinity (first-degree cousins). Her sister and brother had no bleeding manifestations. A female and a male offspring of her mother`s brother have been diagnosed as hemophilia. Her hemostasis screen showed normal bleeding time, prolonged aPTT (56.4 s), decreased FVIII level (6%, normal range 60-150%), vWF antigen 100% (normal range 50-150%), ristocetin cofactor activity of 303% (normal range 50-150%). Platelet aggregation studies including with ristocetin were normal. In both families the mutation analyses of vWF gene showed a homozygous transition (2446 C>T) in exon 19 of the vWF gene at the FVIII:C binding site of the vWF subunite, predicting the exchange of arginine at position 816 to triptophane. Thus, a diagnosis of a vWD type 2N was made. Recognition of vWD type 2N is clinically important, particularly, for the treatment of bleeding episodes and for the aspect of correct genetic counseling. A diagnosis of vWD type 2N should be considered in patients with FVIII deficiency and a bleeding disorder that is not clearly transmitted as an X-linked disorder or in those who respond incompletely to hemophilia A treatment.

Abstract: 336 Poster: 243

CLINICAL PROFILE OF THE LATE HEMORRHAGIC DISEASE OF THE NEWBORN IN A DEVELOPING COUNTRY

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Late hemorrhagic disease of the newborn (HDN) occurs either due to lack of vitamin K prophylaxis or as a manifestation of an underlying disorder or idiopatically anytime in the first year. Between February 2002 and April 2005, 9 infants admitted to our Center with 10 attacks of late HDN. The age at presentation was median 46 (26111) days. All infants were breast-fed and born at term from healthy mothers. One of the babies had meconium aspiration; the rest had uneventful perinatal histories but 4 had no vitamin K prophylaxis. The patients presented with irritability (n:3), grunting (n:2), poor sucking (n:3), vomiting (n:4), hematemesis (n:1), hematochezia (n:1) bruising (n:3), oozing from venipuncture site (n:1), bulging or full fontanel (n:7), convulsions (n:6) diminished or absent neonatal reflexes (n:6) and coma (n:1). All seven infants with intra-cranial bleeding underwent surgical drainage or decompression craniectomies. Two patients with prolonged jaundice were evaluated for metabolic disease (one had galactosemia, one had probably propionic acidemia). There was no surgery related mortality but one survived only for two days with ventilatory support following surgery. Only one of the six survivors had severe neurologic sequel. Two patients with metabolic disease died in the following month due to underlying disease. Prothrombin time (PT) and partial tromboplastin time (aPTT) were prolonged in all the patients. Late HDN frequently presents with intracranial hemorrhage, leading to high mortality and morbidity. Vitamin K prophilaxis of newborns must not be neglected. Physicians must be aware that late hemorrhagic disease may be the manifestation of an underlying disorder.

Abstract: 337 Poster: 244

THE INCIDENCE AND CLINICAL IMPORTANCE OF LUPUS ANTICOAGULANT IN CHILDREN WITH RECURRENT UPPER RESPIRATORY TRACT INFECTION

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Background: Lupus Anticoagulant (LA) is one of the major antiphospholipid antibodies. The presence of LA is an important cause for delayed aPTT test in children. However, it does not increase the risk for bleeding. Diagnosis of LA in asymptomatic children is usually incidental. It is generally determined when the aPTT test is delayed after an upper respiratory tract infection (URTI) or during the screening tests before surgery. The presence of this antibody is usually temporary and is not correlated with clinical status. Aim: In this study, we tried to reveal the incidence and clinical importance of LA positivity in Turkish children who have recurrent URTI. Patients and Methods: One hundred and sixty five patients (77 females, 88 males; mean age: 5 years) who visited the clinics of pediatrics and otolaryngology between June 2004 and April 2005 were enrolled in this study. These patients had recurrent URTI and were candidates for tonsillectomy/adenoidectomy. One hundred and twenty healthy children were enrolled in the study as the control group. LA screening was per-formed by diluted Russell`s Viper Venom Time (dRVVT) test. Results: LA positivity was present in 8 (4.8%) cases of the patient group while only 2 (1.6%) cases were LA (+) in the control group (p=0.03). The annual frequency of infection was not different significantly between the LA (+) and (-) patients (7.5/year and 6.9/year respectively). The mean age of LA (+) patients was significantly lower than LA (-) patients (p=0.02). While 55.8% of the patients had adenoid hyperthrophy, the LA (+) patients had no adenoid hyperthrophy (p=0.009). aPTT test was delayed in 6 of 165 patients (3.6%). Two of these 6 patients were LA (+). These results show that the sensitivity of the aPTT test for revealing LA positivity is low while its spesifisity is high. LA positivity disappeared in 7 of 8 patients (87%) 2 months after the diagnosis. Conclusion: As a conclusion LA positivity incidence is higher in young children with recurrent URTI than healthy children. However LA positivity does not lead to bleeding and/or thrombosis and it disappears in a short time. It is clear that patients who have LA positivity causing delayed aPTT can be operated without any bleeding problem.

Abstract: 338 Poster: 245

RECOMBINANT ACTIVATED FACTOR VII FOR SEVERE GASTROINTESTINAL BLEEDING AFTER CHEMOTHERAPY IN CHILDREN WITH LEUKEMIA

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Recombinant activated factor VII (rFVIIa) is a major alternative for management of hemophiliac patients with inhibitors. Additionally, it has been used off-label for the treatment of massive life-threatening hemorrhage associated with various bleeding situations such as Glanzmann thorombastenia, solid tumors and leukemia. Here in, we describe four cases with leukemia and febrile neutropenia and severe intractable gastrointestinal (GI) bleeding controlled by rFVIIa. Three children with acute lymphoblastic leukemia (ALL) and one with chronic myelomonocytic leukemia (CMML) were treated with rFVIIa for GI bleeding. Gastrointestinal bleeding was diagnosed in neutropenic sepsis period in all of our patients. All of the patients had thrombocytopenia and elevated prothrombin time, but only one patient has elevated activated partial thromboplastin time. In order to treat gastrointestinal bleeding, supportive therapy was administered including the infusion of fresh frozen plasma, apheresis platelets, packed cells and vitamin K. Unfortunately, bleeding persisted and rFVIIa was administered at a dose of 50 mg/kg per dose via intravenous route at 2 hour intervals for a total three doses to control bleeding. Except for the patient with CMML, gastrointestinal bleeding was controlled in three. No adverse event was seen after the use of rFVIIa. In order to control massive GI bleeding, we experienced a good result with the use of rFVIIa in our patients. As it is functional at a key point in the clotting cascade, rFVIIa seems to be a novel therapeutic option for patients with massive bleeding conditions, including children with leukemia.

Abstract: 339 Poster: 246

ARG 506---GLN MUTATION IN FACTOR V AND RISK OF THROMBOSIS DURING PREGNANCY

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A resistance to the anticoagulant activity of protein C (APC), most frequently due to a point mutation in the factor V gene, Arginine 506--- Glutamin (Arg 506--- Gln, the factor V R506Q), represents the most common genetic cause of thrombophilia. Venous thromboembolism is a life threatening complication of pregnancy. Little conclusive information is available on the actual risk of venous thrombosis in pregnant women with thrombophilia. To determine the pregnancy-related risk of venous thromboembolism in women with thrombophilia, modified activated protein C resistance (m-APC-R), protein C, free protein S, antithrombin III, antiphospholipid antibodies (APLs), lupus anticoagulant (LA) and factor V Arg 506--Gln detection by PCR allele specific oligonucleotide hybridization technique were assessed in 30 pregnant women developed venous thromboembolism during pregnancy, 30 normal pregnant women (served to be a control group) as well as 20 age matched non pregnant women from normal population. In this study, factor V R506Q was detected in 50% (13.3% were homozygous & 36.7% were heterozygous), APLs in 6.6%, LA in 3.3% and free protein S deficiency in 6.6% in pregnant women with VTE (when they were present as single defect). Factor V R506Q was the only thrombophilic defect detected in normal pregnant women and it was 16.7% and all were heterozygous. The odds ratio for pregnancy-associated with VTE in the presence of factor V R506Q was 9.5 (95% CI, 3.8 - 49.6). 50% of pregnant women who had past history of obstetric complications -in this study- had factor V R506Q (37.5% were heterozygous and 12.5% were homozygous). From this study we can conclude that factor V R506Q is associated with an increased risk of venous thrombosis during pregnancy and it plays a critical role among females with obstetric complications.

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DECREASED VON WILLEBRAND FACTOR SPECIFIC ACTIVITY IN PATIENTS WITH OTHERWISE NORMAL PRIMARY HEMOSTASIS TEST RESULTS

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Mild mucocutaneous bleeding manifestations are relatively frequent in otherwise healthy persons and definition of significant mucocutaneous bleeding is a debatable issue. vWF:Ag/RiCof Act ratio is used to differentiate between type 1 and type 2 von Willebrand disease subtypes. An increased ratio means presence of relatively dysfunctional von Willebrand molecules with a lowered specific activity. Approximately 60% of all patients referred for platelet aggregation testing with suspicion of a primary hemostasis defect have been found to have normal aggregation tests, von Willebrand antigen (vWF:Ag) and ristocetin cofactor activity (RiCof Act) levels (normal patients). We compared vWF:Ag/RiCof Act ratio of these cases with healthy blood donors. Mean±SD value of the ratio was 0,92±0,27 in healthy controls (N= 81) and it did not differ between O (N= 34) and non-O (N= 47) blood groups although both vWF:Ag and RiCof Act levels were significantly lower in blood group O. Five and 95 percentile values were 0,5 and 1,4 in the control group. The ratio was 1,26±0,61 for the normal patients (N= 55). Five and 95 percentile values were 0,8 and 2,4 in these cases. The ratio was significantly lower in the normal patients ($p< 0,001$). Decreased specific activity of vWF in patients with otherwise normal primary hemostasis test results is an interesting finding that should be confirmed by further studies.

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CLINICAL CHARACTERISTICS OF ADULT VON WILLEBRAND DISEASE PATIENTS FOLLOWED IN A UNIVERSITY HOSPITAL

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The aim of this study was to determine clinical characteristics of von Willebrand disease (vWD) patients followed in the Hacettepe University Medical Shool, Division of Hematology between 1993-2004. This is a retrospective study based on patient records. Age of diagnosis changed be-

tween 1-60 years. Mean age of diagnosis was 17,6±13,7. Eleven patients had been classified as type 3 vWD, 8 patients as type 1 VWD, 5 patients as type 2 vWD and 3 patients as type 2B vWD. No subtype was determined in 6 patients because of missing data. Gum bleeding was the most common (30,3 %) complaint in first admission. Majority (83,3%) of female patients had menorrhagia. One patient with type 3 vWD had recurrent hemarthroses and 2 cases including this case had chronic arthropathy. In vitro bleeding time had been studied by PFA-100 device in 17 patients. The sensitivity of CADP was 94,1% and CEPI was 100%. Skin bleeding time was measured with template method in 19 patients and sensitivity was 84,2 %. Desmopressin test was applied to 9 patients and response was observed 5 patients with type 1 vWD, 1 patient with type 2 vWD. No benefit was observed in 3 patients with type 3 vWD. Blood transfusions were made to 81,8 % and factor replacements were made to 63,6 % of type 3 vWD patients. These rates were higher than other subtypes.

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EVALUATION OF OUR CASES DIAGNOSED AS GLANZMANN THROMBASTENIA

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Glanzmann thrombasthenia is an autosomal recessively inherited bleeding disorder, associated with absence or dysfunction of glycoprotein IIb-IIIa in platelet membrane. The specific laboratory finding is the normal platelet count and morphology, prolonged bleeding time and abnormality of aggregation with all the platelet agonists except ristocetin. In this study, we evaluated the clinical findings in 19 patients followed-up in our clinic between the years 1990-2004. 11 (56%) of the patients were male and 8 (44%) were female. Median age on admission was 5 years (1-10 years) and median age at diagnosis was 3 years (1 month-6 years). There was consanguinity between the parents in 10 patients (55%). The platelet count at diagnosis was 186000-488000/mm3 (median 266000/mm3), bleeding time was 14-30 minutes (median: 20 min). Definite diagnosis was established by the absence of CD41 and CD61 by flow cytometric method in one patient and by the abnormal aggregation test with adrenalin, collagen and ADP but normal aggregation with ristocetin in other patients. As the presenting symptom, purpuric lesions were seen in the following months after delivery in 10 (55%) of the patients. There were recurrent epistaxis episodes in 4 (40%) of the patients: 4 of them (40%) had gingival bleeding and 1 had bleeding after intramuscular injection. During the follow-up period, intracranial bleeding occurred in 2 of our patients after cranial trauma, and one of them died despite the surgical intervention. 2 of our patients with the complaint of severe menorrhagia are still under follow-up. In cases of severe bleeding (surgical intervention, intracranial bleeding, and prolonged menorrhagia) we tried to use leukocyte-filtered platelet suspension derived from a single donor. One of our patients with recurrent menorrhagia responded to FVIIa preparation. In case of mild and moderately severe bleeding, we tried to prevent platelet alloimmunization as much as we can by using local therapies, antifibrinolytic agents and oral contraceptives. Even tough Glanzmann thrombasthenia, the second most common type of bleeding diathesis registered in our Pediatric Hematology-Oncology Clinic, is a severe disorder, by meticulous follow-up, we can prevent most of the problems.

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rFVIIA USE IN OUR CASES OF CONGENITAL FACTOR VII DEFICIENCY

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Between the years of 1990-2004, 17 cases of Factor VII deficiency have been followed in our clinics. 10 of the patients were male and 7 female. The ages ranged between 2 months and 16 years. FVII activity of 8 patients was found to be below 5% and 9 patients above 5%. Patients with severe bleeding episodes were given rFVIIa after the year 2002. In 22 bleeding episodes of 4 patients rFVIIa was given in doses of 15-35 mcg/kg with 4-6 hour intervals. Out of bleeding episodes 5 (23%) were gingival bleeding, 9 (41%) were epistaxis, 5 (23%) were intracranial bleeding one was suspect of intracranial bleeding. The duration of rFVIIa treatment ranged between 1 to 21 days. rFVIIa was administered between 2 to 84 doses. No al-

lergic reaction and trombotic complication was observed during rFVIIa treatment. There was no treatment resistant case.

Abstract: 344 Poster: 251

ANTITHROMBIN III, D-DIMER LEVELS AND INFLAMMATION MARKERS IN LUNG CANCER PATIENTS

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Background: The mechanisms of the coagulation/ fibrinolytic system have been well studied in cases of malignancy. In some cases it is found affected but the mechanism through which it is affected is not always well known. Disseminated intravascular coagulation and enhanced fibrinolytic activity is believed to be due to tissue factors released from the tumor. In some cases the activity of various coagulation factors, fibrinolytic factors and natural anticoagulants are good prognostic factors for the malignant disease and relapse. Aim: The aim of this study was to investigate the activity of antithrombin III and the levels of d-dimers in patients with lung cancer and the possible correlation with inflammation markers. Methods: We studied 50 subjects: 30 patients with lung cancer of different histological types between 50 and 80 years old and 20 healthy age-matched individuals. We measured antithrombin III, d-dimers in plasma and CRP and Ferritin in serum. The lung cancer patients` group was examined shortly after they were diagnosed, before any treatment. We used IL-ATIII kit, IL D-dimer kit and ELISA Olympus kits for Ferritin and CRP according to the manufacturers instructions. Results: The levels of antithrombin III in the lung cancer patients were lower (71.89%) than those of the control group (84.7%) and that was statistically significant (p=0.046). D-dimers, on the other hand, were significantly higher (663.13ng/ml) in the same group, in comparison to the healthy group (290.05ng/ml) (p<0.05). Antithrombin III levels in urine in the patients` group were not detectable in all samples, while d-dimers` levels in urine were higher and plasma levels were also higher. There was no difference in d-dim-ers` levels, between the different types of cancer. CRP and Ferritin values did not differ in the 2 groups. Conclusion: Antithrombin III is reduced in patients with lung cancer. Follow up of the patients could prove possible use of this parameter as index of disease activity. D-dimers were significantly higher in the patients` group. This could also be a useful marker of disease progress

Abstract: 345 Poster: 252

A CASE OF MILD FACTOR- VII AND STORAGE POOL DEFICIENCY

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Hereditary factor VII deficiency is a very rare autosomal recessive disorder of coagulation that occurs throughout the world. Combined deficiency of factors VII and VIII, and combined deficiency of factors VII and IX have been reported. We have been unable to find any report about combined deficiency of factor VII and storage pool deficiency. A 21- year- old male patient, was seen at our hospital with complaints of mild pain, discoloration and swelling on his gluteal region. It was learned that he had a surgical operation "sinus pilonydalis" in another hospital about one year ago. Wound healing and bleeding control has prolonged after the operation. The laboratory tests, including complete blood count (CBC), routine biochemical tests (included liver function tests) and bleeding time were normal. In repeated tests of PT was 16 -17 seconds (control PT<12 seconds), and the aPTT was normal. Hypogranular/agranular platelets on peripheral blood smear were observed. Abdominal ultrasound was normal. Chronic changes due to large subcutanous bleeding were seen on sacral computed tomography.A diagnosis of factor VII deficiency was thought. The one-stage stage factor VII assay using factor VII-deficient plasma as substrate was reduced at 47% (Normal:70% to 130%). Factor VIII, factor IX, von Willebrand factor, ristocetin cofactor and factor XI levels were normal. Platelet aggregation tests were abnormal with ADP, collagen, ristocetin and epinephrine whereas aggregation was normal in response to arachidonate. When patient`s serum was mixed with normal serum (50% proportional), the PT normalized. Results, therefore, eliminated the presence of an antibody to factor VII in patient`s serum. At the

result of these findings, factor VII deficiency and storage pool deficiency was diagnosed in the patient. It`s useful to obtain a bleeding history as well as performing routine clotting tests (including CBC, bleeding time, PT and aPTT) in patients who are prepared for surgical operations. Replacement products must be ready for immediate use if required in moderate or major surgical operations in such cases

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SUCCESFUL USE OF RECOMBINANT FVIIA (NOVOSEVEN) IN THE MANAGEMENT OF CARDIAC SURGERY UNDER CARDIOPULMONARY BYPASS IN A PATIENT WITH CONGENITAL FVIIA DEFICIENCY

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Introduction: Factor VII (FVII) deficiency is a rare congenital coagulation disorder characterized by spontaneous bleeding episodes in severely affected patients, and bleeding after surgical challenge or trauma in the midly affected. Cardiac surgery is occasionally complicated with massive blood loss, refractory to standard hemostatic interventions. Nevertheles cardiac surgery with FVII deficiency is rare and there is only a few case reports in the literature. We present a successful pediatric cardiac surgery case under cardiopulmonary bypass (CPB) with mild FVII deficiency. Case Report: A 4 year-old girl diagnosed with secundum atrial septal defect was referred to our hospital. Preoperative routine coagulation tests showed prolonged prothrombin time (PT) at 16.3 s (reference 11-14s) and normal activated partial thromboplastin time (aPTT). Factor assay analysis revealed an isolated decrease in FVII levels (% 43.5) (normal range: % 60-150). Prior to surgery recombinant factor VIIa (r FVIIa) was administered at 20 mcg/kg, and then continued with 3 doses every 2 hours. This low dose of FVIIa was efficient in this case probably due to the fact that the deficieny was not severe. The defect was repaired with a dacron patch without any bleeding complications. Conclusion: We conclude that under appropriate replacement therapy with rFVIIa concentrate, pediatric cardiac surgery can be performed safely in children with congenital FVII deficiency.

Abstract: 347 Poster: 254

RACCOON EYES

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A 15-month old girl was admitted to hospital with the compliants of bruising around the eyes for 10 days. She had one month history of abdominal pain and accompained by fever and vomiting since last one week. Physical examination demostrated pallor, periorbital ecchymoses (raccoon eyes) and bilaterally mild proptosis (Fig 1). She also had a left sided abdominal mass, which was 5x8 cm in diameter. The laboratory investigation revealed hemoglobin level 6g/dL, white cell count 10.000/mm3, and platelet count 34.000/mm3. Urinary vanillymandelic acid level was high. Bilateral bone marrow aspiration revealed infiltration with neuroblasts. Abdominal CT showed a left surrenal mass (5x7cm in diameter) which was diagnosed as a neuroblastoma on histopathologic examination. Neuroblasts and rulo formations are seen on bone marrow aspiration. The metastatic involvement of the periorbital tissues has been described and the resultant proptosis and orbital ecchymosis has been given the tag of `raccoon eyes`. Orbital metastases can be found in up to 20% of children with stage IV neuroblastoma. The raccoon eyes appearance associated with neuroblastoma is probably related to obstruction of the palpebral vessels by tumor tissue in and around the orbis. This case represents a classical presentation of this appearance. There are a multitude of differential diagnoses for the presentation of periorbital oedema and ecchymosis, e.g. child abuse or trauma, infection of the soft tissues associated with a spreading dental infection and an allergic reaction. Other systemic causes to consider include; myxoedema, other neoplasias such as lymphoma or haematological coagulopathies such as haemophilia. Figure 1. A photograph of the child`s face shows bilateral periorbital ecchymosis (raccoon eyes) and bilateral mild proptosis.

Abstract: 348 Poster: 255

CARRIER DIAGNOSIS OF HEMOPHILIA A BY THE ARMS METHOD OF PCR

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The human factor VIII gene, with 186 Kb length composes about %0.1 of the X-chromosome. This gene with 26 exones after splicing its 25 introns, produces mRNA with 9 Kb length after translation it produce protein with 265 KD comprising 2351 amino acids. The disorder of factor VIII gene includes point mutation, deletion, duplication and inversion which lead to a bleeding disorder. Hemophilia-A are studied. A blood sample was drawn from affected individuals and after DNA purification by proteins-K and boiling methods with ARMS Technique (one of PCR techniques), the situation of factor VIII gene for number 18 and 24 exones were studied. For this reason specific primers designed and synthesized by DNA synthesizer. DNA derived from samples of patients were treated with specific primers then amplified by a specific method with 25 cycle thermocycle instrument. After electrophoresis through agarose gel, the product of PCR was analysed by UV transluminator. In this study the affected individuals because of mutation in 1941 situation of number 18 and 2209 of number 24 exones were deter-mind. After determination of mutation, carrier detection were performed which this procedure was successful and used first for carrier detection in Iran.

Abstract: 349 Poster: 256

IMPLANTATION OF TOTAL HIP PROSTHESIS IN A HEMOPHILIC PATIENT-IS ANTITHROMBOTYC PROPHYLAXIS NECESSARY?

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Hemophilia A is an inherited disorder with a disturbed coagulation system as a result of deficient f-r VIII. In a 48-year old hemophilic patient with initial f-r VIII level 4%, nine months after traumatic injury of the right hip (fra prethrochanterica femoris dex.), a total hip prosthesis was implanted. At the time of surgery he was anti-HCV and anti-HIV negative and no circulating inhibitors were encountered. The supportive therapy was sustained of a purified freeze-dried human f-r VIII (Immunate-Baxter) in doses 50 IU kg-1 body weight twice a day. The initial dose of 3000 IU was administrated 2 hours before the operation and every 12 hours afterwards in the following 3 days. A high f-r VIII level was achieved an hour after the administration (129-160%).From the fourth postoperative day on, the dosage was adjusted according to the recoveries of f-r VIII in the next 6 weeks, with an overall factor consumption of 77000 IU. The first 7 postoperative days, until the patient was completely immobilized, an antithrombotic prophylaxis was carried out using LMWH (20mg Clexane s.c. once a day). The operation and the whole postoperative period passed without any complication. The 21-st postoperative day, the patient was verticalized and a slight physical therapy was started. This is the first case in Macedonia of a successfully implanted total hip prosthesis in a hemophilic patient with a short-term follow-up. Spontaneously ankylosed hips and other joints are very frequent in hemophilic patients, so a much longer follow-up is still needed to ascertain the efficacy of this surgical procedure in hemophilia. We think that a low-dose antithrombotyc prophylaxis is necessary in the first postoperative days but we didn`t find similar information in literature.

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RESULTS OF INHIBITORY DEVELOPMENT IN PATIENTS WITH HEMOPHILIA A AND B FROM A SINGLE CENTRE IN THE SOUTH-EAST TURKEY

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Background: Development of inhibitory is a recent problem for hemophilia patients because of reduction of viral spreading with modern factor concentrates. The frequency of inhibitory formation is 20-30% in severe hemophilia A and 3% in hemophilia B in western countries. Spesific inhibitory is very rare in mild and moderate cases with

hemophilia. It is showed that the frequency of inhibitory in Turkey is similar to western countries. Aims:We aimed tostudy frequency of inhibitory in 33 patients with hemophilia that attended to our center, in Diyarbakır province, in the southeast part of Turkey. Methods: Twenty-nine patients were hemophilia A and 4 patients were hemophilia B. The age was between 4 months and 50 years. In hemophilia A group, 5 patients were severe,10 patients were moderate and 14 patients were mild hemophilia. In hemophilia B group 1 patient was severe, 3 patients were moderate. Results:Only 1 patient with severe hemophilia A has a inhibitory for factor VIII. There were not a inhibitor formation In 4 hemophilia B patients. Summary/conclusion: It is known that age, severity of hemophilia, mutation type, antigenic type of factor concentrates and MHC genes are responsible for inhibitory formation.and fresh frozen plasma causes lower risk for inhibitory. Although only severe and moderate hemophilia patients taken into consideration, in our study the frequency of inhibitory is lower than the other part of Turkey. We think that the possible causes of low incidence of inhibitory are; low factor replacement frequency, many of patients are mild and moderate type of hemophilia, usuallly using of fresh frozen plasma replacement for bleeding episodes and type of mutation.

Abstract: 351 Poster: 258

EVANS SYNDROME: ISTANBUL UNIVERSITY EXPERIENCE

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Evans syndrome is a rare disorder characterized by immune thrombocytopenia, Coombs positive hemolytic anemia and occasional neutropenia. Aim: To analyze the clinical and laboratory features of our Evans patients. Method: The data of 7 Evans patients diagnosed and treated between 1985-2005 were analyzed retrospectively. Results: Out of 7 patients, 5 were female and two were male, median age at diagnosis was 5 years (min 11 months- 12 6/12 years). All patients had petechia, purpura or ecchymoses except for one. The laboratory findings at diagnosis were as follows: Platelets: median 9000/ mm3 (0-52.000/ mm3), Hemoglobin: 7.7 g/dl (6-11,8 mg/dl), white blood cells: 12.000/ mm3 (2400-25600/ mm3)., reticulocyte 6.7% (3,5-9,2%). Direct Coombs test was positive in all patients. The median follow up time was 4 years (3 months-19 years). The treatment regimen was IVIG in one patient, IVIG+steroids in 2 patients, IVIG+steroids +cyclosporine in 3 patients, IVIG+steroids +cylosporine and azathiopurine in 1 patient. Splenectomy was performed in 4 patients who were unresponsive to treatment with 3 or 4 drugs. After splenectomy, complete remission could be achieved in 2 patients, one patient required cyclosporine, the other unresponsive patient was lost to follow up. Conclusion: Evans syndrome is a rare but potentially mortal disorder, where the management is difficult and sometimes refractory. Despite multidrug regimens with IVIG+steroids +cylosporine+ azathiopurine and anti-CD20, the results are not very encouraging. Therefore frequent follow-up of patients is often required.

Abstract: 352 Poster: 259

THIRTEEN GLAZMANN CASES: ONE CENTER EXPERIENCE

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Glanzmann thrombasthenia (GT) is an inherited disease characterized by severely reduced or absent platelet aggregtion in response to many physiologic agonists because of abnormalities of platelet glycoproteins IIb and/or IIIa. Consanguinity raises the possibility of the occurence of the disease. Aim: to study the clinical and labaratory details of patients and to compare the treatment modalities in diffrent bleeding sites. Methods: The data of 13 GT patients who were diagnosed and treated at the İstanbul University, İstanbul School of Medicine, Department of Pediatric Hematology and Oncology between 1990-2005 were evaluated retpospectively. Symptoms at presentation, onset of symptoms, consanguinity, family history, platelet function tests, platelet glycoprotein levels, platelet antibodies, treatment results during bleeding or invasive procedures were analyzed.. Results: The median age of all patients were 105 months with an interval of 43-192 months. Out of 13 patients, 5 were female (38%), 8 male (62%). Consanguinity was positive in 11 patients. Family history of 8 patients re-

vealed bleeding disorders within family members. The onset of bleeding disorder was 3 months (min:1, max:24 months). The leading complaint was mucosal bleeding in 77%, nose bleeding in 33%, gingival bleeding in 23%, bleeding at the injection site in 7% and gastrointestinal system bleeding in 7%. In 7 patients, flowcytometric analysis could be perfomed, which revealed 2 type I patients, 2 type II patients and 3 type III patients. The major complaint of our cases were mucosal bleeding, nose bleeding and gingival bleeding and all patients were anemic at presentation. Eight patients required multiple erithrocyte transfusions. Antiplatelet antibodies were positive in 3 patients out of available 5 patients. During invasive procedures (tooth extraction in 4, renal calculi removal in one, appendectomy in one), platelet transfusions, transecsamic acide, DDAVP, rVIIa ve fibrin glue were used alone or in combination and hemostasis could be achieved. Median follow up time is 30 months (min:1, max:180 months), 6 cases were lost to follow up. One patient with latex allergy was lost due to excessive bronchospasm and anaphylaxis. Conclusion: GT is a rare entity, but in some cases fatal outcomes may be observed. With efficient follow up and rapid intervention, the bleeding of GT patients can be kept under control.

Abstract: 353 Poster: 260

rFVIIA USE IN OUR PATIENTS WITH GLANZMAN TROMBASTENIA

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24 cases with Glanzman Trombastenia was followed in our clinics between the years of 1989-2004. 12 of the patients were male and 12 were female. The ages ranged between 3 months to 16 years. In bleeding episodes of our patients trombocyte suspension and topical agents for mucosal bleedings have been used until 2004. After 2004 in 4 bleeding episodes of our 3 patients rFVIIa was used at a dosage of 90-120mcg/kg. Out of the bleeding episodes 2 were epistaxis and 2 were gingival bleeding. The number of dosages of rFVIIa varied between 2-7. In an episode of epistaxis additional trombocyte suspension was required. No allergic reaction and trombotic complication was observed during rFVIIa treatments.

Abstract: 354 Poster: 261

A RARE AND MISDIAGNOSED BLEEDING DISOR-DER-HEREDITARY BERNARD SOULIER SYNDROME, FOUND IN A FAMILY IN MACEDONIA

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Bernard-Soulier syndrome (BSS) is a rare hereditary autosomal bleeding disorder characterized by prolonged bleeding time, giant platelets, thrombocytopenia and disturbed agglutination of platelets in response to ristocetin. The disease is due to an absence or abnormality of the platelet membrane glycoprotein (GP) Ib-IX-V, the receptor for von Wilebrand factor. We present a case of a 30year old female patient with bleeding problems from her early childhood. Initially she was treated as idiopathic thrombocytopenic purpura and then as Morbus Von-Wilebrand. When her bleeding problems worsened with massive genitourinary hemorrhage and epystaxis, more extensive investigations were done. BSS was suspected on the ground of morphologic changes of platelets: evidence of giant platelets on peripherial blood smear. The platelet count was about 40x10(9)/l, the bleeding time was prolonged. The platelet functional tests showed normal agglutination with ADP but abnormal agglutination with ristocetin. The plasma level of vWillebrand factor was normal. Blood samples from the patient and several members of her family, who also had minor bleeding problems, were sent in Hopital Henri Mondor, Creteil in Paris, where the diagnosis of BSS was confirmed. The immunoelectron microscopic study of the platelets had shown: normal level of vWilebrand factor in alpha granules, normal GPI-b III-a expression and distribution, profound decrease of GP I-b IX immunolabeling, virtually absent from platelet plasma membrane. The ultra structural examination confirmed the uniformly large size of platelets. Any further therapies, predominantly corticosteroids (that had already made many side effects) were stopped in this patient. As a conclusion we can say that very careful investigation must be done for appropriate diagnosing a bleeding disorder. BSS is a rare congenital condition where we don`t have many treatment options. Treatment with cortikosteroids is completely unuseful. Substitution with platelet

concentrates is recommended in case of a severe bleeding episode.

Abstract: 355 Poster: 262

FACTOR VII DEFICIENCY PRESENTING WITH RECURRENT INTRACRANIAL BLEEDING AND RFVIIA PROPHYLAXIS

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Factor VII deficiency is an autosomal recessively inherited bleeding disease with a frequency of 1/500000. Intracranial bleeding may be seen in the newborn and infancy period. In this report, a patient having recurrent intracranial bleedings with the diagnosis of Factor VII deficiency that is treated and given the prophylaxis of rFVIIa is discussed. The patient was a 40 months old boy who was given fresh frozen plasma at the 2 and 4 months of age. He had subdural hematoma, intracranial bleeding and hydrocephalus when he was 5 months of age and ventriculoperitoneal shunt operation was done. Replacement therapy with rFVIIa was given. When he was 11 months of age he had 2 attacks of intracranial bleeding and right cerebellar hematoma was diagnosed at that time. He was treated with 14 days of rFVIIa replacement therapy, without the need of any surgical intervention. In the 15th month he had a 3rd attack of intracranial bleeding and after that bleeding he had left occipital lobe hematoma. The valve of his shunt was replaced. He was treated with 14 days of rFVIIa replacement therapy. During 15-26 months of age the patient was given fresh frozen plasma twice a week for 6 months and then continued with 10 ml/kg of fresh frozen plasma once a week. He had 4 minor mucosal bleeding attack. At the 26th month he had the 4th intracranial bleeding attack and subarachnoid hemorrhage that is treated with 14 days of rFVIIa replacement therapy. No surgical intervention was done. After the 4th attack, once a week rFVIIa prophylaxis was started. He had 4 minor mucosal bleeding during the prophylaxis. At the 34th month due to his social security problems the patient could not get the drug and he had the 5th bleeding and had subarachnoid bleeding in the 35th month. Both replacement therapy and prophylaxis were restarted. The patient is being followed for 3 months with rFVIIa prophylaxis and he had no new bleeding episode.

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VITAMIN B12 DEFICIENCY AS ONE OF THE MAJOR CAUSES OF POST-NEONATAL VITAMIN K DEFICIENCY

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Background: Vitamin K (VK) is essential for activation of clotting factors II, VII, IX and X. The classical VK-deficiency bleeding (VKDB) presents from days two to seven of life in full-term infants. However, poor intake or malabsorption of vitamin K may also produce the coagulation defect causing hemorrhagic disease in postneonatal period. Vitamin B12 deficiency is prevalent in our region (Sanliurfa Province, at the southeast region of Turkey) and it may cause malabsorption of other nutrients such as VK, because of atrophy in the intestinal mucous membrane. Longstanding systemic antibiotic receiving may also be the cause of VK deficiency by disturbing VK2 synthesis by intestinal bacterial flora. Aim: The aim of this study was to determine the major causes of post-neonatal vitamin K deficiency in our region, and to demonstrate whether vitamin B12 deficiency was an important cause of VK deficiency. Methods: Between January 2002 and June 2005, 51 children with postneonatal VK-deficiency were investigated prospectively. The diagnosis of VK-deficiency was made in a child if PT and PTT were prolonged together and responsive to intravenous 3-5 mg VK treatment, while fibrinogen level was in normal limits. Results: The mean age of the children was 11.73±7.91 (1-30) months; 41.2% were female and 58.8% were male. 93.6% of children were breast-feeding and 6.4% were feeding with formula or other foods. 70.6% of children were brought to hospital with bleeding symptoms, while 29.4% were brought with other symptoms and VK deficiency was diagnosed after the investigation due to bleeding after injections or interventions for blood analysis. In neonatal histories of children, 88.2% of children have not received VK, while it is not known whether VK were received in 11.8 % of children. Bleeding sites were injection sites (27.8%), skin (ecchymoses, hematoma) (19.4%), gastro-intestinal tract (19.4%), nose (13.9%), intracranial region (8.3%), circumci-

sion site (5.6%) and mouth (5.6%). When children were investigated according to underlying disorders, 35.3% of children had diarrhea more than 7 days, 13.7% had malnutrition, 66.7% of children had received least one systemic antibiotic more than 7 days before come to our clinic. Mean PT was 70.41±41.96 (17.0-165.0) seconds, mean PTT was 120.86±84.30 (39.0-240.0) seconds, and mean hemoglobin level was 8.72±2.91 (2.50-13.9) g/dL. Vitamin B12 deficiency (< 200 pg/mL) were diagnosed in 84.6% of children (severe deficiency in 54.5% [vitamin B12 levels between 30-100 pg/mL] and more severe deficiency in 18.2% [vitamin B12 < 30pg/ml] of children). Mean vitamin B12 level was 101.32±104.90 (<30 pg/mL-547 pg/mL). Conclusion: These results showed that VKDB is an important problem also in post-neonatal period of childhood in our region, and prophylactic use of VK should be continued. Our results also demonstrated that vitamin B12 deficiency is an important cause of VK deficiency in infancy, either by impairing absorption or impairing nutrition due to lack of appetite.

Abstract: 357 Poster: 264

SUCCESSFUL BILATERAL CATARACT AND CIRCUMCISION OPERATION PERFORMED IN A HEMO-PHILIA-A PATIENT WITH INHIBITORS BY USING RECOMBINANT FACTOR VIIA

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Prothrombin complex concentrates (PCC), active prothrombin complex concentrates (APCC; FEIBA) or recombinant Factor VIIa (rFVIIa; Novoseven) are safely used for the treatment of hemorrhages in hemophiliac patients with inhibitors or during the interventions performed in these patients. A hemophilia-A patient with inhibitors in whom bilateral cataract operation and circumcision were successfully performed by rFVIIa administration was presented. Case: The 13 year old male patient had been diagnosed with severe Hemophilia-A by the detection of a FVIII level below 1% in the factor assay performed due to echhymoses in his body when he was 6 months old. The inhibitor level of the patient who developed bilateral cataract during the follow-up period was determined as 2.95 BU; however the cataract operation had to be delayed due to the absence of an adequate increase in his factor VIII level despite the 2000 U factor replacement administered in July 2002. The patient was readmitted to the hospital for operation in October 2002. However, the operation was delayed again since a safe level of factor VIII wasn`t achieved with Factor VIII replacement. The patient was excluded from follow-up for approximately 2 years. In August 2004, the patient was hospitalized due to echhymosis in the scrotum, and his factor VIII level was measured as 1% and the VIII inhibitor level as 88 BU. IV steroid treatment was initiated in the patient at a dose of 2 mg/kg, with the factor VIII replacement intended at a level of 100 U/kg. 2 doses of 90 microgram/kg of rFVIIa were administered at a two-hour interval due to catheterization for plasmapheresis and subsequently, plasmapheresis program was carried out. The inhibitor level was measured as 25.6 BU after the first plasmapheresis. Factor VIII level of the patient whose FVIII inhibitor level declined to 15.4 BU with these treatments, didn`t exceed 3%. 120 microgram/kg rFVIIa was administered to the patient prior to operation and maintained during the 1st and 2nd days of the operation every 2-3 hours at the same dose. At this operation, right eye small incision cataract extraction and posterior chamber intraocular lens implantation were performed under general anesthesia. A month later, cataract operation was performed in the other eye together with the circumcision operation. A 3-grade increase was achieved in visual acuity of both eyes. Here, the cataract operation together with the circumcision operation performed in a hemophiliac patient with inhibitors was presented, demonstrating that rFVIIa which has been started to be used also in other fields other than hemophilia patients, can be used safely in operations.

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PSYCHOGENIC PURPURA

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Psychogenic purpura is a rare syndrome manifesting itself bleeding from mucosal and skin surfaces, but hemostatic screening tests are completely normal. The disease symptoms may include paroxysmal abdominal pain, nausea, vomit-

ing, joint pains, headache, epistaxis, gastrointestinal hemorrhage, bleeding from eyes and ears. There is no eye bleeding reported in the Western literature, but seven such cases have been reported in Turkey. In cases of psychogenic purpura, dissociative reactions, psychogenic traumas in childhood, symptoms of conversion and hysteria have been reported. In April 2005, a 20-year-old patient was admitted to our outpatient clinic with the complaints of bleeding from eyes, ears and nose. These bleedings last for 15-20 minutes and repeats at least 10 times a week in the last 6 months. Her bleeding complaints started two years ago after a serious psychological trauma. This psychological trauma insisted and she noted that her bleeding symptoms have been exaggerated after psychologically stressful conditions. We also observed one of these bleeding attacs in the examination room.. Physical examination was completely normal. In ophtalmological examination there was no source of bleeding and also there was not any sign of trauma to the eyes. In otorhinolaryngoscopic examination there was no lesion that can cause bleeding. Laboratory studies were as follows WBC 6.7 x109/l, neutrophils 4.2 x109/l, hemoglobin:15 g/dl, PCV 44%, MCV 84 fL, platelets 254.0 x109/l. Peripheral blood smear was normal and there were 10-15 platelets in each high power field, prothrombin time 12.9 sec (Normal: 12.3), partial thromboplastine time 33 sec (Normal: 28-40), plasma fibrinogen level 383 mg/dl (Normal: 200-400), thrombin time 15 sec (Normal: 15-22), bleeding time 6 minutes, faktor VIII 114% (Normal: 60-150), Faktör IX 102% (60150), faktor XI 100% (Normal: 60-140). In the bleeding episode observed in the examination room, tear drop was examined in the microscope and RBCs were seen.. These RBC shaved the same major blood group antigens with the patient`s blood obtained from a peripheral vein. Otoerythtrocyte sensitization test was negative. In Physiatric examination diagnoses of major depressive episode, posttraumatic stress disorder and dissosiative disorder not otherwise specified, have been made.Sitalopram 20 mg/ day and mirtazopine 30 mg/day have been given as drug therapy.For her traumatic disorder psyhoterapy is going on. Her bleeding attacks have dropped to once a week.

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THROMBOELASTOMETRY IN PATIENTS WITH IDIOPATIC THROMBOCYTOPENIC PURPURA

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Platelet transfusion is rarely used to reduce the risk of hemoragy in idiopatic thrombocytopenic purpura (ITP) due to platelet antibodies.In spite of no platelet transfusion adult patients with ITP rarely have serious bleeding events.Rotation thromboelastometry is a new laboratory method and it can predict the bleeding risk better in these patients. We investigated rotation thromboelastometry as a tool to assess bleeding risk in patients with ITP. We investigated 15 patients (7 male and 8 female) with ITP. The median age was 47 years and the median duration of ITP was 42 months. Platelet count was corraleted with both clot formation time (CFT) in INTEG and EXTEG and maximum clot firmness (MCF) in INTEG and EXTEG ($r= -0.779$ $p<0.01$, $r= -0,683$ $p<0.01$, $r= 0,750$ $p<0.01$, $r= 725$ $p<0.01$ respectively). MCF was much more variable from patient to patient when the platelet count was lower. The bleeding risk in ITP can be evaluated with rotation thromboelastometry better than platelet count. Further studies are encouraged evaluating rotation thromboelastometry as a means to predict bleeding in thrombocytopenic patients.

Abstract: 360 Poster: 267

USE OF RECOMBINANT FACTOR VIIA FOR SEVERE BLEEDING EPISODES IN CHILDREN WITHOUT CONGENITAL HEMORRHAGIC DISORDERS

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Objective: Coagulopathy is an important cause of mortality in critically ill children. Traditional therapies to correct coagulopathy lead to great delays and causes fluid overload in patients. The aim of this study was to evaluate the effectiveness of the application of activated recombinant factor VII (rFVIIa) in nonhemophiliac children with coagulation disturbance. Methods: The records of the patients without a diagnosis of hemophilia, congenital platelet function disturbance who were administered rFVIIa for any reason in Ege University Faculty of Medicine, Department of Pediatrics were reviewed retrospectively. Results: Eighth patients age ranged from 2 days to 15

years received rFVIIa from February 2002 to May 2005. Primary diagnosis of the patients were Hemaphagocytic lymphohystiocytosis (n=2), liver failure (n=1), Prematurity, Respiratory Distress Syndrome (RDS) and disseminated intravascular (DIC) coagulation (n=3), sepsis (n= 1), autolog stem cell transplantation for rhabdomyosarcoma (n=1). Severe bleeding resulted from pulmonary (n=3), lower gastrointestinal system (n=3), eosephagus varices (n=1), pulmonary and gastrointestinal system (n=1). Median frequency of rFVIIa administration was 3 per patient (range 2- 15) and median dose of rFVIIa was 90 mcg/kg, ranging from 60 to 120 mcg/kg/ each administration. All of the patients had been given fresh free plasma, vitamin K and if necessary platelet transfusion (n= 7) or fibrinogen concentration (n=1) before administration of rFVIIa. In 5 patients lack of success to control bleeding by conventional methods was the only cause to start rFVIIa. In 3 patients need for volume restriction was also significant contributing factor for decision to switch FFP treatment to rFVIIa. Median PT was 32.9 (range: 19-65) second before rFVIIa administration and it was decreased to 11.6 (range: 10.7-12.8) second, 20 minutes after rFVIIa infusion. Bleeding was stopped completely in 6 patients at least 24 hour and decreased in 3 patients, 30-45 minutes after administration of rFVIIa. One patient had a thrombotic complication after rFVIIa was given. He was a premature newborn with 31 gestational age, had stage 3 RDS and DIC. A venous catheter was implanted. He had a severe melena, hematemesis and intracranial hemorrhage at the 6th day. He did not give a response to FFP, Vitamin K treatment and rFVIIa was given at the dose of 100 mcg/ kg twice a day for 2 days. After the last dose was administered he had both arterial and venous thrombosis in brachial vessels. No other complication was observed in any of the patients. Conclusion: In this retrospective study rFVIIa was found to be effective in the control of severe hemorrhagic symptoms of different etiologies in children without congenital hemorrhagic diseases. In addition to controlling bleeding in a short time, using this agent improved fluid balance in critically ill children. However risk of thromboembolism should be considered before treatment is given.

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USE OF RECOMBINANT ACTIVATED FACTOR VII IN POSTOPERATIVE LIFE THREATENING INTRAABDOMINAL BLEEDING IN A CASE WITH AMILOIDOSIS

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A 10-years-old boy with amiloidosis and end stage renal disease secondary to familial Mediterranean fever underwent laparascopic cholecystectomy because of cholelithiasis. The results of preoperative routine coagulation tests were normal. On postoperative follow-up, a rapid decrease of hemoglobin level was observed and an urgent laparatomy was performed. Active multifocal bleeding primarily from the suture sites and trochar entry sites was seen. Surgeons tried to achieve surgical hemostasis. After the second operation, abdominal distension developed and tachycardia and tachypnea became more severe. His hemoglobin level decreased rapidly. His hemodynamic condition detoriated despite red cell concentrates, fresh frozen plasma and platelet suspension. Intravenous 2.4 mg (86µg/kg) recombinant activated factor VII was administered and soon after that the hemoglobin level became stabil and his hemodynamic state improved. No side effect was seen. In literature, similar several of hemorrhagic complications in systemic amiloidosis cases have been reported. Increased fragility of small vessels due to amiloid infiltration and aquired deficiency of factor X, IX, VII, II, V, increased fibrinolysis, and disseminated intravascular coagulation were shown to be the underlying coagulation defects. Physicians should be aware of spontanous bleedings in patients with amilodosis. In this group of patients, coagulation should be carefully evaluated preoperatively and minimal invasive surgical procedures should be performed. Procedures that increase the abdominal pressure like laparoscopy should be selected with caution.

Abstract: 362 Poster: 269

USE OF RECOMBINANT FACTOR VIIA (NOVOSEVEN) IN THE TREATMENT OF PATIENT WITH TYPE I VON WIILEBRAND S DISEASE WITH REFRACTORY GASTROINTESTINAL BLEEDING

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Recombinant activated coagulation factor VII(rVIIa,NOVOSEVEN) is indicated for the treatment of bleeding episodes or as a prophylactyc hemostatic agent during surgery in patients with inhibitor complicated hemophilia an rare in type III von Willebrand s disease with inhibitors.The use of rVIIa in gastrointestinal bleeding refractory to conventional therapeutic interventions is reviewed in patients with liver disease, hematolgocal disturbances, BMT,platelet function disorders, peptic ulcer disease and Crohn s disease. CASE REPORT: we present 39-year old male with type I von Willebrand s disease, FVIII coagulant activity, FVIII.C 17% RcO 0%, inhibitors to von Willebrand F.0,5 BU, aPTT 45,4sec R1,51, bleeding time>30min, RBC 1,93, Htc 0.17, Hb5.1g/cdcl, WBC 8,2 PLT 125 were the parameters ad the time of admition to hospital. Endscopic exploration presented presense of multiple gastric erosiones with profuse bleeding.Patient was treated with RBC transfusiones, inhibitor of protonyc pump(Controloc) iv amp./per day contineosly, concentrated FVII(Immunate 3000i.j./day during 21 days. After second endoscopic exploration amp.Sandostatin, previosly 2xI iv. pe r day during 10 days and after VI amp.in continous infusion/per day during 3 days were aplicated. There was a little bit of local and clinical ben-efit/melaenas of 100ml /per day, RBC2,46, Hb73, HTC O,22 endoscopic funding show out multiple erosiones in gaster mucosa, permanently bleeding. At that time FVII.: c was 109%,RcoF 14%, aPTT 25,2, R 1,050, bleeding time >30min.rVIIa (NovoSeven) was given in standard dosage of 90ug/kg of BM three days, every 2 hours and one day after bleeding stoped. Gastrointestinal bleeding stopped, endoskopic finding showed out gastris erossiones in recovery phase, and hemostatic paramethers were normalised even at first day of treatment with NovoSeven: bleeding time was< 5min,aPTT 23,9 r 0,75,rbc 3,44 Hb98 HTC 0,31, WBC 8,6, PLT164. Conclusion:The efficancy and safety of rVIIa as a single hemostatis agent or as a part of standard first line therapy for refractory gastrointestinal haemorrhage in haemophylic and nonhaemophylic patients will be better evaluated in prospective randomized clinical trials.

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PARADONTAL NAGATIVE CHANGES DURING THE HEMOPILIA DISEASES

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The paradontal diseases present the most important problem in time of hemophilia. They are common for approximately 98% of the patients. It is confirmed that the gingival liquid at the intact paradontosis presents transudate, i.e. its composition conforms to the composition of blood plasma - globulin, albumin and fibrin. The gingival liquid enters into the gingival fissure with the assistance of high conductivity of blood vessel of this area. According to our opinion, the globulin and fibrin create strong union between gingival epithelia and dental enamel, thus creating the adhesive film. We study the patients that have failure of blood coagulability function (hemophilia, Willebrand syndrome). We divided the abovementioned contingent to the age groups and studied the percent data of paradontosis spreading for every age group (Table 1). Proceeding from the fact that the hemophilia is the genetic coagulopathia, the physiological mechanism of connection of gingival epithelia with dental enamel is injured accordingly. This is one of the most important reasons of high frequency of paradontal diseases` spreading among the contingent given.

Abstract: 364 Poster: 271

SUCCESSFUL TOOTH EXTRACTION WITH TWO DOSES OF RFVIIA IN A PATIENT WITH BERNARD-SOULIER SYNDROME

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A fifteen-year-old female patient with Bernard-Soulier syndrome had admissions to our center with multiple epistaxis attacks, prolonged heavy periods, iron deficiency anemia and had antifibrinolytic therapy, oral contraceptives, platelet transfusions and iron replacement (Hb:6-9,5 g/dl). Her platelet count was 20 000-35 000/ mm3. She had caries in molar teeth and severe ache. After antibiotic administration for seven days, tranexamic acid 10 mg/kg/dose every 8 hour was started 24 hour before the operation. A bolus injection of rFVIIa 90mcg/ kg was administered and extrac-

tion was performed in the following hour. The same dose was repeated 2,5 hour after the first dose. Hemostasis was quite normal during the procedure and the patient experienced no bleeding in the following days. Oral tranexamic acid was withdrawn in the 8th day. Our experience confirm that minor surgical procedures can be successfully managed with rFVIIa in Bernard-Soulier syndrome and development of platelet antibodies and viral contamination can be avoided.

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ACQUIRED-TRANSIENT F-X DEFICIENCY ASSOCIATED WITH ANTI-CARDIOLIPIN ANTIBODIES IN A PEDIATRIC PATIENT WITH EXTENSIVE BURN

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Background: Acquired Factor X (F-X) deficiency has been associated with systemic amyloidosis, pneumonia, liver disease/vitamin K deficiency, myeloma, tumors, and some drugs such as topical thrombin and sodium valproat. This disorder is quite rare in pediatric patients and usually transient. Evidence of F-X specific inhibitors has been demonstrated previously in some cases. Aim: We present a pediatric patient with extensive burn who developed acquired-transient F-X deficiency associated with antiphospholipid antibodies. After teeth extraction, massive bleeding from wounds, gingiva and epistaxis occured together with a leukomoid reaction and disturbation of coagulation tests. Methods: Investigations lead to the diagnosis of acquired isolated F-X deficiency associated with antiphospholipid antibodies. He was succesfully treated with plasmapheresis, steroid and intravenous immun-globulin therapy with an uneventful follow-up period of 7 months. Conclusion: Bleeding diathesis in burned patients can be associated with coagulation factor inhibitors. We propose that plasmapheresis with accompanying IVIG and steroid therapy is a successful treatment.

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FACTOR VII DEFICIENCY WITH MASSIVE SUBGALEAL HEMATOMA: A CASE REPORT

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BACKGROUND: Factor VII deficiency is an autosomal recessive hereditary disorder characterized by a normal partial thromboplastin time and a prolonged prothrombin time. Definite diagnosis of this condition requires a specific Factor VII assay. In patients with congenital FVII deficiency, bleeding manifestations and clinical presentation vary widely, ranging from asymptomatic subjects to patients with hemorrhages that may cause important handicaps. AIMS: To report a case of massive subgaleal hemorrhage in a patient with factor VII deficiency. METHODS: A four year-old male presented 3 months after mild head trauma with progressive scalp swelling. RESULTS: He had a history of epistaxis, easy bruising, and prolonged bleeding after circumcision and no family history of bleeding disorder. The physical examination was normal except swelling on the scalp. He had a normal partial thromboplastin time and a prolonged prothrombin time. Computerized tomography scans demonstrated a large subgaleal hematoma. Quantitative assays of coagulation proteins identified a factor FVII:C deficiency (%1). CONCLUSIONS: Delayed-onset subgaleal hematoma can rarely be an initial manifestation of factor deficiency. FVII:C levels are not a good predictor of bleeding tendency as there is a wide overlap between bleeders and asymptomatic patients. Careful follow-up of patients with prolonged subgaleal hematomas is necessary because of the possibility of the development of infection and proptosis. Persistent bleeding from the circumcision site should alert the physician to the possibility of hemophilia

Abstract: 367 Poster: 274

RESEARCH FOR BLEEDING TENDENCY IN PATIENTS PRESENTING WITH SIGNIFICANT EPISTAXSIS

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Background/Aims: Epistaxis has been discovered as one of the most frequent bleeding symptoms in patients with hereditary primary hemostasis disorders including von Willebrand disease. However, we have rarely observed a patient presenting with nose bleeding to be diagnosed with a hereditary bleeding disorder in our clinical practice. Therefore, we decided to perform a prospective study in the cases presenting with this symptom. Methods: Nineteen consecutive adult patients (9 men, 10 women; median age = 57; range = 24-85)presenting to The Hacettepe University Emergency Service due to epistaxis were evaluated using a detailed questionnaire for clues of a personal and family bleeding disorder. A detailed physical exam including ENT examination and testing for hemostasis were performed in all patients. Hemostasis tests included platelet count, INR, APTT, thrombin time, fibrinogen, factor VIII, factor IX, factor IX, von Willebrand factor and ristocetin cofactor activity levels. Platelet aggregation tests were also recommended if necessary. Results: Seven cases had hypertension with greater than 170 mmHg and 100 mmHg values of systolic and diastolic blood pressures, respectively. Four cases described a significant mucocutaneous bleeding history. Only one case had a decreased von Willebrand factor level considering his/her blood group. This case also had a personal and family history compatible with a bleeding tendency. Interestingly, 10 out of 19 patients had a history of aspirin use within the last one week. Conclusions: In conclusion, aspirin use and hypertension are the leading causes of emergency service admission due to epistaxis in adults.

Abstract: 368 Poster: 275

PURPURA FULMINANS DUE TO STREPTECOCOUS PNEUMONIA

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Purpura Fulminans is an acute, often lethal, syndrome of Disseminated Intravascular Coagulation (DIC) and purpuric skin lesion which is invading progressive with minimal inflamation, necrosis and perivascular hemorrage. Clinically fever, hypotension and sepsis are observed. The main etiologies of purpura fulminans are bacterial Infection and protein C and S deficiency. In addition, skin necrosis by usage of Warfarin and Anti-Phospholipid Syndrome (APA) are rare reasons. Case Report 49 years old male was admitted with high fever and purpuric skin lesions bilaterally spanned on hand and foot, root of nose and ears. Before he came to our hospital, he was administered Novalgine imtramuscular route 12 hours ago, because of high fever. Physical examination revealed a heart rate of 126 beats/min and oral temperature of 39.5 oC. He has disseminated purpuric skin lesions and pneumonia. The patient was diagnosed as purpura fulminans. A complete blood cell count indicated the following values: Hemoglobin:13.8 g/dL, WBC count: 12800 cells/mm3(predominantly neutrophils and bands) and platelet count: 260000 cells/mm3 The patient had and international normalized ratio of 1.77, an activated partial thromboplastin time of 42.6/s, his blood urea nitrogen and creatinine levels were 56 mg/dL and 2.24 mg/dL` respectively. D-Dimer level was 6414 µg/L. The activity of Protein C, Protein S and antithrombin were 34% 55% and 61%, respectively. FactorV Leiden (G1691 A) and Prothrombine (G 20210 A) mutations and MTHFR polymorphism (C 677 T) were negative. Cultures of blood and sputum samples obtained at the time of hospital admission and sputum culture yielded streptecoccus pneumonia. Continious Heparin Infusion therapy controlled by APTT and ampiric antibiotic were administered. The skin lesion was obviously regressed. Left little fingers of hand and distal phalangeus of both foot fingers except big toes were amputated. The condition of this case is due to infection. He was discharged from hospital after nine weeks managed by whole regression of skin lesions and good healing.

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DEFICIENCY OF FACTOR V: ONE OF THE RARE CASE REPORT`S IN THE INTERNATIONAL LITERATURE

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We report the case of a 40-year old woman who presented severe uterus hemorrhage duration of twenty days with a prolonged prothrombin time (PT).In her individual background had two physiological childbirths and one miscarriage caused by placental detachment at the fifth and

half pregnancy month. She also reported the existence of uterine fibroids that in no case are connected with a prolonged prothrombin time (PT). No other underlying personal and familiar diseases have been reported and identified. Laboratory evaluation revealed the following results: number of platelets 300000/mm3 (n.r 200-400 x1000 cmm), prothrombin time (PT) 15.2 sec (n.r 11-14 sec), INR 1.3, partial thromboplastin time (APTT) 39.1 sec (n.r 27-35 sec), fibrinogen 320 mg/dl (200-400 mg/dl), FII 92%(n.r >60%), FV 39%(n.r >60%), FVII 86% (n.r >60%), FX 84% (n.r >60%), FXII 89% (n.r >60%), FVIII 81% (n.r >60%), FIX 101% (n.r >60%), FXI 157% (n.r >60%), FXIII 84% (n.r >60%), vWFAg 101% (n.r 65-125%), Ricof 51% (n.r >40%). Became retest after 2 months with the following results: prothrombin time (PT) 15.5 sec, INR 1.3, FV 41%. In this case wasn`t verified the presence of malignancy, liver disease, intravascular diffuse coagulation (DIC) or hyperfibrinolysis, conditions that cause the decrease of factor V levels. The relative deficiency of FV is an infrequent hemorrhagic disorder that should be recorded for the follow-up of the patients and the prevention of severe hemorrhagic episodes.

Abstract: 370 Poster: 277

THE EFFICACY OF FRESH FROZEN PLASMA IN FACTOR X DEFICIENCY

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Background: Factor X deficiency is one of the rarest inherited coagulation disorders. It is an autosomal recessive inherited disease. Case: A 19-year-old male was admitted with complaints of progressive swelling on the right thigh for 4 days. In physical examination, painful swelling was found in front of right thigh and on right knee. Hematoma was detected by ultrasound. There was no abnormality in complete blood count, and in biochemical parameters. Bleeding time was 2 minutes. Prothrombin time which was performed for 3 times was as long as undetectable. Also active thromboplastin time was performed for 3 times and was found as 118.7, 97.6, 107.6 seconds (Normal: 25-40 seconds). Lupus anticoagulant was negative. It was assessed as factor deficiency in common way of coagulation cascade. Fibrinogen level and thrombin time was found as normally. Factor IX, factor VIII and von Willebrand factor level was found normal. Factor X level was found 21.45% (Normal level: 70-150%). The patient was accepted as factor X deficiency case. He was given fresh frozen plasma (FFP) of his blood type twice a day for 4 days. The painful swelling on the right knee was progressively smaller and than disappeared. After treatment prothrombin time and active thromboplastin time was found 28.0 and 42.4 respectively. Conclusion: As we know, there is no factor X form. There are forms of factor II, VII, VIII, IX and also active combinations of these factors. The administrations of these factors together with are thrombosis risk. Also, inhibitor factor risk increases with factor administration. Administration of FFP to the patient may present from these risks.

Abstract: 371 Poster: 278

RENAL HAEMOPHILIC PSEUDOTUMOUR

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In haemophilic patients, untreated haemorrhages may lead to pseudotumour formation. We report a rare case of giant intrarenal haematoma mimicking a proximal pseudotumour in a patient with haemophilia A. In this case, surgical removal had been successfully performed while the patient was on appropriate factor replacement therapy.

Abstract: 372 Poster: 279

BLEEDING DISORDERS; AN OVER REVIEW

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Normal homeostasis has to have normal thrombus formation, fibrinolysis and healing process. For the normal thrombus formation; normal Platelets, Coagulation and Vascular phase need to be. Defect in any of those lead to abnormal homeostasis. Bleeding control start with Vascular phase, release of vasoconstriction agents. Endothelial release of tissue factor to initiate coagulation cascade and von-Willebrand factor to initiate Platelets adhesion, where electrochemical signals initiate to call for aggregation and Platelets activation

to provide template for coagulation factors. Finally end with cloth formation and bleeding control. This processes controlled with normal inhibitors and fibrinolysis. Defect may involve any phase. Hereditary, acquired, quantitative or quantitative. Inheritance may include autosomal, X-linked, dominant or recessives pattern. Immune thrombocytopenic purpura considered the most common acquired bleeding disorder, while von-Willebrand disease is the most common hereditary one. Investigations for bleeding disorders include two parts; general (screening) tests which in lead to diagnosis direction and specific tests for definitive diagnosis. Treatment is both supportive and specific replacement therapy. This paper is a review on bleeding disorders, pathophysiology, diagnosis and treatment. In addition to approach to patients with bleeding disorders, with children consideration in particular. CHRONIC LYMPHOCYTIC LEUKEMIA AND RELATED DISORDERS

Abstract: 373 Poster: 280

THE EFFICACY OF RITUXIMAB IN REFRACTORY AUTOIMMUNE HEMOLYTIC ANEMIA OF CHRONIC LYMPHOCYTIC LEUKEMIA

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Background: Autoimmune hemolytic anemia (AIHA) is the best known autoimmune complication of B-CLL and encountered in 10-20% of cases. Steroids are the first-line agents in the treatment of autoimmune complications. Splenectomy, intravenous immunoglobulin and immunosuppressive drugs have been used with varying degrees of successs. Here, we present our patient diagnosed with CLL stage Rai II 3.5 years previously and whose AIHA was refractory to all treatment modalities. The patient`s AIHA was successfully treated with four doses of weekly rituximab. Rituximab is highly effective for the treatment of steroid-refractory AIHA of CLL. Case Report: A 71-year-old male patient had presented to our department in January 2000 with fatigue and weight loss. At the time of diagnosis, his hemoglobin was 6.8 g/dl; hematocrit, 26%; leucocytes, 81800/mm3 (with 94% mature-appearing lymphocytes on peripheral blood smear); platelets, 123000/mm3; total bilirubin, 2.5 mg/dl; indirect bilirubin, 1.7 mg/dl; LDH, 758 U/L. Direct Coombs test was (+++). He had multiple peripheral lymphadenopathies, hepatomegaly (8 cm) and splenomegaly (9 cm). Flow cytometric analysis confirmed the diagnosis of B-CLL. He was administered chlorambucil and steroids for 4 cycles with which his lymphocytosis and organomegaly were successfully treated. Hemoglobin level increased up to 10.9 g/dl; however, did not normalize. The patient was lost to follow-up for 3.5 years. In August 2003, he came again with worsening fatigue. Laboratory values were as follows: hemoglobin, 5.1 g/dl; hematocrit, 15%; leucocytes, 16600/mm3; platelets, 152000/mm3. His AIHA was ongoing. He was administered 4 cycles of COP (cyclophosphamide, vincristine, prednisone). His hemoglobin increased up to 8.1 g/dl. He developed steroid myopathy and became cushingoid; and, in the meanwhile he had a lower extremity deep venous thrombosis for which he was anticoagulated. The patient did not give permission for splenectomy; and, in order to control ongoing hemolysis intravenous immunoglobulin (IVIG) was given. IVIG was not at all effective and the patient used oral cyclophosphamide for 7 months. He was hospitalized again in August 2004 with fatigue. His hemoglobin was 7.8 g/dl; hematocrit, 24.1%; leucocytes, 5400/mm3; platelets, 133000/mm3; indirect bilirubin, 1.2 g/dl; LDH, 579 U/L; direct coombs test was (++++). The patient was given rituximab 375 mg/m2/day for 4 weekly cycles. His hemoglobin level started to increase after 2 weeks. On his last follow-up, his hemoglobin was 13.3 g/dl; hematocrit, 39%; leucocytes, 9100/mm3 (with 22% lymphocytes); platelets, 251000/mm3. The patient felt himself very well and he had no organomegaly. Conclusions: Rituximab alone can be safely administered to CLL patients who have autoimmune complications refractory to other treatment modalities. It renders the patients safe from side effects of long-term steroid usage and postsplenectomy sepsis.

Abstract: 374 Poster: 281

LARGE GRANULAR LYMPHOCYTE LEUKEMIA PRESENTING WITH HEMOLYTIC ANEMIA AND IMMUNOGLOBULIN A NEPHROPATHY

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Large granular lymphocyte (LGL) leukemia is a rare and probably underdiagnosed disorder caused by the clonal proliferation of cytotoxic (CD8+) T cells. In normal peripheral blood %10-15 of mononuclear cells are granuler lymphocytes and the majority of these are natural killer (NK) cells but in most of the LGL leukemias the malign cell is CD8+ cell. The disease has usually an indolent course. Patients come to medical attention becase of cytopenias. Neutropenia is found in 85% of the cases, half the patients have anemia and 20% have thombocytopenia. Modest splenomegaly and hepatomegaly can be seen, enlarged lymph nodes are rare. Increased number of LGLs` are seen in peripheral blood smear. Immunophenotyping shows an increase in CD3, CD8, CD57 pozitive cells. Agressive forms are reported in patients expressing CD3 and CD56 (a NK marker) together. In order to establish the diagnosis, T cell proliferation has to be demonstrated to be clonal by gene rearrengement studies. LGL leukemia is associated with autoimmune diseases like rheumatoid arthritis, autoimmune hemolytic anemia and thrombocytopenia. Hemotologic diseases like pure red cell aplasia, aplastic anemia, myelodysplasia and paroxismal nocturnal hemoglobinuria. Treatment options include methotrexate, cyclophosphamide, cyclosporine A, pentostatin, fludarabin, alemtuzumab. Because of the indolent course of the disease only observation can be a choice. Both G-CSF and GM-CSF help management of recurrent infections secondary to neutropenia. Prednisone improves cytopenias in most patients but sustained remission is rare. Here we report a case of LGL presenting with hemolytic anemia. Our patient is 62 year old man. On his first admission to the hospital he had 2.8 gr/day proteinuria and mild anemia (Hemoglobine 10gr/ dl). His white blood cell (WBC) count was 6300 with a differential count of 20% mature appearing lymphocytes. He was diagnosed as IgA nephropathy by renal biopsy. His staining pattern was like secondary forms. No underlying cause was found and his anemia was considered as anemia of chronic disease. With immune supressive treatment by steroid and mycophenolate mofetil, his proteinuria and anemia healed. A year after the discontiuation of therapy he again admitted to the hospital with anemia (hemoglobine 8.4 gr/dl). This time his WBC was 7100 with 57% lymphocytes most of which had granules in their large cytoplasms. His reticulocyte count and lactate dehidrogenase (LDH) value increased (6.22% and 456 respectively), direct antiglobuline test was negative, antinuclear antibody was positive with 1/80 titers. Immunophenotyping showed positivity for CD3, CD8 and CD16/56 (%23). He was diagnosed as LGL leukemia and hemolytic anemia. At the second month of prednisone therapy hemoglobine, lymphocyte, reticulocyte, LDH values became normal. At the office visit which was after 4 weeks of temination of steroid therapy, he again had a differential conut of 75% large, granular lymphocytes, this time without anemia. Because he had osteoporosis, diabetes mellitus and cushingoid appearence due to steroid treatment we decided to switch therapy to methotrexate Hemolytic anemia is frequently reported with LGL leukemia but we couldn`t find a report in the literature suggesting a connection between IgA nephropathy and the disease. Although we do not have enough data to support a relationship a possibilty should be kept in mind.

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PROGNOSTIC IMPORTANCE OF SOLUBLE CD23 IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA

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Background: CD23 is a 45 kD type II transmembraneous glycoprotein of the hematopoietic cells. It functions as a low affinity receptor for IgE (1). There are two isotypes: CD23a and CD23b. CD23a activates phopholipase C by G-protein, causes increase in cAMP and induces B lymphocyte proliferation and inhibition of B lymphocyte apoptosis (2). Soluble CD23 (sCD23), a soluble protein found in the serum, is the 25 kD fragment of CD23. It acts as a cytokine and together with inter-leukin-1, induces proliferation of normal and leukemic B lymphocytes. In recent years, higher serum sCD23 levels were reported in patients with B-CLL. It was proposed that it could be a marker of the disease activity and prognosis (3). Aims: First, correlation of serum sCD23 levels of our patients with the known clinical parameters if it reflects the disease activity and tumor mass or not, and second if it is possible to predict prognosis with serum sCD23 levels earlier. Methods: In this prospective study, prognostic significance of sCD23 was examined according to its relation with the other prognostic parameters (lymphocyte doubling time, Binet clinical staging system and

bone marrow histopathology) and survival of the patients. Serum sCD23 levels of thirty-six B-CLL patients, followed-up in our clinic between 1999 and 2005, and 15 healthy subjects were measured with ELISA kit. Results: Mean serum sCD23 level of the B-CLL patients (210.72±193.67 U/ml, 6-600 U/ml) was significantly higher than the control group (18.20±14.30 U/ml, 6-50 U/ml). Seventy-eight percent of the B-CLL patients with LDT<12 months and 24% of patients with LDT>12 months had high sCD23 levels (p=0.008). Meanwhile, 81% of the patients with diffuse bone marrow infiltration and 33% of patients with non-diffuse infiltration had high levels of serum sCD23 (p=0.029). A significant difference was found between B-CLL patients with Binet stages A and C (p=0.009). Cumulative and the progression free survivals of the patients with low serum sCD23 levels were 60.1±5.7 (95% CI; 49.0-71.2) and 51.1±6.6 (95% CI; 38.0-64.1) months, respectively. However, they were 43.8±6.5 (95% CI; 31.0-56.6) and 26.5±6.4 (95% CI; 14.0-39.1) months in patients with high levels. Conclusion: Serum sCD23 is increased in B-CLL patients and can be used in the clinical follow-up of the disease in prediction of the tumor mass and prognosis.

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HYPERCALCEMIA IN A YOUNG, B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA PATIENT

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Background: Hypercalcemia in chronic lymphocytic leukemia(CLL) is rare and occurs in less than 5 % of patients. It seems to be associated with poor survival. Its occurrence may indicate development of Richter`s syndrome. PTH-rP may have a role in the pathogenesis. Case presentation: A 28-year old male patient was admitted with extensive bone pain, and masses in servical, axillary regions. Physical examination revealed multiple lymph nodes in servical, axillary, and inguinal regions. WBC: 33600/mm3, Hb: 13.1 g/dl, PLT: 298000/mm3 with a lymphocytic predominant differential was established. Calcium was 10.4 mg/dl. Bone marrow biopsy and immunophenotyping of bone marrow cells with CD5, CD19, CD20, CD23 positivity led to `CLL Stage I` diagnosis. Ig G, A, M levels were normal. He underwent CHOP therapy. After the first cycle his lymph nodes completely regressed and bone pain disappeared. After 6 cycles he lost follow for 15 months. Then he was admitted with weakness and bone pain. WBC:209000/mm3, Hb:2.9 g/dl, PLT:45700/ mm3, urea:69 mg/dl, creatinin: 2.1 mg/dl, calcium:12.4 mg/dl values were established. Fludarabin was initiated. After the third cycle cytopenias resolved, lymph nodes regressed but he did not take therapy for 3 months and was admitted with WBC:52900/mm3, Hb:5.7 g/dl, PLT: 32700/mm3, calcium:13.5 mg/dl, urea:103 mg/dl, creatinin:3.2 mg/dl values. Forth fludarabin therapy was initiated. Skeletal X-ray showed multiple lytic lesions in the bones of iliaca, humerus, scapula, costa, cranium. Lymph node biopsy was done. It was consistent with low grade small lymphocytic lymphoma. The therapy was switched to fludarabin+rituximab combination and he took four more therapies and then isolated rituximab therapy. One month after the last cycle he was admitted with calcium level of 18 mg/dl. Therapies to lower calcium level were initiated urgently. Stem cell transplantation was planned but during this time hypercalcemia relapsed. WBC:16300/mm3, Hb:7.8 g/dl, PLT:63000/ mm3 values were determined. Blast-like cells appeared on peripheral blood smear. Lymph node biopsy was repeated and Richter`s transformation was detected. At this time Vitamin D level was 20 ng/ml (11-70) and PTH level was 1 ng/ml (12-72). He underwent DHAP therapy but succumbed to invasive pulmonary and sinonasal aspergillosis. He was in the third year of his follow up. Conclusion: As stated in the literature hypercalcemia in CLL is associated with a poor prognosis. Hypercalcemia in CLL may indicate relapse of the disease but it may not indicate Richter`s transformation every time.

Abstract: 377 Poster: 284

ASSESMENT OF THE SAFETY OF FLUDARABIN BASED COMBINED CHEMOTHERAPY REGIMENS REGARDING INFECTIONS IN PATIENTS HAVING CLL/INDO-LENT LYMPHOMA OF AGE GREATER THAN 50

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Objective: Documenting the infections, toxicity and efficacy in patients of age >50 having CLL or indolent lymphoma who are treated with fludarabin in combination with cyclophosphamide. Our hypothesis was to increase the efficacy of fludarabin by combining it with cyclophosphamide without augmenting fatal infectious complications even in very old age group. Methods: Between October 2002 and February 2005, a total of 16 patients were studied retrospectively. They had normal BUN, Cre, and no myelosuppression. Median age was 68.5 (range 50-91). Treatment consisted of minimum 2 maximum 4 cycles of fludarabin 25 mg/m2/d iv; days 1-3 every 4 weeks or until recovery of myelosuppression, cyclolphosphamide 250 mg/m2/d iv; days 1-3 every 4 weeks concomittantly. All the patients received prophylaxis with TMP/SM for PCP starting with the therapy until 6 months after the completion of the last cycle. All the infections were documented clinically and the possible increase of the morbidity and mortality due to infections or other toxicities, and the effect of the combined therapy on overall survival was tested with one way anova statistic test. Results: In pretreated patients (n=12) an overall response of 66.7 % was obtained. In newly treated patients (n=4) overall response was 75 %. According to NCI toxicity grading, grade 3-4 neutropenia was observed in 7 (43.75 %), grade 3-4 anemia in 3 (18.75 %), grade 3-4 thrombocytopenia in 4 (25 %). A total of 47 clinical infectious events were documented in one year time after the beginning of the chemotherapy, including the late herpetic reactivation zona zoster. Serious infectious toxicity was found to be similar with other fludarabin studies, not showing difference for this older age group. Also the main toxicity was again found to be hematological toxicity (mainly thrombocytopenia) similar with other fludarabin studies. Conclusions: Combined therapy with fludarabin and cyclophosphamide for older aged group showed similar safety or toxicity profile with the younger group when compared with the literature. We concluded that when given as prior therapy in this age group the main benefit was the disease and treatment free time that eased the life of these old patients. Though an effective regimen in CLL/indolent lymphoma we must emphasize that a priori combined therapy did not show benefit for prolonged survival for our study group.

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PROLONGED REMISSION AND LONG-TERM SURVIVAL IN HAIRY CELL LEUKEMIA TREATED WITH DEOXYCOFORMYCIN

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Hairy cell leukemia (HCL) is a chronic lymphoproliferative disease of adults characterized by pancytopenia, monocytopenia, splenomegaly without lymphadenopathy and by presence, in the peripheral blood and bone marrow, of neoplastic lymphocytes with irregular cytoplasmatic borders, characteristically tartrate-resistant acid phosphatase positive, with markers of B-cells always positive, FMC 7 positive and panel of four antibodies specific for HCL (CD 11c, CD 25, CD 103 and HC 2). The mainstay of the treatment of HCL comprises the two nucleoside analogues, pentostatin (DCF) and cladribine (2-cdA). Both agents induce a high rate (>80%) of complete remission. We present three cases with long-term survival (14.5; 13.5 and 21 years) and prolonged remission after deoxycoformycin (Pentostatin) treatment (5-11 years). Case 1. (A.N., male, 1953) Initial diagnosis in 1984; immunophetype CD 19+. FMC7+, CD 11c+, CD25+, kappa + (75%); splenectomy was done 1988; Interferon alpha treatment administered for 7 years; DCF treatment applied with 8 doses in 1997 with remission of 5 years; relapse occurred in 2002 treated with 2-cdA with second CR. Total survival 21+ years. Case 2. (F.B., male, 1961) Initial diagnosis in 1990; immunophenotye CD19+, CD11c+, CD25+. FMC7+, kappa + 70%; splenectomy was done and interferon treatment applied for 10 months with minor response; DCF treatment administered in 1991-92 with 13 doses with CR lasting > 11 years. Relapse occurred in 2003. Total survival 14.5+ years. Case 3. (C.V.,female, 1940) Initial diagnosis in 1991; immunophenotye CD19+, CD11c+, CD25+, lambda + 85%. DCF treatment applied in 1993 with 11 doses with CR lasting 5 years. Relapse occurred in 1999 with stable disease without further therapy. Total survival 13.5+ years. Conclusions: Splenectomy and IFN-alpha were early treatments with palliative value. In our cases DCF induced durable remissions in HCL. Relapse occurred in the period of 5-11 years with possibility of second remission with 2-cdA.

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CLADRIBINE (2 CDA) IN TREATMENT OF HAIRY CELL LEUCEMIA (A SINGLE CENTER EXPERIENCE)

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Hairy cell leukemia is a rare chronic lymphoproliferative disease characterized by circulating B lymphocytes displaying prominent cytoplasmatic projections and infiltrating the bone marrow and spleen in a unique way. Patients are often elderly men who present with pancytopenia, splenomegaly or recurrent severe infections. During the past decade, the successful introduction of three effective systemic therapies interferon-alfa (INF), 2-deoxy-conformicin (DFC) and 2-chlorodeoxyadenosine (2-CDA) has dramatically and favorably altered the treatment options and prognosis for patients with this disease. We have treated at our Department 6 patients with hairy cell leukemia with 2 CDA, three of them as front line therapy and other in still active disease after previously treatment with chemotherapy (3 pts), splenectomy (2 pts), INF (2 pts), DFC (1 pts). Patients characteristics were: 6 male patients, median age 47 years (range 31-68) initially presented with pancytopenia and splenomegaly. The diagnosis of hairy cell leucosis was based on morphology, bone marrow histology and imunophenotiping. In all patients 2-CDA was administrated as a single continuous 7 day intravenous infusion at a dose 0.09mg/kg/d. Complete remission was achieved in all 6 patients, with disappearance of all evidence of disease with normalization of the blood count and clearance of hairy cells from the bone marrow biopsy. After a follow-up of 36-72 months, 6 patients maintain in complete remission. The treatment was well tolerated. In the period of aplasia postchemotherapy 3 pts had fever of unknown origin and received antibiotics therapy. Granulocytic-colono stimulating factor was administered in 3 patients. 2-CDA is a safe and effective treatment for patients with hairy cell leukemia. The treatment is able to induce complete remission as first line therapy and also in patients previously treated and resistant to other drugs.

Abstract: 380 Poster: 287

COEXISTENCE OF CHRONIC LYMPHOCYTIC LEUKEMIA AND HASHIMOTO THYROIDITIS

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Although, in chronic lymphocytic leukemia (CLL) patients, autoimmune manifestations observed frequently, development of autoimmune thyroiditis reported very rarely in the literature. A 66-year old male CLL patient admitted for regular control visit. Complaints of sweating and weight loss lasting for six months were present in his medical history. CLL was diagnosed three years ago and six courses of fludarabine were administered. Nodular goitre and splenomegaly extended left arcus costarum 5 cms were present in physical examination. In complete blood count, values were as follows; WBC: 2,80 x10e9/l, RBC: 3,88 x10e12/l, hemoglobin: 10,4 g/dl, hematocrit: 31,8%, platelet: 149 x10e9/l. The levels of free T3, free T4 and TSH were normal while the levels of anti-thyroglobuline antibody and anti-TPO antibody were highly elevated. Ultrasonography of thyroid revealed nodular hyperplasia of thyroid gland with heterogenous echo patern (thyroiditis). Biopsy specimen obtained from a large nodule displayed by ultrasonography was negative for malignancy. Diagnosis of `coexistence of CLL and Hashimoto`s thyroiditis` was made according to these findings. Regular controls were suggested for the patient with no treatment for present conditions. Coexistence of CLL, fludarabine treatment and development of Hashimo-to`s thyroiditis was discussed in this case report.

Abstract: 381 Poster: 288

SEVERE PROLONGED PANCYTOPENIA DUE TO IMATINIB MESYLATE TREATMENT IN CHRONIC MYELOID LEUKEMIA

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A 65-years-old woman with chronic myeloid leukemia was treated with imatinib mesylate. She was admitted to our hospital with severe pancytopenia. She received 400mg of imatinib mesylate for 40 days before the agent was discontinued. A

bone marrow biopsy on the 30th day after the last imatinib mesylate administration demonstrated severe hypocellularity. She needed many erytrocyte and thrombocyte transfusions and filgastrim administration. Grade 3 neutropenia continued for 35 days and grade 3 thrombocytopenia continued for over 30 days. Imatinib mesylate an agent targeting BCR-ABL, is expected to be useful as an effective therapeutic agent for chronic myeloid leukemia (CML).However the present case suggests that its appropriate dose is individually variable and we should carefully consider the former treatment of the disease before initiating imatinib treatment. Imatinib mesylate a signal transduction inhibitor,acts selectively on BCR/ABL gene product which is an intracellular pro-ten with elevated tyrosine kinase activity necessary for the transforming ability of the BCR/ABL gene and proliferation of leukemic clone. Side effects include nausea, vomiting, edema, muscle cramps, diarrhea, headache and abdominal pain. Low grade neutropenia and thrombocytopenia may occur occasionally in chronic phase. Dose reduction (best not to treat with less than 300mg /day) or temporary cessation occasionally required about 1% of patients.A 65 year old female, have been followed with interferon alpha and hydroxyurea for eight years. Imatinib mesylate was started 2 years ago with 400mg/ day. In the 4th day of treatment severe urticarial lesions with angioedema manifested. The drug was stopped and restarted with steroids. Similar but less severe lesions were observed. This time the drug was stopped for 6 months. Two months ago it was to be restarted. On the 40th day pancytopenia was detected. WBC count was 0.6x103/µL, Hb concentration was 7.0x106 g/dL and platelet count was 12X103/µL. Bone marrow biopsy revealed severe hypocellularity. Other causes of pancytopenia were investigated. Parvovirus B19 Ig M was found to be negative. She needed many erythrocyte and platelet transfusions with filgastrim administration. On the 35th day WBC count was 4.58 x103/µL, Hb concentration 10.2x106g/dL and platelet count 149 x103/µL.Imatinib mesylate is highly effective in patients with chronic phase CML who are resistant or intolerant to interferon and has an acceptable toxicity that is mostly mild to moderate in severity. The most frequently reported adverse events were superficial edema, nausea, muscle cramps, diarrhea, vomiting, and skin rash. Myelosuppression (thrombocytopenia and neutropenia) was also reported especially in patients with advenced disease. The disturbance in all cell lines is a rare condition. The mean discontinuation time of therapy was 4 weeks but usually one of the three cell lines was affected. In our case we had to discontinue therapy for more than 9 weeks

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INCIDENCE OF GALLSTONES IN PATIENTS WITH CHRONIC MYELOCYTIC LEUKEMIA: EXPERIENCE OF TURGUT OZAL MEDICAL CENTER IN TURKEY

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Objectives: The aim of the present case-control study was to determine whether the incidence of gallbladder stones (GBS) was increased in patients with Chronic Myelocytic Leukemia (CML) and to investigate clinical and laboratory characteristics of CML patients with GBS. Methods: This study included 56 patients with CML and 55 sex and age-matched healthy controls (HC). All participants were performed abdominal ultrasound and their main clinical and laboratory characteristics were recorded. Results: GBS were detected in thirteen patients with CML (23,6%) and three HC (5,4%) ($p<0,05$). The mean follow-up time of CML patients after diagnosis was 54,6 months (range: 3-129). Hemoglobin levels were higher in the HC group, and unconjugated bilurubin, lactic dehydrogenase levels, leukocyte and thrombocyte counts, frequency of splenomegaly and hepatomegaly were higher in the CML group ($p<0,05$). Other clinical and laboratory values were not significantly different between the groups. The clinical and laboratory values of CML patients with and without GBS were also compared. Unconjugated bilurubin levels, age and follow-up time of CML patients after diagnosis were higher in the CML patients with GBS ($p<0,05$). Conclusion: We detected higher incidence of GBS in CML patients than HC. We suggest that CML may increase frequency of GBS, apart from other risk factors. This risk is related to unconjugated bilurubin, which determines hemolysis, age and follow-up time of CML patients after diagnosis.

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ACTIVITY, INDUCTION OF APOPTOSIS AND PHARMACOKINETICS

OF THE TYROSINE KINASE INHIBITOR AMN107 IN BCR-ABL + CELL LINES AND IN IMATINIB RESISTANT PRIMARY CELLS FROM CML PATIENTS

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The kinase inhibitor imatinib eradicates bcr-abl+ cells in chronic myeloid leukemia patients (pts). However, a significant number of pts eventually relapse with leukemia because of point mutations within the imatinib-bind-ing site, amplification of the Philadelphia chromosome or other mechanisms, e.g. clonal evolution. AMN107 (Novartis Pharma AG) is a new anilino-pyrimidine derivative structurally related to imatinib. AMN107 was tested in 3 human bcr-abl positive lines (K562, KCL-22, Lama84) and in primary cells derived from 3 bcr-abl + blast crisis CML pts who were resistant to imatinib, as well as in 2 newly diagnosed pts. In all pts sequencing of the bcr-abl kinase domain excluded any point mutations, but cytogenetic analysis revealed clonal evolution in the resistant pts including t(1;5) and t(3;21) translocations, trisomy of chromosome 8 and monosomy of chromosome 7. Determination of the proliferative activity (XTT-assay) demonstrated a decrease of the IC50 in imatinib versus AMN107 treated samples from 0.08µM to 0.0075µM in Lama 84, from 0.25µM to 0.08µM in K562 and from 0.45µM to 0.03 in KCL-22 cells. In primary cells from imatinib-resistant pts, a decrease of the IC50 in imatinib versus AMN107 treated peripheral blood cells from 0.75µM to 0.25µM and from 4 to 0.4µM and from 2.5 to 0.75 was detected. In addition, in primary cells from 2 newly diagnozed pts the IC50 of AMN107 was reduced. Immunoblotting showed that in LAMA84 cells 0.01µM AMN107 completely inhibited the kinase activity in contrast to almost 5µM in imatinib treated samples. Apoptosis was detected using annexin V and propidium iodide staining. After 48 hours of incubation with either 0.25 µM imatinib or 0.005 µM AMN107 induction of early apoptosis was detected in 8.8% of imatinib treated and 26% of AMN107 treated cells. HPLC analysis in HL-60 cells showed increased uptake by 1,5 fold for AMN107 when compared to imatinib. In MDR1 over-expressing CCRF cells co-culture with either AMN107 or imatinib revealed elevated AMN107 levels (3.7 fold) indicating that this substance is less susceptible to MDR1 driven resistance than imatinib.Conclusions: 1. AMN107 showed elevated activity when compared to imatinib in bcr-abl + cell lines and primary cells. 2. Inhibition of the bcr-abl kinase activity and induction of apoptosis was achieved at lower concentrations in AMN107 treated samples. 3. Preliminary data indicate favourable cellular uptake of AMN107.

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EFFECTS OF IMATINIB MESYLATE AND INTERFER-ON-ALPHA COMBINED WITH GRANULOCYTE COLONYSTIMULATING FACTOR ON CHRONIC MYELOGENOUS LEUKEMIA CELLS IN VITRO

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Aim. In the treatment of patients with chronic myelogenous leukemia (CML), neutropenia is a dose-limiting factor on the combination therapy of imatinib mesylate and interferon-alpha (IFN-alpha). If imatinib combined with IFN-alpha effects on decreasing BCR-ABL-positive cells and granulocyte colony-stimulating factor (G-CSF) has an effect on increasing normal neutrophils, the combination therapy may improve current remission rates in CML. We evaluated in vitro combined effect of imatinib, IFN-alpha and G-CSF on primary bone marrow cells from patients with CML in chronic phase (CP). Material and Methods. The primary bone marrow mononuclear cells (BMMNC) from patients with CML-CP were incubated in the medium containing imatinib (1µM) and/or interferon-alpha (100 U/ml) with or without G-CSF (100 ng/ml). Apoptosis was detected by the flow cytometry analysis with Annexin V (AV) and propidium iodide (PI) double staining. The colony formation assays of BMMNC were performed by methylcellulose method. And then, BCR-ABL positive colony and normal cell colony