

# Acute myeloblastic leukemia-associated Marfan syndrome and Davidoff-Dyke-Masson syndrome: a case report

*Akut myeloblastik lösemi ile Marfan sendromu ve Davidoff-Dyke-Masson sendromu birlikteliği: Bir Olgu Sunumu*

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## Abstract

We present herein a 23-year-old man with acute myeloblastic leukemia (AML) associated with Davidoff-Dyke-Masson syndrome (DDMS) and Marfan syndrome (MS). The diagnosis of DDMS was based on findings including left facial asymmetry, left hemiparesis, mental retardation, right cerebral hemiatrophy, dilatation of the ipsilateral lateral ventricle and calvarial thickening. The diagnosis of MS was based on clinical findings including tall stature, myopia, retinitis pigmentosa, blue scleras, scoliosis, pectus excavatum, arachnodactyly and low ratio of upper/lower body segment. The patient developed hepatosplenomegaly, gingival hypertrophy and pancytopenia. Peripheral blood film and bone marrow examination showed that most of nucleated cells were blasts; immunophenotype of those cells showed CD11+, CD13+, CD14+, CD33+ and HLA-DR+. These findings confirmed the diagnosis of AML (FAB-M5). After induction chemotherapy, remission was obtained. To the best of our knowledge, our case is the third report of AML in MS syndrome, while AML associated with DDMS and MS has not been previously reported in the literature. (*Turk J Hematol 2008; 25: 198-200*)

**Key words:** Acute myeloblastic leukemia, Davidoff-Dyke-Masson syndrome, Marfan syndrome.

Received: May 1, 2007

Accepted: June 20, 2008

## Özet

Burada Davidoff-Dyke-Masson sendromu (DDMS) ile Marfan sendromu (MS) birlikteliği olan 23 yaşında erkek bir akut miyeloblastik lösemi (AML) olgusu sunduk. DDMS tanısı sol fasiyal asimetri, sol hemiparezi, mental retardasyon, kafa kemiklerinde kalınlaşma, serebral hemiatrofi ve ipsilateral lateral ventrikül dilatasyonu ile kondu. MS tanısı uzun yapı, miyopi, retinitis pigmentosa, mavi skleralar, skolyoz, pektus excavatum, araknodaktili, ve üst/alt vucut segmenti oranının düşük olması ile kondu. Hastada hepatosplenomegali, dişeti hipertrofi ve pansitopeni bulunmaktaydı. Periferik yayma ve kemik iliği incelemesinde çekirdekli hücrelerin çoğunun blast olduğu görüldü. İmmunofenotipik incelemede blastların CD11, CD13, CD14, CD33 and HLA-DR pozitif olduğu belirlendi. Bu bulgularla olguya AML (FAB-M5) tanısı kondu. İndüksiyon kemoterapisinden sonra remisyon elde edildi. Bilgilerimize göre AML ve MS birlikteliği olan 2 olgu sunumu bulunmakta olup, daha önce DDMS ve MS ile birlikte AML olan olguya literatürde rastlanmamıştır. (*Turk J Hematol 2008; 25: 198-200*)

**Anahtar kelimeler:** Akut myeloblastik lösemi, Davidoff-Dyke-Masson syndrome, Marfan syndrome.

Geliş tarihi: 1 Mayıs 2007

Kabul tarihi: 20 Haziran 2008

## Introduction

Davidoff-Dyke-Masson syndrome (DDMS) is characterized by variable degrees of unilateral loss of cerebral volume and compensatory changes of the calvaria [1-3]. Marfan syndrome (MS) is an autosomal dominantly inherited genetic disorder of the connective tissue, which affects many organ systems including the skeleton, lungs, eyes, heart and blood vessels. The basic defect has recently been identified as a mutation in the fibrillin gene on chromosome 15. The condition affects both men and women of any race and ethnic group [4]. On the other hand, acute myeloblastic leukemia (AML) is a clonal malignant disease of hematopoietic tissue [5,6]. AML occurs at any age but is more common in adults, with increased frequency as age advances. It is slightly more common in males. The etiology of AML is unknown, even if a number of inherited conditions are known to carry an increased risk of AML. Although two cases of AML associated with MS have been reported [7,8], AML associated with DDMS has not been previously reported. To date, no association between MS or DDMS and AML could be shown. Herein, a 23-year-old male with AML associated with DDMS and MS is reported.

## Case Report

A 23-year-old male was admitted to our hospital with complaints of weakness, pallor, nonproductive cough, weight loss, and night sweating. He was otherwise well until 15 days before admission except for a history of cerebral palsy after birth. There was no history of exposure to toxic agents, smoking, or use of alcohol or illicit drugs. There was also no history of any hereditary disorders in his first-degree relatives.

On admission, the patient's general condition was poor; he was fully oriented, and his speech was slow and mildly dysarthric. His temperature was 36.7°C, pulse 120/min, and blood pressure 140/80 mmHg. On physical examination, he had a tall stature, a thin and long face with intermaxillary narrowness, and paleness (Figure 1). His height was 183 cm and weight 55 kg. Length of the lower segment was 97 cm. The ratio of upper/lower segment (Us/Ls) was 0.88. His fingers were long, thin (arachnodactyly), and hyperextensible. Ophthalmologic examination revealed blue-like scleras, myopia astigmatism, and bilateral partial retinitis pigmentosa. His ears appeared large. He had gingival hypertrophy, mild scoliosis and pectus excavatum. Pansystolic murmur on the apex of the heart (I/VI degree) was noted. Radiograph of the chest was normal. Electrocardiogram revealed no abnormality. There was no mitral valve prolapse (MVP) or aortic root dilatation on echocardiographic examination. The liver and spleen were palpated just below the costal margin. Neurological examination revealed left hemiparesis, flexion contractures and muscular atrophy on the left upper and lower extremities. The deep tendon reflexes were hyperactive. There was no Babinski sign on the left side, and left cerebral tests spoiled. Right cerebral tests were normal. Cranial magnetic resonance (MR) imaging showed diffuse right cerebral atrophy. There was cerebral volume loss, widening of subarachnoid space, prominent cortical sulci, calvarial thickening and dilatation

in ipsilateral lateral ventricle (Figure 2). Mild atrophy was seen in ipsilateral cerebral peduncle, thalamus, and contralateral cerebellar hemisphere. There was no enlargement in mastoid air cells or paranasal sinuses. An arachnoid cyst 3x2 cm in diameter and not showing any mass effect was diagnosed in the right temporal lobe. The diagnosis of DDMS was based on facial asymmetry, hemiplegia, mental retardation, and cerebral hemiatrophy. The diagnosis of MS was established on the characteristics of tall stature, intermaxillary narrowness, myopia, retinitis pigmentosa, blue sclera, scoliosis, pectus excavatum, arachnodactyly and diminished ratio of Us/Ls.

On the day of admission, hematological and biochemical studies were performed and showed pancytopenia (Table 1). A stained blood smear confirmed a markedly decreased platelet and neutrophil count, accompanied by numerous monoblasts. Imprint of bone marrow material and bone marrow biopsy were packed with blasts. Morphological, cytochemical (periodic acid Schiff [PAS] was negative and peroxides weak positive) and immunophenotypic (CD11+, CD13+, CD14+, CD33+ and HLA-DR+) studies confirmed the diagnosis of AML (FAB-M5).

Transfusions of packed red cells were started. He was given chemotherapy regimen for remission induction of AML, a 3+7 day regimen of daunorubicin (45 mg/m<sup>2</sup>) and cytarabine (100 mg/m<sup>2</sup>). Platelet transfusion was given twice from a single donor during that period. The patient developed febrile neutropenia on the first day of treatment, and appropriate antibiotic therapy was started. Complete remission (CR) was obtained following induction chemotherapy. The post-remission therapy of AML was planned, and the patient was discharged from the hospital. A few months later AML recurred and the patient died.

## Discussion

We describe herein a case with AML associated with DDMS and MS. This case was interesting since each of these three diseases has a different etiologic base.

DDMS is a condition characterized by seizure, facial asymmetry, contralateral hemiplegia or hemiparesis, and mental retardation. These findings are due to cerebral injury that may occur early in life or in utero [1,2]. The radiological features are unilateral loss of cerebral volume and associated compensatory bone alterations in the calvaria, like thickening, hyperpneumatization of the paranasal sinuses and mastoid cells and elevation of the petrous ridge [1]. Our patient had facial asymmetry, hemiparesis and mental retardation.

MS is an inherited genetic disorder with characteristic ocular, skeletal, and cardiovascular abnormalities [4]. Diagnosis is made on the overall pattern of malformation; many manifestations are age- or maturation-dependent. Older individuals display tall stature and a long, thin face with intermaxillary narrowness, as in our case. Ocular abnormalities reflect the connective tissue defect and include blue sclera and myopia, as seen in our patient. Examination of the musculoskeletal system discloses dolichostenomelia, and the arm span substantially exceeds height. Tall stature with an abnormally low Us/Ls ratio is the most consistent presenting feature, as seen in our case. Hand findings are nonspecific and include long, thin and hyperextensible fin-

gers. Long, gracile ribs may contribute to various sternal anomalies including pectus excavatum, and the increased risk of scoliosis among affected adolescents, as in our case. Progressive MVP is the most common cause of morbidity in children with MS. Longevity in MS is diminished in comparison with population norms, primarily because of the increased risk of cardiovascular complications.

AML is a clonal malignant disease of hematopoietic tissue [5]. Most patients have not been exposed to an antecedent causative factor. Exposure to high linear energy transfer radiation from alpha-emitting radioisotopes such as thorium dioxide increases the risk of AML. AML may develop from the progression of other clonal disorders of hematopoietic stem cells [5,6]. Furthermore, a number of inherited conditions, for example Down syndrome, Fanconi anemia, Bloom syndrome, Wiskott-Aldrich syndrome, dyskeratosis congenita, Werner syndrome, Shwachman syndrome, Blackfan-Diamond syndrome, and Klinefelter syndrome, carry an increased risk of AML [5,6].

In the literature, two sporadic cases of AML associated with MS have been reported. The first case of acute leukemia in MS during the neonatal period was described by Sharief et al. [7]. The second case of an 18-year-old male who had acute monoblastic leukemia associated with MS was reported by Lee et al. [8]. To our knowledge, this is the first case in the literature of AML associated with both DDMS and MS, while it is the third case of AML associated with MS. Immunodeficiency is observed during neoplastic disease, and several data suggest that individuals with hereditary immunodeficiency may have an increased risk of cancer. Since MS is a genetically transmitted disease characterized by immunodeficiency, subjects with this disease may have a higher risk of cancer. However, there is no knowledge regarding AML association with MS and DDMS in the liter-

ature. We conclude that the association between these rare disorders of the connective tissue and acute leukemia is coincidental. We would like to point out that such cases with these rare disorders of the connective tissue require prolonged follow-up in view of leukemia.

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