

Mucopolipidosis type II in a low birth weight preterm infant: A case report

Düşük doğum ağırlıklı preterm bir infantta mukopolipidozis tip II. Bir olgu sunumu

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ABSTRACT

Mucopolipidosis type II and III are autosomal recessive lysosomal storage disorders caused by the deficiency of the enzyme N-acetylglucosamine-1-phosphotransferase. In this case report we present a preterm born infant with significant developmental delay, secundum atrial septal defect, central hypothyroidism, inguinal hernia, hearing loss and chronic bronchopulmonary disease. She was evaluated for metabolic disorders because of her psychomotor retardation and diagnosed with mucopolipidosis type II. Mucopolipidosis type II is a very rare metabolic disorder. The presenting symptoms are very much like mucopolysaccharidosis type I but it has an early onset and there is no mucopolysacchariduria. So we should think of mucopolipidosis type II in a relatively younger patient with symptoms like mucopolysaccharidosis type I.

Keywords: Mucopolipidosis, lysosomal storage disorders, preterm infant

ÖZ

Mukopolipidozis tip II ve tip III, N-asetilglukozamin-1-fosfortransferaz enzim eksikliđinin neden olduđu otozomal resesif geçiřli lizozomal depo hastalıđıdır. Bu olgu bildiriminde, kronik bronkopulmoner hastalıđı, iřitme kaybı, sekundum atriyal septal defekti, santral hipotiroidi ve belirgin gelişme geriliđi olan preterm doğan bir infant sunulmuřtur. Geliřim geriliđi nedeni ile metabolik hastalıklar açasından deđerlendirildi ve mukopolipidozis tip II tanısı aldı. Mukopolipidozis tip II çok ender görülen bir metabolik hastalıktır. Mukopolisakkaridoz tip I ile semptomları çok benzer fakat mukopolipidozis tip II erken bařlangıçlıdır ve mukopolisakkaridüri saptanmaz. Mukopolisakkaridoz tip I ile benzer semptomları olan yařı daha küçük hastalarda mukopolipidozis tip II tanısı aklımıza gelmelidir.

Anahtar kelimeler: Mukopolipidozis, lizozomal depo hastalıđı, preterm infant

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INTRODUCTION

Mucopolipidosis type II (I-cell disease) and mucopolipidosis type III (pseudohurler polydystrophy) are autosomal recessive lysosomal storage disorders. Their phenotypical features resemble mucopolysaccharidosis type I (Hurler disease), but the onset is earlier and there is no evidence of mucopolysacchariduria^(1,2).

Mucopolipidosis type II is caused by a defect in proper lysosomal enzyme phosphorylation and localization, which results in accumulation of lysosomal substrates. It is phenotypically more severe than the allelic disorder mucopolipidosis type III. Mucopolipidosis III produces less severe symptoms and progresses more slowly^(3,4).

The clinical features include small or low-

birthweight infant for its gestational age, coarse facial features, craniofacial abnormalities, restricted joint movements, skeletal abnormalities (clubfoot, thoracic deformity including kyphosis, dislocation of the hips, deformed long bones), psychomotor retardation, generalized hypotonia, inguinal hernia, and gingival hypertrophy ^(5,6). ML II alpha/beta is caused by a homozygous or compound heterozygous mutation of the GNPTAB gene. This gene is located on chromosome 12 at 12q23.2 ⁽⁷⁾. Mutations in GNPTAB result in a deficiency in N-acetylglucosamine-1-phosphotransferase (GlcNAc-1-phosphotransferase). This deficiency results in improper lysosomal enzyme phosphorylation, causing an accumulation of lysosomal substrates in several organs and tissues, specifically in the skeletal system ⁽⁸⁾. In this case report we present a preterm newborn diagnosed with mucopolipidosis type II.

CASE REPORT

A 4-month-old female patient was admitted to hospital with chronic bronchopulmonary disease. She was born by cesarean section at 34 weeks of gestation after a normal pregnancy. Her birth weight was 1140 gr which showed intrauterine growth retardation. Her parents were relatives. The mother was 28 years, and the father was 31 years old and both of them were healthy. Two siblings aged 6 and 3 years were healthy. In the family history the mother's cousins passed at early age because of an unknown reason.

On physical examination, she appeared dysmorp-



Figure 1. Coarse facial features.

hic, with coarse facial features, including a flat face, depressed nasal bridge, micrognathia, protruded round eyes and enlarged tongue (Figure 1). She had left inguinal hernia, significant global developmental delay and generalized muscular hypotonia.

At birth the infant had respiratory problems so she was intubated and admitted to the intensive care unit. She was ventilator-dependent and extubation failed several times. She stayed at intensive care unit for 76 days. After being discharged she had several hospital admissions because of pneumoniae and sepsis. Because of motor and mental retardation she was evaluated for genetic, and metabolic disorders.

Her thyroid-stimulating hormone levels were high so she was diagnosed with central hypothyroidism and received levothyroxin treatment. She was evaluated for cardiac disorders using transthoracic echocardiography. Echocardiogram demonstrated a secundum atrial septal defect. Her ophthalmologic examination was normal. Her hearing tests showed hearing loss. Tandem mass spectrometric findings were within normal limits. X-ray surveys of the patient didn't show any skeletal anomalies.

Urine tests were performed in search for oligosaccharides, sialic acid and mucopolisaccharides. Trace dermatan sulphate was seen in the urine samples. To confirm the diagnosis of metabolic disorders, former enzymatic tests were performed. Plasma beta - hexosaminidase A+B and alpha-mannosidase levels showed consistency with mucopolipidosis type II-III (Beta - hexosaminidase A+B: 22641 umol/l/h, alpha-mannosidase: 5011 umol/l/h) and she was diagnosed with mucopolipidosis type II. Genetic tests were not applied in this patient.

DISCUSSION

We present this case, because it is a very rare disorder and it resembles mucopolysaccharidosis type I, but with an early onset. To our knowledge, this is the first case report of mucopolipidosis type II in a preterm infant.

Mucopolipidosis type II and mucopolipidosis type III

are rare disorders. They have an early onset compared to mucopolysaccharidosis. Various lysosomal enzyme activities can be measured in serum and in cultured fibroblasts for diagnosis. The activities of beta-hexosaminidase, iduronate sulfatase, and arylsulfatase A are deficient in cultured fibroblasts, but their serum levels are 10-20 times higher than their reference ranges^(2,3).

Our patient was a preterm newborn with severe respiratory problems and severe developmental and growth delay. She had several hospital admissions because of sepsis and pneumonia. She had coarse facial features, inguinal hernia, hypotonia and secundum atrial septal defect as well. Cardiac manifestations reported in the published reports include cardiomyopathy, right and generalized ventricular hypertrophy, valvular thickening and mitral valve regurgitation were the most frequent findings⁽⁹⁾. In patients with mucopolipidosis type II ocular findings such as corneal clouding, retinopathy and astigmatism may be seen, but our patient's ophthalmological examination was normal.

We suspected mucopolisaccharidosis due to the clinical features. Urinalysis showed trace dermatan sulphate levels, and also enzymatic tests were performed. Beta-hexosaminidase A+B and alpha-mannosidase levels showed consistency with mucopolipidosis type II-III.

Mucopolipidosis II appears to differ radiologically early on from the other mucopolipidoses and mucopolysaccharidoses. Talocalcaneal stippling, sacrococcygeal sclerosis, severe generalized vertebral body sclerosis, vertebral body rounding of the lower thoracic/lumbar spine and rickets/hyperparathyroidism-like changes in the early years of life strongly suggest the diagnosis of mucopolipidosis II. Periosteal cloaking (outline of periosteal margins), is observed around the diaphyses of the large long bones and this transient phenomenon is rarely detectable after the first year of life⁽¹⁰⁾. We performed radiological surveys of our patient and no radiologic anomalies were detected.

The diagnosis of mucopolipidosis type II/III is based

on clinical, radiological, biochemical and molecular findings. A mutation study of GNPTAB is important in terms of confirmation of the disease and prediction of prognosis. Genotypes with compound heterozygotes consisting of nonsense and frameshift mutations are not expected to produce RNA product, and they are associated with a more severe phenotype⁽¹¹⁾. In our case we couldn't perform any molecular and genetic tests to the patient. A mutation study gives important information about the prognosis and helps to confirm the diagnosis.

The prognosis of mucopolipidosis is poor and it usually has a fatal outcome. Most patients die because of cardiorespiratory insufficiency in early childhood. Treatment is usually symptomatic and supportive. Bone marrow transplantation or hematopoietic stem cell transplantation has been attempted in some children but the information on their outcomes is not yet available⁽¹²⁾.

A patient with coarse facial features, dysmorphic phenotypical features and frequent respiratory tract infections should remind us metabolic disorders. Mucopolipidosis type II is a very rare metabolic disorder and the symptoms are very much like mucopolisaccharidosis type I but it has an early onset and there is no mucopolysacchariduria. So we should think of mucopolipidosis type II in a relatively younger patient with symptoms like mucopolisaccharidosis type I.

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