Chanarin-Dorfman Syndrome: A Case Report

Chanarin-Dorfman Sendromu: Olgu Sunumu

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ABSTRACT

Chanarin-Dorfman syndrome is a multisystem inherited metabolic disorder associated with congenital ichthyosis and accumulation of lipid droplets in various types of cells. Mutation of *ABHD5/CG158* gene in the short arm of the 3rd chromosome is responsible from the main metabolic defect. Clinically, the disease is presented with ichthyosis, hearing loss, hepatomegaly, splenomegaly, cirrhosis, cataract, keratopathy, myopathy, and mental retardation. Here we present a case of Chanarin-Dorfman syndrome in a 2 years girl with who had ichthyosis, elevation of liver enzymes, hepatomegaly and mutation of *ABHD5*.

Key Words: Chanarin-Dorfman syndrome; Ichthyosis; Jordan anomaly; hypertrophic cardiomyopathy; *ABHD5* gene

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ÖZET

Chanarin-Dorfman sendromu, konjenital iktiyozis ve çeşitli hücrelerde lipit damlacıklarının birikimi ile ilişkili kalıtsal bir metabolik bozukluktur. *ABHD5/ CG158* geninin 3. kromozomun kısa kolundaki mutasyon ana metabolik kusurdan sorumludur. Klinik olarak hastalık iktiyozis, işitme kaybı, hepatomegali, splenomegali, siroz, katarakt, keratopati, miyopati ve zeka geriliği ile kendini gösterir. Burada iktiyozis, karaciğer enzimlerinin yükselmesi, hepatomegali ve *ABHD5* mutasyonu olan 2 yaşındaki bir kız çocuğunda Chanarin-Dorfman sendromu olgusunu sunuyoruz.

Anahtar Sözcükler: Chanarin-Dorfman sendromu; İktiyoz; Jordan anomalisi; hipertrofik kardiyomiyopati; *ABHD5* geni

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INTRODUCTION

Chanarin-Dorfman syndrome (CDS) is a multisystemic, lipid storage disease inherited autosomal recessively and characterized by lipid accumulation in neutrophil leukocytes. Chanarin and Dorfman have defined the syndrome in 1975 (1). Mutation of *ABHD5/CG158* gene in the short arm of the 3rd chromosome is responsible from the main metabolic defect (2,3). Clinical symptoms arise from accumulation of lipids in granulocytes in muscle, liver, eye, ear, central nervous system and bone marrow. The syndrome is diagnosed by ichtiosiform dermatosis with presence of lipid vacuoles in monocytes or granulocytes (Jordan's sign) in peripheral blood smear of the patients (4). Here we present a case of CDS in a 2 years girl with who had ichthyosis, elevation of liver enzymes, hepatomegaly and mutation of ABHD5.

CASE REPORT

Two years old girl was referred to our outpatient clinic with elevated transaminase levels. There was first degree consanguinity between parents. She was diagnosed as ichtyosis due to her scaly skin which was not healed although treatment with different topical medicines. After detection of high levels of transaminases during routin tests she was referred to our clinic. There was no history of jaundice, bleeding or changes in urine colour.

On physical examination; she was 11 kg in weight (25 P), 86 cm in length (25-50 P) and her head circumference was 47 cm. She had evident dry skin, mid erythema, multiple hyper pigmented squamous lesions on her back and body and widespread hyperkeratosis Abdominal examination revealed generalised abdominal distention and liver was palpable four cm below the right costal margin, was non tender and firm in consistency. There was no splenomegaly and no lymphadenopathy. Examination of other systems revealed no abnormalities.

On laboratory evaluation, full blood count, urinalysis, serum electrolytes, cholesterol, and lipid levels were normal. His liver functions were as follows: ALT 73 U/L, aspartate aminotransferase (AST) 79 U/L, total serum bilirubin 0.5 mg/dL and the direct fraction 0.08 mg/dL, alkaline phosphatase (AP) 267 U/L, gamma glutamyl transpeptidase (GGT) 22 U/L, serum albumin 4.3 g/dL, prothrombin time 12.3 s, and international normalised ratio (INR) 1.1. The serum creatine kinase (CK) level was elevated 706 U/L. Peripheral blood smear revealed cytoplasmic vacuoles in most neutrophils.

Abdominal ultrasound showed a enlarged and fatty infiltration of liver. Otherwise, scanning of the gall bladder, spleen, and kidneys was normal, and there was no ascites. Ophthalmological and otorhinolaryngological examinations were normal. Electromyography (EMG) was also normal. Muscle biopsy was not performed. Echocardiography revealed that concentric hypertrophic cardiomyopathy.

The patient was found to have a homozygous mutation p.I198fs (c.594dupC) in the *ABHD5* gene. This resulted in addition of a cytosine base to the cDNA sequence following the 594th base, which resulted in the formation of a frame shift mutation and premature stop codon. This mutation has previously been defined (Human Gene Mutation database no. 0016006).

The clinical and laboratory findings indicated that the patient had CDS, and this diagnosis was confirmed by the finding of the *ABHD5* gene mutation.

DISCUSSION

CDS is a rare autosomal recessive metabolic disease, characterized by accumulation of lipid vacuoles in different organ systems. Mutation in *ABHD5/CG 158* gene which is responsible for the activation of enzyme hydrolysing triacylglycerol, triglyceride lipase is the main metabolic defect (5). Mutation in *ABHD5/CG158* gene causes accumulation of lipid molecules in leukocytes, fibroblasts, liver and muscle cells by inhibition of lipolysis which is responsible for the symptoms like ichtyosis, loss of hearing, hepatomegaly, splenomegaly, cirrhosis, cataract, myopathy and mental retardation (6-8). The disease is frequent in Mediterranean countries and especially in some middle east countries in which widespread consanguineous marriage has been seen. There was also first degree consanguineous marriage between parents of our case.

Variety of symptoms can be seen in different lipid metabolism diseases occurred due to different enzyme defect. In CDS hepatic involvement usually with hepatomegaly have been seen in 2/3 of the patients (7). Although hepatosteatosis is the most frequent finding, fibrosis also has been seen in the liver biopsy of the patients.

Elevated levels of transaminases, hepatomegaly and ultrasonographically detected hepatosteatosis were also present in our case. Bud we couldn't perform liver biopsy due to refusal of the parents.

Another important clinical sign of the syndrome is myopathy, and it exists in 60% of the cases (9). It may manifest clinically as weakness or it may remain as subclinical myopathy. Despite an elevated CK level in our patient, the EMG at the age of two was still normal. Other neurological symptoms like mental retardation, microcephaly, seizure, gait abnormalities or sensor neural hearing loss were not seen in our case. Other reported associations include growth retardation, cataracts, ptosis, nystagmus, splenomegaly, intestinal anomalies, short stature and cardiomyopathy (it was documented in our case by echocardiography).

İchtyosis in CDS appears like non bullous congenital ichtyosiform erithroderma. The lesion is characterised a fine scaling over erythematous background. On the other hand CDS associated non erythrodermic ichtyosis also had been reported (7). In a case serie conducted by Pena-Penabad and colleagues ichtyosis was shown in all of the patients even without erythema (6). Although we didn't observed in our patient hyperkeratosis and ectropion are also frequent findings of the syndrome.

Although there is not a specific treatment for CDS a diet rich in middle chain fatty acids and poor in long chain fatty acids had shown to have some beneficial effects on liver and skin lesions (10). Local emollients may also be used for symptomatic treatment of the skin lesions. As a systemic treatment regimen retinoids like acitretin had been shown to be useful for skin and muscle manifestations (12). We observed no improvement in symptoms of our case after eight months of diet.

In conclusion, we report a Turkish child presenting with CDS, a disease of the lipid metabolism, which is caused by various mutations of the *ABHD5* gene. Although CDS is an infrequent lipid storage disease, should be kept in mind specially in patients with congenital ichtyosis and associated symptoms besides skin lesions. When the diagnosis is made, screening of almost all organ systems for the aforementioned abnormalities may help start the required support early before the symptoms set in.

Conflict of interest

No conflict of interest was declared by the authors.

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