

Dorfman-Chanarin syndrome: a case with hyperlipidemia

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SUMMARY: Düzovalı Ö, İkizoğlu G, Turhan AH, Yılğör E. Dorfman-Chanarin syndrome: a case with hyperlipidemia. Turk J Pediatr 2006; 48: 263-265.

Dorfman-Chanarin syndrome is a rare, autosomal recessive disorder characterized by congenital ichthyosis and presence of intracellular lipid droplets in most tissues. Here, we present a patient from Turkey, who is the fourth Turkish case in the literature with this syndrome, and we review the previous reported cases. He was also the second case reported with hyperlipidemia.

Key words: congenital ichthyosis, lipid storage disease, cytoplasmic vacuoles.

Dorfman-Chanarin syndrome (DCS, neutral lipid storage disease) is an autosomal recessive entity characterized by congenital ichthyosis, lipid droplets within leukocytes, and variable involvement of other organ systems¹. Since the first description by Dorfman et al.⁶ in 1974, approximately 40 cases with this syndrome have been reported, most from the Middle East and Mediterranean countries.

We present a four-year-old Turkish boy with DCS, who is the fourth reported case from Turkey.

Case Report

A four-year-old Turkish boy was born at term as the first child to consanguineous parents who were first cousins. He had a scaly skin at birth, but there was no evidence of a definite collodion membrane. One sister who did not have skin involvement at birth died at one month of age. His younger brother was reported as healthy. There were no other known cases of skin disease in the family.

Dermatological examination revealed generalized erythema and fine desquamating scales over his entire body surface, including flexural areas. Facial skin was erythematous and dry, but ectropion was absent. His hands, feet, palms, soles, and hair were normal, but there was diffuse, whitish scaling of the scalp. The nails appeared normal. His parents stated that they had observed a slight improvement in summer months.

On physical examination, his weight and height were at the 25th and 50th percentiles, respectively. His liver and spleen showed

enlargement upon palpation. Firm hepatomegaly 5 cm below the right costal margin and firm splenomegaly were detected. Neurological examination, muscle power, and psychomotor development were normal, and there were no hearing abnormalities. Ophthalmological examination was normal.

Laboratory investigations showed a normal blood count, erythrocyte sedimentation rate, urea, creatinine, electrolytes, alkaline phosphatase, total protein, albumin, globulin, glucose, and urinalysis. The results of other biochemical tests were as follows: aspartate aminotransferase (AST) 351 U/L, alanine aminotransferase (ALT) 374 U/L, gamma-glutamyl transferase (GGT) 87 U/L, total bilirubin 3 mg/dl, total cholesterol 307 mg/dl (normal range 112-205 mg/dl), triglycerides 458 mg/dl (normal range 35-110 mg/dl), very low density lipoprotein (VLDL) 92 mg/dl (normal range <40 mg/dl), high density lipoprotein (HDL) 12 mg/dl (normal range 35-85 mg/dl), creatine phosphokinase 343 U/L (normal range 0-170 U/L), and lactic dehydrogenase 1545 U/L (normal range 0-615 U/L). Abdominal ultrasound showed hepatomegaly, splenomegaly, and slightly enlarged lymph nodes in the portal hilum. Chest X-ray was normal. His bone age was two.

On examination of the peripheral blood smear, cytoplasmic vacuoles within granulocytes, eosinophils and monocytes were detected (Figs. 1, 2). Lymphocytes, red blood cells, and platelets were normal. Lipid stains (oil red O and Sudan red) confirmed that the vacuoles contained neutral lipid.

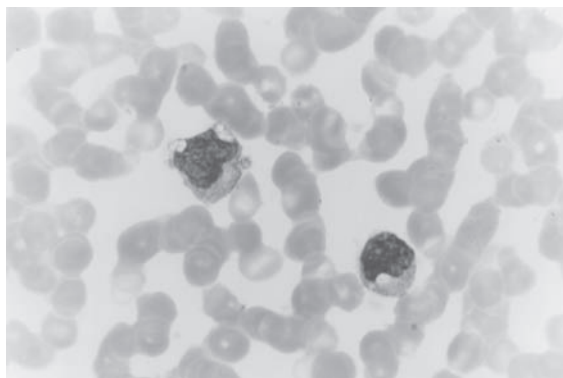


Fig. 1. Giemsa-stained peripheral blood smear showing lipid droplets in polymorphonuclear leukocytes, X100.

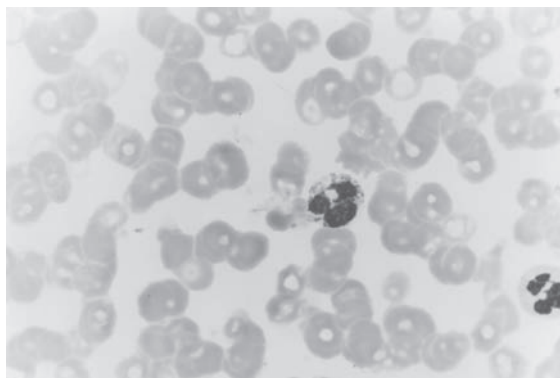


Fig. 2. Lipid-containing vacuoles in monocytes, X100.

Although the father was clinically unaffected, his peripheral blood smear showed vacuoles in some of the neutrophils and monocytes. No other relatives were examined.

After Jordans' anomaly was detected (i.e. vacuoles in neutrophils), further investigation of the patient was planned, but his parents did not allow a skin or liver biopsy to be performed. Based on the dermatological and laboratory findings, a diagnosis of DCS was made.

Discussion

Dorfman-Chanarin syndrome, also referred to as "neutral-lipid-storage disease with ichthyosis", is a rare, autosomal recessively-inherited lipid storage disease characterized by congenital ichthyotic erythroderma, lipid vacuoles in neutrophils (Jordans' anomaly), and variable involvement of liver, muscle, and central nervous system²⁻⁴.

Lipid inclusions within monocytes and leukocytes were first described by Jordans in 1953, and in 1966, Rozenszajn et al.⁵ reported a kindred with similar leukocyte lipid droplets and ichthyosis. Two members of this kindred, with two additional patients, characterized by a multisystem disorder of lipid metabolism, were reported by Dorfman et al.⁶ in 1974. One year later, Chanarin et al.⁷ reported another case with similar findings and pointed to an abnormality of intracellular triglyceride metabolism. By electron microscopy, these lipid vacuoles, containing neutral lipid, were nonmembrane bound and cytoplasmic⁵. Ultrastructural studies showed mitochondrial involvement, suggesting a defect in mitochondrial fatty acid oxidation⁸. It is suggested that neutral lipid, in the form

of triacylglycerol, accumulates in most cells due to an enzymatic error in the recycling pathway converting triacylglycerol to phospholipids⁹. In recent years, mutations in CGI-58, the gene encoding a new protein of the esterase/lipase/thioesterase subfamily, have been detected in DCS, suggesting a genetic influence¹⁰.

Although liver, muscle, ear, eye and central nervous system involvement is frequent, DCS may present clinically as monosymptomatic ichthyosis. Systemic involvement usually does not interfere with a normal life span^{2,11}. Clinical diagnosis is based on the demonstration of lipid vacuoles in neutrophils in patients with congenital ichthyosis. On histopathological examination of the skin, lipid droplets in basal and granulocytic cell layers, as well as in epidermal Langerhans cells, fibroblasts, Schwann cells in both myelinated and unmyelinated nerves, smooth muscle cells, and sweat gland cells are detected^{2,5,12-14}. Unfortunately, a skin biopsy could not be performed on our patient.

Myopathy has been observed in some patients with this syndrome^{9,11,15}. Lipid droplets within muscle fibers, Type I fibers being more severely affected, can be demonstrated by oil red O staining and electron microscopy^{1,5,16}. In our patient, there was no clinical evidence of myopathy, but creatine phosphokinase level was elevated. Muscle biopsy, like skin biopsy, could not be performed as consent was not given.

Neurologic impairment characterized by ataxia, nystagmus, neurosensory deafness, as well as by developmental delays and learning disabilities has been reported^{1,5,6}. In our patient no neurologic impairment was observed.

Ophthalmologic findings such as a mild degree of ectropion, cataracts, and retinal dysfunction were reported in the literature^{1,6,11,15,16}. There were no ocular manifestations in our patient.

The liver is reported to be the most frequently affected organ. Patients usually present with hepatomegaly, elevated liver enzymes and fatty liver. Severe fatty degeneration is a common histopathological finding^{1,5,6,9,15,16}. Although not frequently reported, splenomegaly can also be seen¹. We suspected hepatic involvement based on hepatomegaly and elevated liver enzymes. However, it could not be confirmed because of the missing histopathological findings.

Aortic insufficiency, slight right ventricular overload, cardiomyopathy, and electrocardiographic abnormalities are reported to be related with DCS^{5,6,16}. Our patient had no cardiac abnormalities.

No alterations in serum lipids have been reported, with the exception of a patient reported by Williams et al.⁵, who had a high VLDL and low HDL. Our patient, to the best of our knowledge, is the second case with such a lipid profile. In addition, fasting cholesterol and triglyceride levels were found to be elevated.

Heterozygous carriers of the syndrome are asymptomatic, but they can be identified by the presence of similar, though fewer, vacuoles in myeloid leukocytes, especially in eosinophils^{1,15,16}. Vacuolization was demonstrated on the peripheral smear of our patient's father.

There is no known effective treatment, but a diet low in long-chain fatty acids and enriched with medium-chain fatty acids is reported to improve skin and liver manifestations. Acitretin is useful in the treatment of skin and muscle manifestations^{9,11,15}.

We have presented the fourth Turkish case of Dorfman-Chanarin syndrome, based on clinical and laboratory findings. Splenomegaly and hyperlipidemia are findings not frequently reported in association with this syndrome. Since extracutaneous manifestations range between no extracutaneous involvement to multisystem involvement, inspection of a fresh blood film should be a routine test in all patients with congenital ichthyosis in order to not miss the diagnosis.

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