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**Case report**
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# A case with full clinical manifestations of Dorfman-Chanarin syndrome

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**Abstract:** Dorfman-Chanarin syndrome (DCS), is a rare, autosomal recessive disorder associated with lipid metabolism. It is characterized by ichthyosiform nonbullous erythroderma, lipid vacuoles in peripheral leukocytes and variable involvement of organs. We report a Turkish man with the complete syndrome, who described family history of ichthyosis. To best of our knowledge this is the sixth case from Turkish origin to date. In addition to congenital ichthyosis he had also strabismus, horizantal nystagmus, bilateral neurosensory hearing loss, hepatomegaly and splenomegaly. Liver biopsy revealed hidrophic degeneration in hepatocytes, steatosis, enlargement and inflammation in portal areas and portal central fibrosis, consistent with cirrhosis. Write stained peripheral blood smear examination revealed lipid vacuoles in all of the neutrophils consistent with Jordan's anomaly. We think that, it is essential to evaluate the peripheral blood smear of the patients with ichthyosis and also patients with DCS should be informed and warned about the results of consanquinous marriage.


*Keywords: Dorfman-Chanarin Syndrome, ichthyosis, leucocytes vacuoles*

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## 1 Introduction

Dorfman-Chanarin syndrome (DCS), is a rare and autosomal recessive disorder. It is characterized by ichthyosiform nonbullous erythroderma, lipid vacuoles in peripheral leukocytes and variable involvement of organs such as liver, muscle, central nervous system, eyes and ears [1–3]. Clinical manifestations of this syndrome related with the affected organs are; ichthyosis, myopathy, liver steatosis, sensorineural hearing loss, growth retardation, mental retardation, cataract and a variety of neurological symptoms. To our knowledge, 45 cases of DCS have been reported in the worldwide [4–8]. The majority of patients were of Middle-Eastern origin [2, 9] and five of the cases were Turkish origin [6, 8, 10]. Herein, we report a Turkish man with the complete syndrome in addition to organ calcifications who described family history of ichthyosis.

## 2 Case report

Fifty year old Turkish man, with congenital ichthyosis admitted to the hospital complaining with inguinal pain, dysuria and generalized muscle pain together with weakness. He is married with his cousin, and also he was born of a consanquinous marriage. In his history; he had bilateral cataract operation four years ago, and thirteen years ago he had brain trauma due to traffic accident. He had no cigarette, drug or alcohol exposure. In family history, his father had died at the age of 72 year old due to liver cirrhosis. He had 4 sisters and 4 brothers. One of his sisters was said to be born with ichthyosis and had died while she was 3 years old. The case has two healthy children.

The patient's pyhsical examination revealed generalised squamatous skin lesions in dorsal spine, abdomen, arms and legs including all flexures. The facial skin was shiny and dry. He had short status (height 1.57 m). Ophtalmological examination revealed strabismus and horizantal nystagmus, audiological examination revealed bilateral neurosensory hearing loss. The liver was palpabl to 5 cm below the costal margin. Laboratory parameters revealed increased levels of aspartate aminotransaminase (77 U/L; normal range: 0-40), alanine aminotransaminase (71 U/L; normal range: 0-40), lactate dehydrogenase (314 U/L; normal range: 125-243), creatine phosphokinase (783 U/L; normal range: 25-175), triglyceride (283 mg/dl; normal range: 50- 200) and very low density lipoprotein (57 mg/dl; normal range: 10–40). Other parameters including fasting blood sugar, serum blood urea nitrogen, creatinine, calcium, uric acid, sodium, potassium, albumin, bilirubin and gamma glutamyl transferase were all within normal ranges. The count of red blood cells, leucocytes, and trombocytes were within normal ranges. Wright stained peripheral blood smear examination revealed lipid vacuoles in all of the neutrophils consistent with Jordan's anomaly (Figure 1). Urinalysis revealed microscopic hematuria, without proteinuria. Hepatitis markers including Hepatitis B surface antigen, anti hepatitis C virus antibody, anti hepatitis A immunoglobin M antibody were negative. Additionally, antinuclear antibody, immunoglobulin levels (A, G and M), compleman 3, compleman 4, antimitochondrial antibody, anti neutrophil stoplasmic antibody, liver kidney microsomal

antibody and anti smooth muscle antibody were all negative. Light microscopic examination of the skin biopsy was inconclusive. Chest X-ray, electrocardiogram, cranial tomography were normal. Abdominal ultrasonography revealed hepatomegaly, splenomegaly, parancymal calcifications in the spleen, bilateral renal cortical cysts and shiny echogenic mass of 4 mm diameter (Cyrstalloid) at the left kidney. Pelvic ultrasonography showed periuretral calcification of prostate gland. Abdominal tomography showed similar findings with abdominal ultrasonography. He was evaluated for microscobic hematuria. Acidoresistant bacteria and tuberculose culture in the urine were negative. Urinary calcium, phosphate, oxalate excretion and angiotensin converting enzyme and intact parathormon levels in the serum were within normal levels. He didn't give consent for kidney biopsy. Echocardiography revealed left ventricular hypertrophy. Due to mucle pain, he was evaluated for myopathy, but electromyelography revealed no pathology. Light microscopic examination of liver biopsy revealed extend hidrophic degeneration in hepatocytes, microvesicular and macrovesicular steatosis involved 30 % of hepatocytes, enlargement and inflammation in portal areas and portal central fibrosis, consistent with cirrhosis.

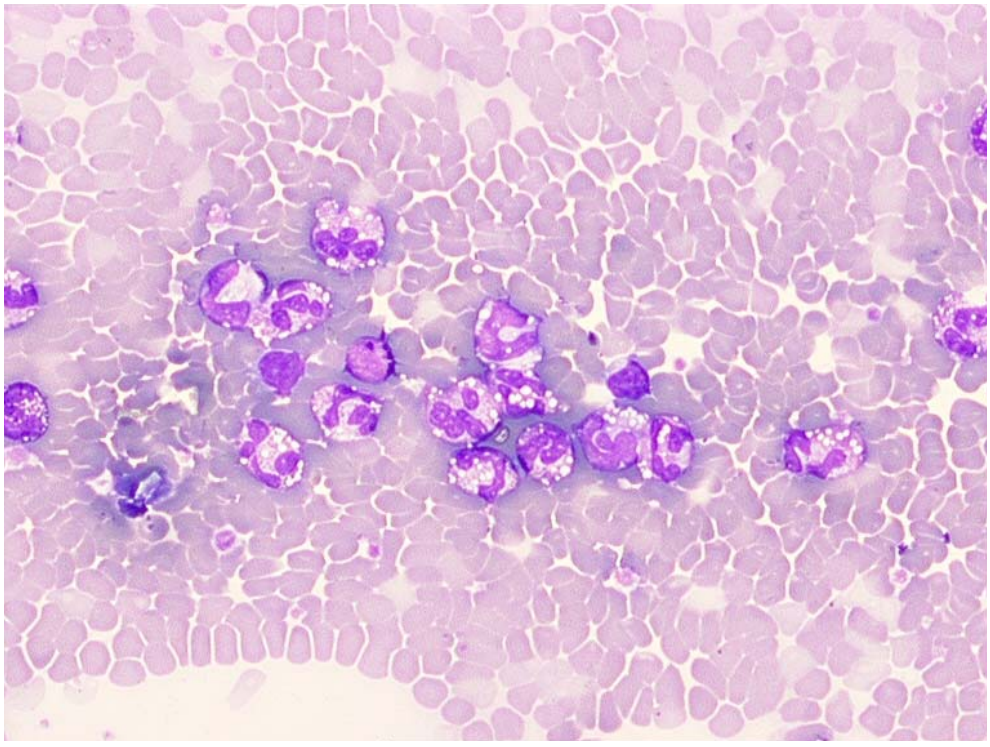

**Fig. 1** Wright stained of peripheral blood smear: Jordan'a anomaly in neutrophils.

## 3 Discussion

This inherited lipid storage disease was first recognized by Dorfman in 1974 and subsequently by Chanarin in 1975 [2], coined the name in 1975. To our knowledge, since first description, 45 cases were reported to date in the world literature, most of whom have been observed in consanguineous families from the Middle East origin. The present case

was also born of consanguineous marriage. In literature, there are five cases of Turkish origin reported with DCS characterized by ichthyosis, lipid vacuoles in the leucocytes and also liver involvement has observed in three cases of them [6, 8, 10]. The wide spread tissue deposition of neutral lipids result in a broad spectrum of systemic manifestations. The most important feature of DCS is; congenital nonbullous ichthyosiform erythroderma and lipid vacuoles in the leucocytes (Jordan's anomaly) in the peripheral blood smear [2]. Most of cases present with skin manifestations of moderate to severe nonbullous congenital ichthyosiform erythroderma. The presence of lipid containing vacuoles in the neutrophils, eosinofils and monocytes (Jordans anomaly) is an important diagnostic criteria of this syndrome. Peripheral staining of the present case showed lipid vacuoles in 100 % of neutrophils, which is described as Jordan's anomaly.

Variable organs can be affected in DCS [11]. It is interesting that, there is association between clinical features and ethnic background in the DCS [4]. It is shown that Japanese patients have usually myocardial involvement without skin lesions, contrastly, the patients who are from Mediterranean region usually have skin disorders without cardiac involvement [4]. Extracutaneous manifestations including fatty liver, myopathy, cataract, neurosensory hearing loss and neurologic symptoms show clinical variability [3, 10]. It has been reported that, the most frequently affected organ is the liver (64 % of cases) [12]. Hepatic steatosis with steatohepatitis can progress to cirrhosis rapidly [5]. In the presence of fatty liver hepatic enzymes can be in normal ranges [10]. It is considered that liver biopsy is variable in the diagnosis of DCS [3]. The prognosis of this disorder mainly depends on the course of liver disease and extend of hepatic fibrosis. In the present case, liver biopsy revealed extend hidrophic degeneration in hepatocytes, microvesicular and macrovesicular steatosis and portal central fibrosis. In the neurologic involvement of DCS, myopathy with or without elevated serum muscle enzymes and abnormal electromyelography, ataxia, areflexia, diffuse hypotonia, ptosis, cranial nerve palsies, nystagmus, facial weakness, developmental delay are reported [9, 11]. Clinical myopathy usually begins in the thirties [3]. In the present case, although electromyelography showed no pathology, he had muscle pain and increased serum muscle enzymes. The most frequent ocular presentation is cataract, which occurs in 42 % of cases [12]. Other oculer manifestations are; strabismus, nystagmus, myopia, retinal dysfunction, mild ectropion (as a result of facial involvement by ichthyosis) [11, 12]. In our case, eye involvement was characterized by findings of nystagmus, strabismus and cataract. Deafness can be seen in DCS, it can occur at any age and it can be progresive [3, 11]. In this case odyologic examination revealed bilaterally sensoryneural hearing loss. The present case was have full clinical manifestations of DCS, including soft tissue calcifications. No causative factor was found to be responsible for organ calcifications.

The prominent histological finding is presence of lipid droplets in basal and granulocytic layers of the skin [9, 11]. However skin biopsy was nonspesific in the present case. Additionally, it has been shown that, in the skin involvement, there is no correlation between the clinical severity and the microscobic findings [3, 13].

The pathogenetic defect of this disorder seems to be associated with abnormality of

intracellular triglyceride metabolism, especially in the catabolism of long-chain fatty acids or in the recycling pathway of triglycerol-derived monoacylglycerols or diacylglycerols into phospholipids [9, 14]. ABHD5 (abhydrolase domain containing 5 {CGI-58} ) is a gene which encodes an enzyme with an $\alpha\beta$-hydrolase fold and esterase-lipase-thioesterase activity [5]. Mutation in both copies of this gene causes DCS [5]. The role of enzyme which is coded by ABHD5, and how the mutation in both copies of this gene, also how the product of ABHD5 contributes to cellular lipid storage is unknown [5, 14]. Recently, CGI-58 mutations are identified in DCS families, who are from Mediterranean area [14].

In conclusion, despite a rare disorder, DCS should be suspected in patients with ichthyosis in the presence of other clinical findings of this syndrome. We also conclude that these patients should be informed and warned about the results of consanquineous marriage.

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