Vacuolated Leukocytes in the Peripheral Blood Smear of a Child With Chanarin-Dorfman Syndrome

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To the Editor,
Chanarin-Dorfman syndrome (CDS) is a rare autosomal recessive inherited neutral lipid metabolism disorder (NLSD) characterized by lipid vacuoles in leukocytes (Jordan's anomaly) on a peripheral blood smear and ichthyosiform erythroderma with involvement of multiple tissues in the body including liver, skin, muscle, eyes, ears and central nervous system. More than 100 cases have been documented worldwide mostly from the Mediterranean and Middle-East region [1-4].

A 4-month-old boy with congenital ichthyosis was referred to pediatric hematology department because of leukocytosis and thrombocytosis. It was learned that the baby was born at full term as a collodion baby by caesarean section as the first alive child of the family. One brother died of respiratory failure when he was 10 days old in the family history. There was consanguinity between parents and there was no similar patient in the family. Physical examination was normal except non-bullous ichthyosiform erythroderma on his scalp, face, trunk and flexures (Figure 1a). Blood count revealed leukocytosis (18.5 x 10³/µL) and thrombocytosis (674 x 10³/µL). Biochemical examinations were normal except mild aspartate
aminotransferase elevation (AST) (75 U/L). The peripheral blood smear revealed vacuoles in neutrophils and monocytes consistent with Jordan's anomaly (Figure 1b, c, d, e). Serum lipid analysis showed elevated serum triglyceride 257 mg/dl (0-149) and very low density lipoprotein cholesterol 51 mg/dl (10-40). Urine culture revealed E. coli (>100,000 CFU/ml) and the patient's leukocytosis and thrombocytosis were thought to be due to urinary tract infection. Due to the presence of ichthyosis and vacuoles in leukocytes, CDS was suspected and genetic analysis was performed. ABHD5 gene analysis revealed homozygous c.594_595insC (p.Arg199Glnfs*11) mutation on exon 4 consistent with CDS. This mutation was previously identified (HGMD number: CI013354) in a Turkish family and a Kurdish origin child [5,6]. ABHD5 gene encodes a protein which is a member of the esterase/lipase/thioesterase subfamily. To date, 37 different types of ABHD5 mutations have been reported in CDS patients [7].

In CDS, lipid droplets accumulate in the cytoplasms of various tissues as a result of abnormal catabolism of triacylglycerols being irrelevant to lysosomes Non-bullous ichthyosiform erythroderma or fine scaling on erythematous skin since birth is a characteristic finding of CDS [8]. Apart from skin manifestations, steatohepatitis, sensorineural hearing loss, subcapsular cataract, nystagmus, strabismus, myopathy and mental retardation can be seen. NLSD skeletal myopathy and cardiomyopathy are two clinical variants of NLSDs in which ichthyosis is not observed while the vacuoles are detected in leukocytes [9].

There is no specific treatment for CDS. However, a diet, low in fatty acids with medium chain triglycerides (MCT) was reported to decrease hepatomegaly and normalize hepatic enzymes, especially when initiated early in diagnosis with the combination of vitamin E and ursodeoxycholic acid [4]. Emollient cream, artificial tear drops and MCT containing diet were started to our patient, and he has been followed up for 5 years since the initial diagnosis. His thrombocytosis and leukocytosis improved and hemogram values remained normal ranges until 5 years of age. At the age of 5, the patient has had persistent ichthyosis (Figure 1f), mild mental retardation and multi-organ involvement. The liver was 3 cm palpable below the costal margin with moderate increase in transaminases (AST 118 IU/L, (normal 0-40 U/L); ALT 134 IU/L, (normal 0-55 U/L)) and there was no splenomegaly. He developed grade II hepatosteatosis at the age of 2.5, punctate keratopathy at the age of 3, and mild hearing loss at the age of 5. Myopathy has been reported in a patient with the same mutation as our patient [6]. However, our patient did not have myopathy. Except for NLSDs, leukocyte vacuolization can be seen in acquired conditions (infections, alcoholism, toxin exposure, diabetic ketoacidosis) and in inherited conditions (carnitin deficiency, multiple sulfatase deficiency, Refsum disease, Wolman disease). In acquired conditions, leukocyte vacuolization is temporary and there is no accompanying ichthyosis. However, in the inherited conditions mentioned above, there are persistent leukocyte vacuolization accompanying ichthyosis except carnitin deficiency. We excluded these disorders in our patient with the presence of ABHD5 gene mutation [6].

In conclusion, CDS should be kept in mind in a patient presenting with the combination of marked ichthyosis and persistent leukocyte vacuolation in the blood smear.

References


Figure 1. Non-bullous ichthyosiform erythroderma on the scalp, face, trunk and flexures (a), lipid vacuoles in leukocytes (b, c, d, e), persistent ichthyosis (f).