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Letter to the Editor

Chanarin-Dorfman Syndrome Presenting with Ichthyosis and Persistent Hypercreatinekinasemia: Value of the Peripheral Blood Smear

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Introduction

Chanarin-Dorfman syndrome (CDS) is a rare autosomal recessive non-lysosomal lipid storage disorder characterized by the accumulation of neutral lipids in various tissues such as the skin, skeletal muscle, liver, eye, ear, central nervous system, and bone marrow (1). The disease is caused by mutations in the [alpha/beta hydrolase domain 5 (ABHD5) -containing, comparative gene identification-58 (CGI-58)] gene located on the short arm of chromosome 3 (2). Diagnosis is based on the presence of ichthyosiform skin lesions and the demonstration of lipid vacuoles in neutrophils or monocytes in a peripheral blood smear. Defective lipolysis leads to intracellular triglyceride accumulation and the pathognomonic Jordans' anomaly in leukocytes (1,3). In this case report, we present a two-year-old girl with ichthyosis, muscle enzyme elevation, and vacuolated neutrophils, illustrating how a simple peripheral blood smear can direct timely molecular confirmation and counselling.

At one year of age, the patient developed scaly lesions beginning on the upper extremities and spreading to the whole body. Family history revealed second degree consanguinity. On physical examination, her height, weight, and head circumference were within normal percentiles. Systemic examination revealed marked skin dryness, hyperpigmented scaly patches on the back and trunk, and generalized hyperkeratosis (Figure 1). Neurological findings were normal. Laboratory tests showed elevated creatine kinase (CK) at 1.046 IU/L (reference: 0-190 IU/L). Muscle tissue associated enzymes, namely aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and aldolase, remained within reference limits. Thyroid, parathyroid, viral serologies, autoimmune panel, serum lipids, and a targeted inborn-error screen (plasma amino acids, acylcarnitine profile, urine organic acids) were unremarkable. Due to unexplained hyperCKemia and skin findings, a peripheral blood smear was performed, revealing marked vacuolization in neutrophils (Figure 2). Based on this finding, CDS was considered. The Denver developmental screening test, audiological and ophthalmological examinations, and metabolic workup were normal. Electromyography, echocardiography, and abdominal ultrasonography revealed no abnormalities. Muscle biopsy could not be performed due to a lack of consent. Genetic analysis revealed a homozygous ABHD5 (NM_016006): c. 594dupC (p.Arg199Glnfs*11) mutation.

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Figure 1. Marked dryness in the skin, hyperpigmented squamous lesions in places, hyperkeratosis appearance in the body skin

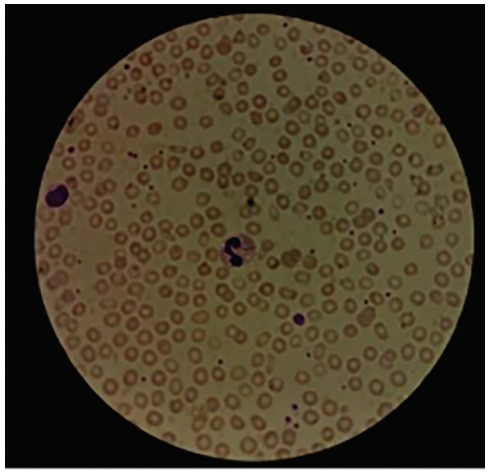

Figure 2. Marked vacuolization observed in neutrophils on the peripheral blood smear

CDS was first described by Jordan in 1953 through identification of lipid vacuoles in leukocytes in two brothers with progressive muscle disease. Later, Chanarin and Dorfman demonstrated that the condition involved defective intracellular triglyceride metabolism, with lipid accumulation in leukocytes, hepatocytes, and other cell types (1). The disorder results from a defect in the CGI-58 protein, essential for triglyceride lipase activation and triacylglycerol hydrolysis in adipose tissue (2). To date, around 120 cases of CDS have been reported in the literature, with higher prevalences found in regions such as the Mediterranean and Middle East, where consanguineous marriages are more common (1). Besides cutaneous manifestations, systemic involvement is frequent, including hepatomegaly, elevated transaminases (AST/ALT), steatosis, cataract, nystagmus, strabismus, sensorineural hearing loss, mental retardation, and myopathy (1,4). Cutaneous findings usually mimic non-bullous congenital ichthyosiform erythroderma. A collodion baby appearance may be present at birth, although hair, nails, mucosa, and teeth are typically spared (1). While serum lipid abnormalities are not common, some cases have shown elevated very low-density lipoprotein and reduced high-density lipoprotein levels (5).

CK elevation is a recognized clue; however, published cohorts frequently show concurrent rises in LDH and/or transaminases, likely reflecting subclinical myopathy or hepatic steatosis. Çetinarslan et al. (6) reported on four Turkish children in whom CK elevation coincided with increased LDH and/or AST/ALT. Our patient exhibited isolated CK elevation-an uncommon but noteworthy biochemical footprint-underscoring phenotypic heterogeneity.

Management focuses on early diagnosis, genetic counselling, surveillance for organ involvement, and nutritional measures: a diet low in long-chain fatty acids and enriched with medium-chain triglycerides may delay hepatic complications. Emerging data on systemic retinoids and lipid-lowering agents remain anecdotal.

This case underlines three teaching points: (i) persistent hyperCKemia in a child with ichthyosis should prompt a peripheral blood smear; (ii) Jordans' anomaly is a rapid, low-cost diagnostic gateway to CDS; and (iii) molecular confirmation enables tailored follow-up before irreversible hepatic or neuromuscular damage occurs. We advocate including CDS in the differential diagnosis of ichthyosis accompanied by muscle-enzyme elevation, even when LDH and transaminases are normal.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.T.T., Ö.D., Concept: B.T.T., Design: B.T.T., Data Collection or Processing: B.T.T., Ö.D., Analysis or Interpretation: B.T.T., Ö.D., Literature Search: B.T.T., Ö.D., Writing: B.T.T.

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