Dorfman–Chanarin Syndrome: A Case Report

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Abstract An 8-year-old male child, diagnosed case of congenital ichthyosis presented with abdominal distension, hepatomegaly and pancytopenia. His peripheral blood and bone marrow showed clear punched out intracytoplasmic vacuolations in leucocytes (Jordans' anomaly). He had convergent strabismus, ectropion, blepharitis and genu valgum. He was diagnosed as a case of Dorfman–Chanarin syndrome.

Keywords Congenital ichthyosis · Jordans' anomaly · Dorfman–Chanarin syndrome

Abbreviations

CNS	Central nervous system
CPK	Creatine phosphokinase
DCS	Dorfman–Chanarin syndrome
DLC	Differential leucocyte count
GGT	Gamma glutamyl transferase
GIT	Gastrointestinal tract
Hb	Hemoglobin
PBS	Peripheral blood smear
RBCs	Red blood cells
SGPT	Serum glutamate pyruvate transaminase
TAG	Triacylglycerol
USG	Ultrasonography
WBC	White blood cell

Introduction

Dorfman–Chanarin syndrome (DCS) is a multisystem inherited metabolic disorder associated with congenital ichthyosis and accumulation of lipid droplets in various types of cells. However, there is great variability in dermatologic severity and pattern and degree of systemic involvement. The disease is rare and since the initial case report by Dorfman et al. [1], only 30 cases have been reported, majority of which are from the Middle East. We report a case of DCS from Maharashtra in an 8-year-old boy who had generalized ichthyosis since birth and abdominal distention since 2–3 months. Leucocytes in his blood showed lipid vacuoles. Prior to this, three cases have been reported from India [2].

Case History

An 8-year-old male child from Maharashtra born at term as the second child of 1st degree consanguineous marriage presented with complaints of short stature, failure to gain weight since 2–3 years, and increasing abdominal distension since 2–3 months. On examination, he was short for age, was afebrile and had mild pallor. His skin was rough and showed dry fish like scales all over the body (Figs. 1, 2). Abdomen was distended. Liver was palpable 2 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. He also had bilateral genu valgum (Fig. 2).

Ophthalmic examination showed ectropion and blepharitis of both eyes and convergent strabismus (Fig. 3). Fundoscopic examination was normal.

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Fig. 1 Dry fish like scales on forearms

Fig. 3 Strabismus

Fig. 2 Dry fish like scales on thighs and legs with genu valgum

Fig. 4 Peripheral blood smear showing punched out vacuoles in polymorphs—100×

Initial laboratory work up showed Hb—10.9 g%, WBC count—3,600/cmm, DLC: Polymorphs—33%, Lymphocytes—64%, Monocytes—2%, Eosinophils—1%. Platelet count—68,000/cmm. PBS examination revealed normocytic normochromic RBCs with mild anisocytosis and mild leucopenia. Neutrophils and eosinophils showed punched out clear intracytoplasmic vacuolations (Figs. 4, 5). Platelets were diminished on smear. Coagulation study showed a normal prothrombin time and an abnormal activated partial thromboplastin time (44 s). Biochemical investigations revealed: Total bilirubin—0.6 mg%, Total protein—

7.0 g%, Albumin—3.6 g%, Globulin 3.4 g%, Serum triglycerides—240 mg%, SGPT—69 IU/l, S. Alkaline phosphatase—490 U/l, S. Cholesterol—165 mg%, CPK—142 IU/l, GGT—48 U/l. USG showed mild hepatomegaly with mild fatty changes and minimal splenomegaly.

In order to rule out a storage disorder, bone marrow aspiration and biopsy was done. Bone marrow aspirate showed mildly hypercellular marrow particles. Erythroid series showed predominantly normoblastic erythropoiesis. There was mild maturation arrest at intermediate stage.

Fig. 5 Peripheral blood smear showing punched out vacuoles in eosinophil—100×

Fig. 6 Bone marrow aspirate showing punched out vacuoles in myeloid precursors—100×

Many myeloid precursors showed clear intracytoplasmic punched out vacuolations (Jordans' anomaly) (Fig. 6). Megakaryocytes were adequate. There was mild increase in reticulum cells, which showed intracytoplasmic clear punched out vacuolations. However, no definite storage cells or parasites were seen. Trephine biopsy did not show fibrosis or granulomas.

X-ray knee joints showed periarticular osteopenia and flaring of metaphyses.

Patient was stable and discharged. Orthopaedic reference was advised on follow up.

Discussion

DCS, also known as neutral lipid storage disease with ichthyosis is characterized by congenital ichthyosis and deposition of lipid droplets in multiple organs like skin, muscle, liver, CNS, GIT and leucocytes in blood and bone marrow. It shows a variety of clinical features like neurological abnormalities, myopathy, growth retardation, sensorineural deafness, cataract, strabismus and retinal dysfunction [2].

The first case of DCS was described by Dorfman et al. [1]. Prior to that, Jordans had reported two brothers with Erb's type of progressive muscular dystrophy whose peripheral blood leucocytes showed fat vacuoles (Jordans' anomaly). One year later, Chanarin et al. reported another case with similar findings and pointed to an abnormality of intracellular triglyceride metabolism. This is an autosomal recessive lipid storage disease, often caused by mutations in hydrolase CGI-58 (recently renamed as ABHD5) gene on chromosome 3p21. This gene encodes a protein of esterase/lipase/thioesterase subfamily, although its exact function is still unknown [3]. Because of this mutation, Triacylglycerols (TAG) accumulate in cytosolic droplets in multiple organs. The pathway that leads to cytosolic TAG accumulation is not known with certainty. However, labeling studies suggest that the lipolytic activity that uses diacylglycerols derived from TAG for phospholipid synthesis is impaired, resulting in TAG accumulation in DCS.

The majority of reported cases of DCS are from Middle Eastern countries. A few European and Asian patients have also been reported. Diagnosis of DCS is based upon a characteristic and diagnostic spectrum of clinical, laboratory and histochemical features. Clinical features include congenital ichthyosis either isolated or associated with systemic involvement usually not interfering with a normal life span. The liver is reported to be the most frequently affected organ and patients usually present with hepatomegaly, elevated liver enzymes and fatty liver. Although not frequently reported, splenomegaly can also be seen [4].

Our patient had congenital ichthyosis, ectropion, strabismus, genu valgum and characteristic findings on PBS and bone marrow. Mild hepatomegaly with fatty changes in liver, minimal splenomegaly on USG and raised serum triglyceride levels were also noted in our patient.

There is no effective treatment for DCS, but a diet low in long chain fatty acids with minimal saturated fat and enriched with medium-chain fatty acids is reported to improve skin and liver manifestations. Symptomatic treatment can be provided in the form of local application of emollients. Retinoids such as acitretin, which are the systemic therapeutic modality of choice in lamellar ichthyosis, are found useful in the treatment of skin and muscle manifestations in DCS but cannot be given in the

presence of impaired liver function which is common in DCS. Response of gastrointestinal symptoms and muscle weakness to a gluten-free diet has been reported. Treatment is only symptomatic, but functional studies of the ABHD5 protein may help to define new therapeutic strategies.

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