Gene 575 (2016) 359–362

Contents lists available at ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

Short communication

Chanarin Dorfman syndrome: a case report with novel nonsense mutation

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ARTICLE INFO

Article history:
Received 8 February 2015
Received in revised form 19 August 2015
Accepted 1 September 2015
Available online 6 September 2015

Keywords:
Chanarin Dorfman syndrome
Ichthyosis
Lipid storage disorder
Liver involvement
ABHD5 mutation

ABSTRACT

Chanarin Dorfman syndrome (CDS) is a very rare neutral lipid metabolism disorder with multisystem involvement. It is inherited as an autosomal recessive manner. It is characterized with congenital ichthyosiform erythroderma and involvement of liver, muscle, and central nervous system. Demonstration of lipid vacuoles in neutrophils from peripheral blood smears in patients with ichthyosiform erythroderma leads to the diagnosis. We report a novel ABHD5 truncating variant in a twenty nine month old female child, who presented with icthyosiform erythroderma.

1. Introduction

Chanarin Dorfman syndrome (CDS) is a rare autosomal recessive neutral lipid storage disorder. It is characterized by congenital ichthyosis, lipid vacuoles in peripheral leucocytes (Jordan's anomaly), and multisystem involvement. Only few cases have been reported from India (Nanda et al. 1990; Tullu et al. 2000; Gupta and Kaur 2005; Tamhankar et al. 2014; Srinivasaraghavan et al. 2014). Here we present a case of CDS with multi-organ involvement.

1.1. Case report

A 29 month old female child presented with complains of scaly skin lesions since birth, gradually progressing abdominal distention since one and half years of age and delayed motor development. Child was third in birth order and born to a third degree consanguineous married couple (Fig. 1). Child was born as preterm at 32 + 6 weeks gestation with a birth weight of 1.9 kg and cried immediately after birth. There were no previous abortions and no history of exposure to drugs, radiation, smoking or alcohol during pregnancy. There was history of a similar scaly skin lesion in other female sibling, who had a sudden demise due to unknown cause, at 9 months of life.

The child was admitted at 5 months of age for skin problems in dermatology and diagnosed as a case of congenital non bullous icthyosiform erythroderma and discharged on emollient cream for symptomatic relief. There was no history of abdominal pain, jaundice, vomiting, seizures, altered sensorium, blood transfusion, oliguria and hematuria. Developmental milestones were delayed in all spheres with developmental age of 12–15 months. The length-for-age, weight-for-age and head circumference for age were below the third percentile. Cutaneous examination revealed generalized scaling. The scales were fine and occasionally pruritic involving whole body (Fig. 2a). Abdominal examination revealed distention, soft, nontender liver 5 cm below from right costal margin (span 8 cm) and spleen 2 cm below from left costal margin with normal bowel sounds normal (Fig. 2b). Child had central hypotonia. There was no limb weakness, ataxia, deafness, nystagmus, strabismus or any focal neurological deficits. On investigation, complete blood counts were normal, but the peripheral smear showed microcytic hypochromic picture and later on leucocytic vacuolations were also noted. Liver functions tests revealed 2–3 fold elevated transaminases (SGOT 115 IU/L, SGPT 97 IU/L) and mildly elevated serum alkaline phosphatase (626 IU/L) with normal prothrombin time. Lipid profile revealed elevated (>95 percentile) serum triglycerides 124 mg/dl

Abbreviations: ATGL, Adipose triglyceride lipase; CDS, Chanarin Dorfman syndrome; ECHO, Echocardiography; HDL, High density lipoproteins; LDL, Low density lipoproteins; PAS, Periodic acid Schiff; SGOT, Serum glutamic oxaloacetic transaminase; SGPT, Glutamate–Pyruvate Transaminase; VLDL, Very low density lipoproteins.

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http://dx.doi.org/10.1016/j.gene.2015.09.004
0378-1119/

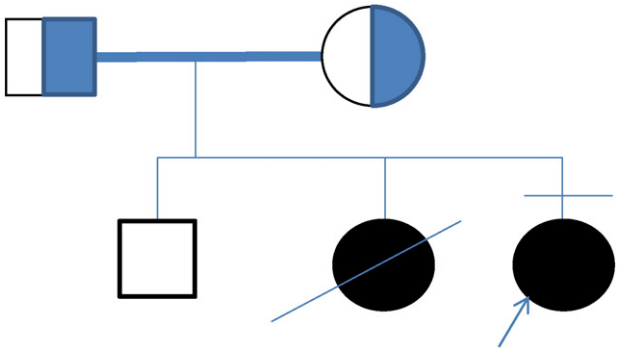

Fig. 1. Shows the pedigree.

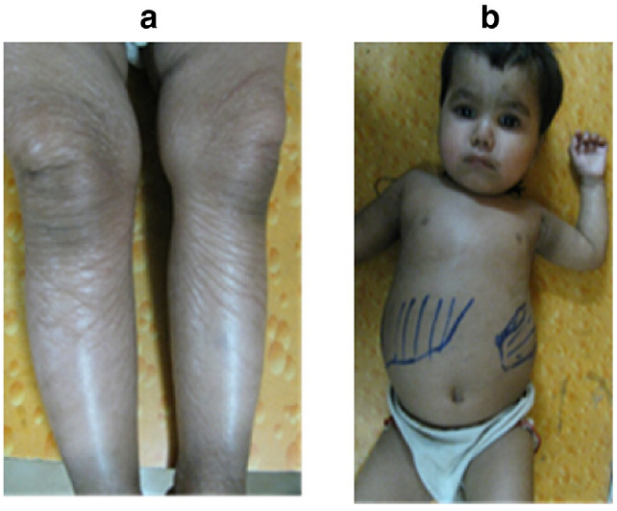

Fig. 2. a) Shows the presence of shiny skin and scaling b) shows presence of hepatosplenomegaly.

(91.1 ± 29.85) serum cholesterol 234 mg/dl (134.5 ± 27.1), LDL cholesterol 136 mg/dl (80.1 ± 21.65), while low HDL cholesterol 52 mg/dl (46.3 ± 14.8) and VLDL cholesterol 46 mg/dl (143.3 ± 27.0). Creatine phosphokinase and coagulation profile were normal. Skeletal survey revealed normal bone age. Thyroid profile was found to be normal. Ultrasound abdomen revealed hepatomegaly with fatty change along with mild splenomegaly. Levels of various sulphatase enzymes such as aryl suphatase A, Iduronate 2 sulfate, β glucosidase, chitotriosidase, beta galactosidase (GM-1) were within normal range. Liver biopsy revealed distortion of globular architecture, portal triaditis, with presence of lymphocytes, eosinophils and histiocytes. Hepatocytes show diffuse ballooning and cytoplasm content brightly positive with PAS showing diastase sensitivity around 70% of biopsy parenchyma shows predominantly macro vesicular and focal micro vesicular steatosis (Fig. 3 A–D). Peripheral smear using Wright's stain and Oil red O stain for the presence of vacuolated granulocytes was positive for Jordan's anomaly (Fig. 4). Peripheral smears from both parents were also normal. The baseline ECHO was normal. Ophthalmic examination revealed multiple corneal opacities, while ear examination was normal. Mutation analysis of the *ABHD5* gene was performed by previously described methods by Lefevre et al.[11] after obtaining an informed consent from the parents. Pathogenicity of mutation was verified using Mutation Taster software.

Results: A novel nonsense mutation c.297C > A (p.C99X) (GenBank number- KM659022) in exon 3 of *ABHD5* gene in homozygous status was identified in the patient, while in her parents the same mutation was detected in heterozygous status (Fig. 5). Mutation Taster software predicted this mutation to be pathogenic with a probability of 1 (score: 0–1). The mutation was further not found in 100 control individuals from the same ethnicity. However, further RNA or protein studies could not be carried out. The patient was started on a low fat with medium chain triglycerides, low-protein, high-carbohydrate diet with ursodeoxycholic acid and vitamin E along with emollients cream for local application. Parents were explained the nature of disease, treatment options and for adherence of follow up. In follow up of about 6 months, repeat lipid profile showed almost similar levels as

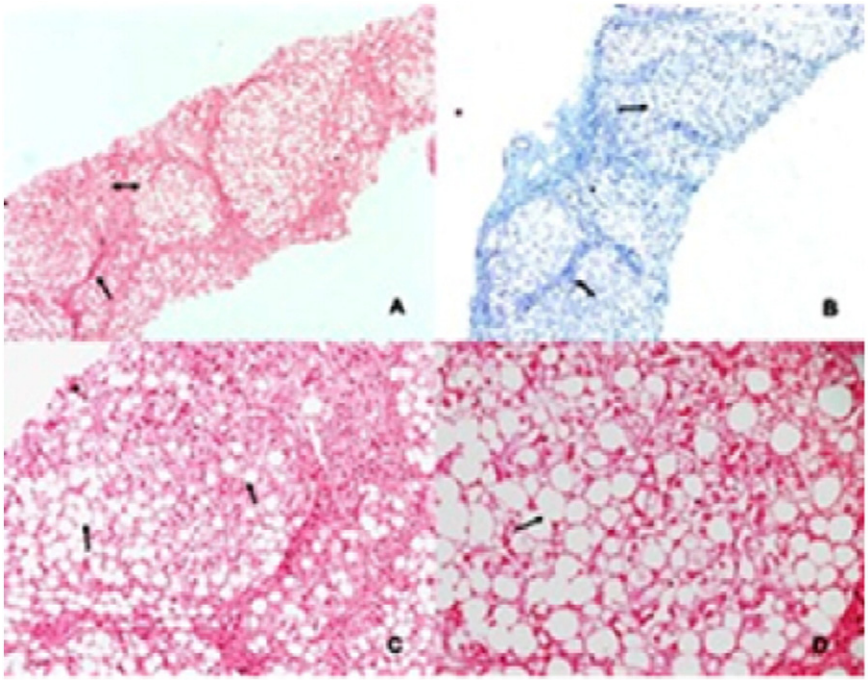

Fig. 3. Photomicrographs of the trucut liver biopsy show distorted liver archietecture with the presence of micronodular cirrhosis (arrow-nodules) [Fig. A, H&E; B, Masson's trichrome stain × 40]. Higher power photomicrographs show the presence of extensive macrovesicular steatosis (arrows) with ballooned hepatocytes. Inflammation is sparse [Fig. C & D, H&E, C x 100; D x 200].