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Case Report

Atypical Gauchers Manifesting as Neonatal Cholestasis

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ABSTRACT

Deficiency of lysosomal enzyme glucocerebrosidase leads to Gauchers disease which is the most common sphingolipidosis. A non-neuronopathic form of gauchers disease as a result of sapocin-C deficiency is a rare entity. Sapocin-c is required for degradation of glucosylseramide and its deficiency results in an atypical form of Gauchers disease. Neonatal cholestasis is defined as a prolonged elevation of conjugated bilirubin beyond 14 days of life. We hereby present a 10 month old male child who presented with neonatal cholestasis due to sapocin-C deficiency, which is the first rare case being reported in literature.

Key words: *Neonatal cholestasis, Sapocin-C deficiency, Atypical Gauchers disease*

INTRODUCTION

Mutations in the glucocerebrosidase GBA gene leads to deficiency of glucocerebrosidase enzyme which results in Gauchers Disease (GD). In addition to this above mechanism, the degradation of this sphingolipids also depends upon the role of sphingolipid activator proteins. The post-translation cleavage of prosaposin PSAP gene yields four proteins named sapocins A,B,C and D.[1] The variant form of GD is a result of Sapocin –C deficiency. The most common causes of neonatal cholestasis include biliary atresia, infections, inborn errors of metabolism and congenital malformations.[2] This case report highlights the need for a thorough evaluation of storage disorders as a cause of neonatal cholestasis.

CASE REPORT

10 months old male child born of 3rd degree consanguineous marriage presented with yellowish discolouration of skin since 15 days of life and abdominal distention since 3 months of life. There was no history of fever, vomiting, itching, clay coloured stools, convulsions, altered sensorium or constipation. Child weighed 2 kgs at birth, with antenatal history of fever and rash in the mother during 1st trimester of pregnancy and was developmentally normal.

Child had no dysmorphic features, heart rate of 110/min, respiratory rate 30/min and weight and height less than 3rd percentile. Pallor, icterus and hepatosplenomegaly were present however the ophthalmological evaluation was normal.

Hb 9.6gm/dl, Tlc 20,200 with Neutrophils 28, Lymphocytes 65, Eosinophils 3.3 and Platelets 60/µl. Liver function test was suggestive of direct hyperbilirubinemia with total bilirubin 25.6mg/dl, direct bilirubin 15.9mg/dl, indirect 9.7mg/dl and elevated SGPT and SGOT levels. Prothrombin Time, Activated Partial Thromboplastin Time, GGTP, Bleeding time, Clotting time, Alkaline phosphatase, Thyroid profile and serum ammonia were normal. Aarterial Blood Gas levels, Random Blood sugar, HIV, HBsAg, HCV, TORCH titres, Karyotyping, sepsis and inborn errors of metabolism screening were also normal. Ultrasonography of abdomen showed gross hepatosplenomegaly with gall bladder sludge. HIDA scan showed slow uptake with no evidence of biliary atresia. 2D-Echo and X-ray long bones were normal. Liver biopsy showed Per Acidic Schiff (PAS) staining was intensely positive with crumpled tissue paper appearance suggestive of Gauchers disease. Beta glucosidase enzyme assay was normal (value - 5.20nmol/ml/hr) with elevated levels of chitotriosidase (value - 115.71nmol/hr/ml). Mutation analysis of the common exons was normal. The diagnosis of Sapocin–C deficiency was based on normal Beta-glucosidase enzyme activity, elevated chitotriosidase enzyme

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levels, PAS staining positive and non-neuronopathic presentation.

DISCUSSION

Sapocin C is an essential activator for glucocerebrosidase enzyme, whose deficiency leads to GD. The most vital gene encoding Sapocin C is PSAP gene. Despite a normal in-vitro enzyme activity, if there is a mutation in the PSAP gene, the patient will present with Gaucher like phenotype.[3]

The rearrangement of lipids in the lysosomal membranes which results in substrate accessibility to glucocerebrosidase enzyme is enhanced by Sapocin C.[4] As this case presented with non neuronopathic symptoms, massive hepatosplenomegaly and thrombocytopenia. There is normal beta glucosidase activity with increase level of chitotriosidase. Liver biopsy was PAS positive.

Liver biopsy, Enzyme assays and mutation are mandatory investigation. Storage disorders are corrected by enzyme replacement therapy. To the best of our knowledge, this is the first case in world literature of an infant with Atypical Gauchers disease, manifesting as neonatal cholestasis.

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