A rare case of chronic diarrhoea in an infant

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Introduction:

Johanson-Blizzard syndrome (JBS) is a very rare autosomal recessive disorder first described in 1971 by Johanson and Blizzard [1]. It is characterized by exocrine pancreatic insufficiency, nasal wing hypoplasia, ectodermal scalp defect, growth retardation and other abnormalities. It is caused by mutations of the UBR1 gene, which is highly expressed in pancreatic tissue (2).

Less than 100 cases of JBS have been reported worldwide and very few from India. We here report a rare case of JBS who presented with steatorrhoea and failure to thrive.

Case report:

Two month old female baby presented with complains of chronic diarrhoea with greasy stools since birth. She was first child of her parents, born out of consanguineous marriage at full term. Her birth weight was 2 kg and was exclusively breastfed. She also had failure to thrive with weight at presentation of just 1.7 kg. She had peculiar dysmorphic facies with hypoplastic alae nasi, upslanting palpebral fissure and patchy loss of hair on scalp (Image 1)

Her routine investigations including complete blood count, liver function tests, serum electrolytes were normal. TSH was normal. Stool for fat globules showed 30 droplets/high power field. Ultrasound abdomen showed fatty infiltration of pancreas. Echocardiography was normal. BERA and fecal elastase were not done.

Her characteristic facies with evidence of exocrine pancreatic insufficiency (steatorrhoea & fatty infiltration of pancreas) led to syndromic diagnosis of Johanson Blizzard Syndrome. Her blood sample for genetic testing of JBS was sent. She was started on pancreatic enzyme supplementation (2000 IU lipase per feed, with estimated 20000 IU/day for 8-10 feeds/day) along with fat-soluble vitamin supplements.

Image : 1 : Characterstic facies of the baby

Outcome:

Baby was lost to follow up and later on enquiry found to have died at home at 3 months of age.

Later genetic testing confirmed the heterozygous missense mutation (c.1688C>A, p.Ala563Asp) in exon 44 in both alleles by Sanger sequencing and diagnosis of Johanson blizzard syndrome.

Discussion:

Classic cases of JBS present in early infancy with syndromic features and severe exocrine pancreatic insufficiency. The genetic defect of JBS is a homozygous loss-of-function mutation in the Ubiquitin-Protein Ligase E3 Component N-Recognin 1 (UBR1) gene, located on chromosome 15q15-21.UBR1 is essential in the development and maintenance of acinarcells and mutation in this gene results in in-utero destruction of acinar tissue followed by fatty

replacement (3). This defect leads to almost complete absence of pancreatic enzymes in duodenal secretions. Additional features include: short stature (>80%), dental abnormalities (>80%), sensorineural hearing loss (80%), mental retardation(77%), scalp defects including alopecia (76%), hypothyroidism (40%), imperforate anus (39%), and genitourinary malformations (38%)[2]. Abdominal imaging of affected patients shows replacement of the exocrine pancreas by lipomatous and connective tissues [1, 2].

An exocrine pancreatic defect is a constant feature of this condition. The diarrhoea caused by pancreatic enzyme deficiencies leads to hypoproteinaemia, edema, anaemia, and failure to thrive. Hence pancreatic enzyme replacement with fat-soluble vitamins supplementation is the mainstay of the treatment.

Pancreatic insufficiency and severe hypo-proteinaemia may lead to death in infancy or early childhood.

It is important to recognize this rare syndrome with characteristic facies in infants associated with severe exocrine pancreatic insufficiency. Early supplementation of pancreatic enzyme is required in neonatal period along with nutritional support. Prenatal counseling should be done for future pregnancies owing to autosomal recessive mode of inheritance of this condition.

References:

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