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Case Report

Biochemistry Section

An Infant with Chronic Diarrhoea and Failure to Thrive: Familial Hypobetalipoproteinemia

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ABSTRACT

Diarrhoea is a common clinical problem for treating clinicians in developing countries. Mostly, it is attributed to malnutrition and infection. We, as clinicians, tend to miss some of cases who have inherited enteropathies because of lack of suspicion and non availability of diagnostic facilities. Here, we report a case of homozygous hypobetalipoproteinaemia in a nine-month-old female patient presenting with chronic diarrhoea and failure to thrive. Simple parental screening of lipid parameters led to correct diagnosis and early intervention in present case.

Keywords: Abetalipoproteinaemia, APOB gene, Malnutrition

CASE REPORT

Nine-month-old female, born to nonconsanguious parents, presented with history of on and off loose stools for 1 month progressive paleness of body for 1 month and swelling of bilateral feet for 2 days. Loose stools were large in amount, non watery, occurred 7-8 times per day, difficult to flush, with no blood and mucus in it. Child developed progressive paleness of body since last one month.

There was no history of fever, signs of dehydration, vomiting, abdominal distension, any seizures, and focal weakness of body. Such episodes of loose stools were present since the child's birth. Each episode used to last for 5-7 days and subsided with oral medications. Child had received blood transfusion for pallor of body 3 months back. No adequate work up was done before giving transfusion so, causes could not be ascertained from the past records. Perinatal period was normal. Examination revealed severe pallor with no icterus, cyanosis, clubbing, petechiae, lymphadenopathy, no sign of vitamin deficiency and hepatosplenomegaly. Her anthropometric parameters were: length (64 cm < 3rd centile), weight (6.3 kg < 3rd centile), weight for length (~ - 1 z score). She had IAP Grade I malnutrition. There was no other obvious sign of malnutrition except stunting and that the child was underweight. Neck holding was attained at age of 4 months and she could sit with support, can hold the objects shown to her and speak in monosyllables. There was no dysmorphology.

Blood investigations revealed anaemia, leucocytosis with normal platelet count. Red blood cell indices were normal. Liver function test showed mild elevation of SGOT with low albumin. Immune work up (IgA, IgM, IgG, IgE, CD3, CD19, CD56), HIV parents were negative. Faecal ion gap was more than 50 suggestive of osmotic diarrhoea. [Table/Fig-1] depicts the lipid profile of child and her parents. Peripheral smear showed anisocytosis with presence of microcytes and macrocytes. Bone marrow aspiration and biopsy showed feature suggestive of megaloblastic anaemia. Fundus examination was normal. Stool examination for pathogenic organism was negative. Non-quantitative estimation of stool for fat globules was positive.

The diagnosis of familial hypobetalipoproteinaemia was kept and the child was put on low fat diet, adequate supplementation with fat soluble vitamins and iron and folic acid supplementation. At 3 month follow up, diarrhoea subsided; child started gaining weight (2.5 kg in 3 months). Her height increased to 69 cm at 12 months, showing consistent gain in anthropometric parameters. Her haemoglobin improved to 10 g/dl.

DISCUSSION

Abetalipoproteinaemia (OMIM # 200100) and familial hypobetalipoproteinaemia (OMIM # 107730) are congenital disorders of diarrhoea that presents with intractable diarrhoea, failure to thrive and retinal degeneration, neuropathy and coagulopathy [1]. The basic defect lies in improper packaging and secretion of apolipoprotein (apo) B containing particles. Genetic defect lies in mutation in MTP gene and APOB gene, leading to abetalipoproteinaemia and familial hypobetalipoproteinaemia phenotype respectively [2,3].

Presentation of our patient has following unique features: Neonatal onset of diarrhoea, severe stunting and undernourished child. Large watery and bulky stools suggestive of malabsorptive process [Table/Fig-1]. Possibilities of immune deficiency, congenital Diarrheal Disorders (CDD), malignancy were kept. Congenital immune deficiency was ruled out as immunoglobulin profile (IgA, IgM, IgG, IgE), CD Markers (CD3, CD19, CD56) were normal. Peripheral smear and bone marrow examination were not suggestive of malignancy. The above constellation of symptoms helped us to categorize our patient under category of congenital Diarrheal Disorders (CDD). The presence of increased faecal anion gap (> 50) suggested Osmotic diarrhoea [4]. Blood biochemistry (low cholesterol and very low apo B lipoproteins) were indicative of abetalipoproteinaemia, familial hypobetaliporoteinaemia, chylomicron retention disease. Lipid profile of parents showed half normal levels of apo B- containing lipoproteins, thus favouring a likely diagnosis of homozygous hypobetalipoproteinaemia (HHBL) [1] [Table/Fig-1].

Our case, first presented to health facility in neonatal period, was diagnosed at age of 9 month. The diagnosis was delayed because of attribution of common clinical presentation to malnutrition and infection, lack of suspicion on part of treating clinicians and lack of adequate facilities to diagnose such condition. An updated diagnostic approach suggested by Terrin et al., helped us reach the correct diagnosis [4].

The importance of present case lies in highlighting the idea that rare, treatable disorders present with common problems. So, clinicians should be aware of such rare conditions and apply diagnostic algorithm approach to reach correct diagnosis for proper management of case. There have been only few case reports of hypobetalipoprotenaemia and abetalipoprotenaemia from India that presented beyond infantile age group [5-7]. A late

A: Clinical	Proband (Reference range)	Mother (Reference range)	Father (Reference range)
Chronic diarrhoea	+	--	--
Failure to thrive	+	--	--
Fat malabsorption	+	--	--
B: Biochemical			
Total Cholesterol (mg/dl)	71 (106-186)	112 (125-230)	120 (125-230)
Triglycerides (mg/dl)	136 (65-234)	54 (125-230)	65 (125-230)
HDL-C (mg/dl)	12.9 (24-84)	31.2 (35-80)	37 (35-80)
LDL-C (mg/dl)	21 (34-111)	41 (55-160)	45 (55-160)
Apo- B (mg/dl)	10 (39-90)	35 (45-117)	39 (45-117)

[Table/Fig-1]: Clinical and biochemical profile of proband and parents

diagnosis in the above cases leads to irreversible neurologic and hepatic complications, unlike ours where early diagnosis halted the disease progression and improved the outcome of case. The median age of diagnosis in familial hypobetalipoproteinaemia was 21 years in a series of 27 patients [8]. Literature search found only few cases of hypobetalipoproteinaemia presenting in infancy and neonatal period [9,10]. There has been no Indian case report of hypobetalipoproteinaemia. Findings in above case reports were similar to ours as they presented with chronic diarrhea and failure to thrive. Simple dietary adjustment improved the diarrhoea in present case and will further halt the disease progression. Low fat diet is advocated as there is defect in secretion of lipoproteins, needed for fat absorption. Medium chain triglycerides are added as they are directly absorbed, they quickly correct malnutrition. As there is defect in fat absorption, fat soluble vitamins are also supplemented.

Associated anaemia in our case was of nutritional in origin (megaloblastic), which was corrected with vitamin B12, folate and iron supplementation. There have been reports of cases presenting with neurological, ophthalmological and hepatic complications due to delay in diagnosis and treatment [5]. We screened our case for presence of complications and found no abnormality. The child showed improvement in anthropometric parameters and loose stools subsided at follow up of 3 months.

CONCLUSION

Diarrhea is an important clinical presentation of many diseases in paediatric age group. Despite treating common diarrhoeal causes, the presence of important clues (failure to thrive, neonatal onset of symptoms) should alert the treating clinicians to look for work up of rare inherited disorders that require additional investigations. If diagnosed early, it improves the outcome of disease. Genetic counselling of the family is also a very important step.

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