INTRODUCTION

Abetalipoproteinemia (ABL) is a monogenic autosomal recessive disorder associated with absence or great reduction of apolipoprotein-B (apo-B) containing lipoproteins [(chylomicrons, low density lipoproteins (LDL) and very low density lipoproteins (VLDL)] in serum.\(^1\) It results from mutations in microsomal triglycerid transfer protein (MTP) gene. This mutation leads to the absence of 97-KDa subunit (894 amino acid protein product) of MTP and results ABL. A region on chromosome 4q 22-24 that encodes the large sub-unit of MTP has been found to be the site of mutation. To date at least 33 mutations have been identified.\(^2\) This rare metabolic genetic disorder has variable prevalence in different countries. Its overall global frequency is 1:100,000, but in Israel, the Ashkenazi Jewish community has a very high carrier frequency, i.e. 1:131.\(^3\) Patients have, chronic diarrhoea with fat and fat soluble vitamins’ malabsorption since birth leading to their deficiency, which is known to cause a wide range of effects.\(^4\) As it is a quite rare genetic and metabolic entity, the case is marked for reporting.

CASE REPORT

An infant Saudi boy developed chronic diarrhoea and failure to thrive since 3 months of age. His stools were steatorrhic, 3-6 times per day, associated with mild abdominal distention. His development was also delayed. He was breast fed and was also receiving soya based lactose free formula. His parents were normal and non-related. His single elder brother was healthy.

On examination he was severely malnourished with weight of 3.4 kg at 5 months of age, length of 54 cm and head circumference of 36 cm. All measurements were below the 5th centiles for his age according to NCHS standard charts. The vital signs were stable. His hair were brittle, sparse and hypopigmented. The abdomen was mildly protuberant without visceromegaly. Rest of the examination was unremarkable.

Investigations showed haemoglobin level of 12.1 g/dl, WBC count of 21x10\(^9\)/l, with 16% polymorphs and 79% lymphocytes and ESR was 3 mm after first hour. Peripheral blood picture revealed abundant acanthocytes and few target cells (Figure 1). His AST was 266 IU/l, ALT 174 IU/l; GGT was 42 IU/l and ammonia level was 81 mg/dl (normal 19-95). Stool analysis showed many fat globules, traces of occult blood, normal pH and absence of reducing substances. Lipid profile showed cholesterol level of 34 mg/dl (normal 50-200), triglyceride level of 2 mg/dl (normal 50-190), HDL of 32 mg/dl (normal 30-70), and level of LDL 1 mg/dl (normal 50-190) while chylomicron and VLDL were undetectable. Parental lipid profiles were normal. Jejunal mucosal biopsy histologically showed multiple fat globules especially in apical areas of enterocytes. Villi were normal in size. According to Marsh criteria, mucosal epithelial cells of villi were of grade zero. The cells also lacked the esssential protein, MTP. Phenotype mutation

ABSTRACT

Abetalipoproteinemia is a rare genetic disorder. A 5-month-old Saudi boy presented with chronic diarrhoea and failure to thrive since 3 months of age. He was cachectic. His peripheral blood picture showed many acanthocytes and he had very low lipid profile. He improved on medium chain triglyceride (MCT) formula and administration of fat soluble vitamins.

Key words: Abetalipoproteinemia. Infant. Saudi. Chronic diarrhoea. Failure to thrive.
in MTP was present. Homozygous 481 kb deletion between markers RH 8338 and RH 59351 was found. Contiguous deletion included MTP and six other genes. On lipoproteins electrophoresis beta hypoprotein was found to be absent. Rest of the relevant investigations like renal functions, urinalysis, serum glucose, proteins, electrolyes, calcium, phosphorous, alkaline phosphatase and ultrasonography of abdomen were within normal limits. On the basis of his clinical picture and results of laboratory investigations, he was diagnosed as a case of abetalipoproteinemia. Treatment was started with MCT formula and high doses of fat soluble vitamins after which his diarrhoea improved and he started thriving.

**DISCUSSION**

Abetalipoproteinemia is associated with chronic diarrhoea since birth, severe fat malabsorption, steatorrhhic stools and failure to thrive, with slow intellectual development. Most of these findings were present in this case. After the first decade of life, intestinal symptoms become less severe, but ataxia develops, and there is loss of position and vibration sensations with intention tremors, reflecting involvement of the posterior column, cerebellum, and basal ganglia. In adolescence and later life, atypical retinitis pigmentosa, coagulopathy, neuropathy and myopathy develop. Steatorrhea-induced vitamin D and calcium malabsorption seems to be the cause of rickets in this entity. Deep tendon reflexes are absent as a result of peripheral neuropathy, secondary to vitamin E deficiency. This vitamin's deficiency is also critical for many aspects of fetal development during pregnancy. There may be congenital ophthalmological abnormalities and some other fetal anomalies which are most probably associated with vitamin A deficiency. These fetuses are frequently aborted in early pregnancy and the liveborns also have high mortality. This disorder also has some endocrinological disturbances e.g. female patients have low production of progesterone probably due to low serum LDL and cholesterol. Diagnosis rests on finding acanthocytes in the peripheral blood, significantly lipid laden entocytes with normal villi on jejunal biopsy and multiple fat globules on stool examination. There is extremely low plasma levels of cholesterol (< 50 mg/dL) and triglycerides (< 20 mg/dL). Chylomicron and VLDL are not detectable, while LDL fraction is virtually absent. After first decade of life, when there is significant impact of the disease on muscles and nerves, evoked motor unit potential in the muscles are significantly reduced and creatinine kinase is increased. Moreover, electron microscopy of nerves shows a marked reduction in large myelinated fibers. Genetic studies show mutation in MTP gene. Early diagnosis and treatment with high doses of fat soluble vitamins and other necessary dietary managements (MCT formula, linoleic acid supplements, avoiding long chain fatty acids and limiting fat intake to 5-20 grams/day etc.) may slow the progression of some problems such as retinal damage and reduced vision. All these findings are consistent with this patient's investigations. Patient's ESR was very low due to inhibition of rouleaux formation by acanthocytes which is also found in another study. Normal parental lipid profiles ruled out possibility of hypobeta-lipoproteinemia diagnosis. Mildly disturbed liver enzymes in this case are also found in another study. However, in contrast to the above mentioned studies, this patient had high WBC count with absolute lymphocytosis, which is most probably due to a concomitant viral infection. This case had only few findings because these develop with age.

Early diagnosis and early start of management are essential to prevent/slow the progression of manifestation following fat-soluble vitamins deficiencies.

**REFERENCES**


