The Turkish Journal of Pediatrics
Volume 27, No. 4, October - December 1985

ABETALIPOPROTEINEMIA*

A case report

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Key words : abetalipoproteinemia, hemolytic anemia

Abetalipoproteinemia is a rare molecular disorder which is observed clinically only in a homozygous condition[1]. Since first-cousin marriage is very frequent in Turkey, several genetic disorders are seen fairly often, but to the best of our knowledge this is the first report of abetalipoproteinemia. This might indicate that the gene for this disease is very rare in Turkey as elsewhere[2]; about 50 cases of abetalipoproteinemia had been reported up to 1980[3].

Case Report

A six-month-old girl, the child of first cousins, was referred from another hospital to Hacettepe Children's Hospital with the complaints of failure to thrive and enlargement of the abdomen. Although her birth weight was not known, she had been seen with the above complaints at about 20 days of age, at which time her weight had been 2700 grams. Malabsorption-like bowel movements, four to eight times a day, had been the main complaint since the age of three months. At five months of age, on admission to the other hospital, her height had been 53 cm and weight 3800 grams, despite peritibial edema and marked hepatomegaly (6 cm below the right costal margin). During the following month she lost 800 grams, although energy (120 kcal/day) and protein (3 g/kg/day) requirements were supplied. Anemia (hemoglobin: 8.8 g/dl, hematocrit: 27%), hypoproteinemia (4.2 g/dl), glucosuria and a high alpha fetoprotein level (195 ng/ml) were detected, and the patient was referred to our hospital after open liver biopsy was obtained which was not diagnostic.

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On physical examination she was found to be severely emaciated (weight 3160 g, height 54 cm) and microcephalic (head circumference 37 cm). She had oral moniliasis, craniotabes and a large abdomen (liver palpable 5 cm below the costal margin) with venous collaterals. The results of other clinical examinations, including eye ground and neurologic examinations, were normal.

Laboratory findings indicated marked anemia (hemoglobin: 6.3 g/dl, hematocrit: 24%) with reticulocytosis (8%). On the peripheral smear, normoblastemia, acanthocytosis (Figure 1), anisocytosis, poikilocytosis, polychromasia and

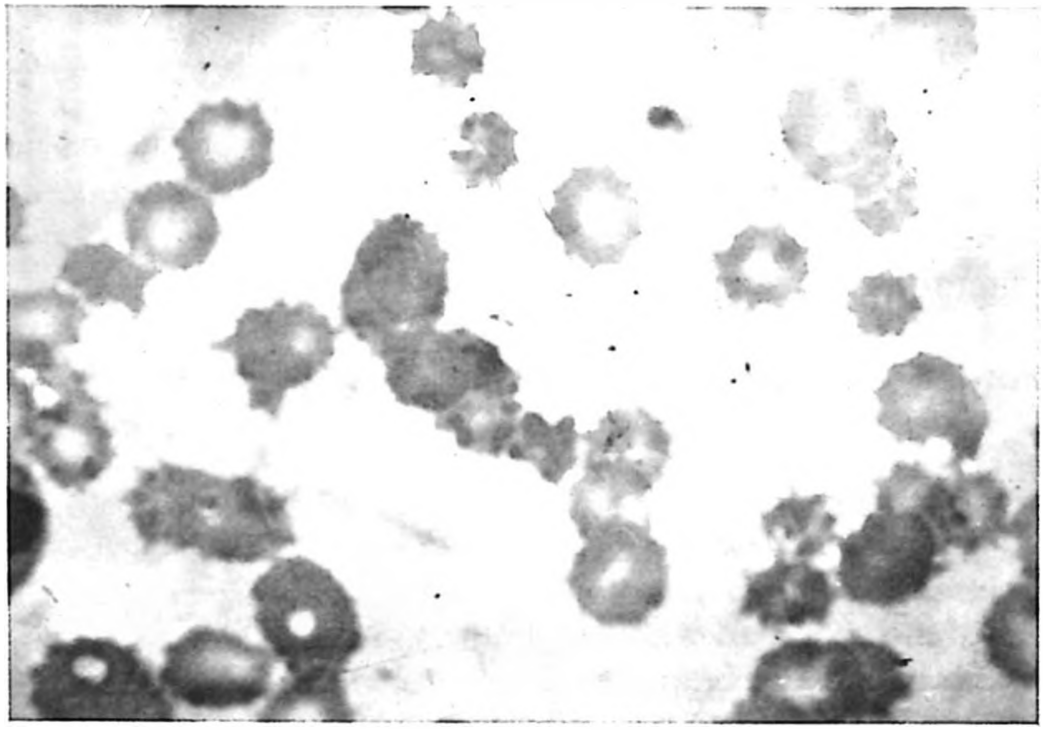


Figure 1
Acanthocytosis is seen on the peripheral smear.

basophilic stippling were detected. A direct Coombs' test was negative, and results of a hydrogen peroxide test (8%; control: 15%) and autohemolysis test were normal. Urinalysis was normal with the exception of generalized aminoaciduria despite a normal serum amino acid pattern. Findings from liver function tests were normal except for marked hypocholesterolemia (63 mg/dl) and hypolipidemia (210 mg/dl). On lipoprotein electrophoresis only the alpha band was present (Figure 2). Low density lipoproteins (LDL) and very low density lipoproteins (VLDL) were not seen, but high density lipoprotein (HDL) was detected (11%). Hypoproteinemia (4.6 g/dl), hypoalbuminemia (2.5 g/dl) and hypergammaglobulinemia (2.5 g/dl) were present. Despite breast milk feeding and vitamin supplement (including vitamin E 100 U/kg), the patient's hypoalbuminemia became very marked (1.5 g/dl), ascites with pitting edema developed and she died at home within a month. Permission for autopsy was not granted.

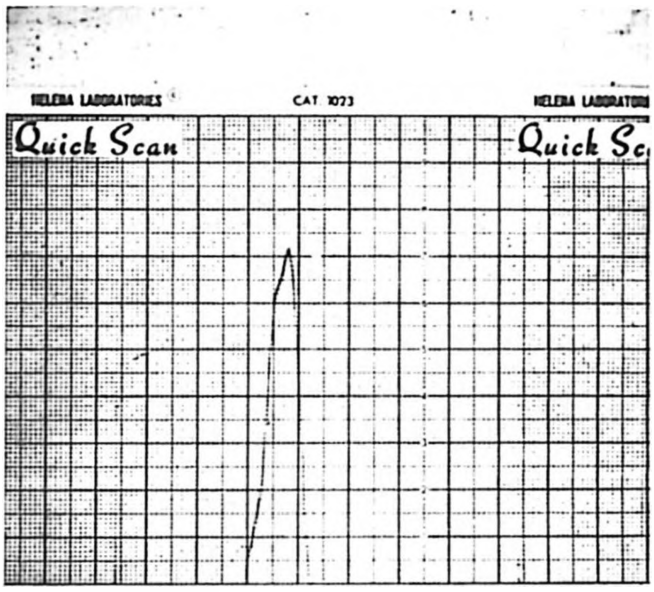
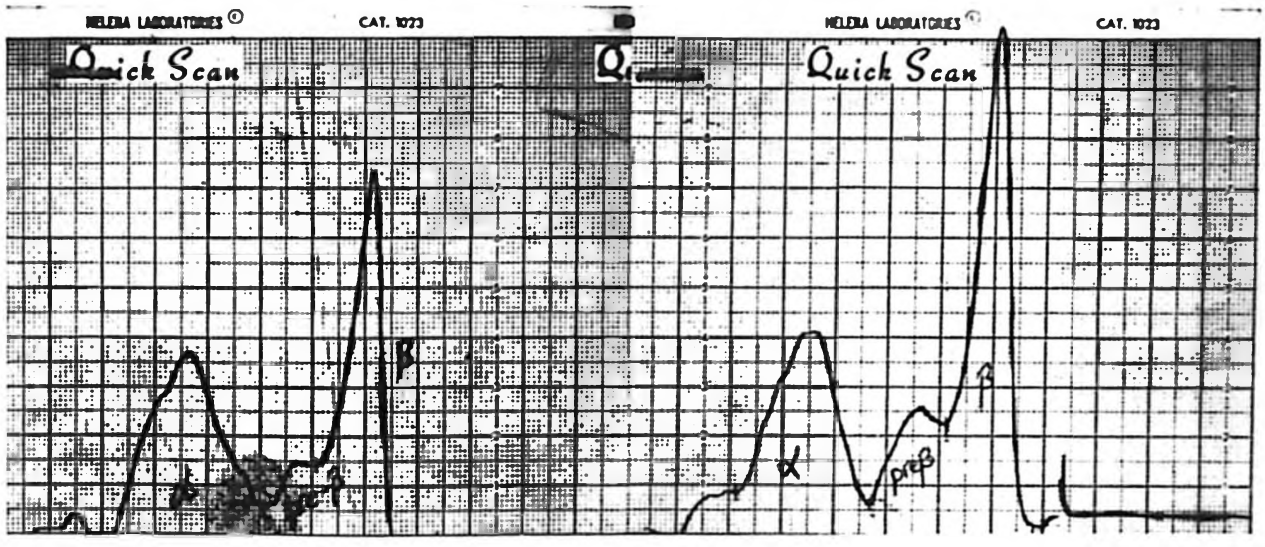


Figure 2

Lipoprotein electrophoresis of the patient. The β- and prebetabands are not seen; only the alpha band is present.

The mother and father were 22 and 24 years old respectively. They had no health complaints, and their cholesterol, lipid and triglyceride levels as well as lipid electrophoresis were normal (Figures 3-a and 3-b).



Figures 3-a and 3-b

The mother's and father's lipid electrophoresis showing normal pattern.

Discussion

Abetalipoproteinemia, also called the Bassen-Kornzweig syndrome, is a disease characterized by fat malabsorption, retinitis pigmentosa, acanthocytosis and ataxia[1]. Profound hypocholesterolemia with total absence of LDL in the plasma is due to the absence of betalipoprotein in homozygotes. About 70% of the plasma cholesterol is carried physiologically in the LDL; therefore, in the absence of LDL striking hypocholesterolemia is expected. Virtually all the plasma cholesterol in abetalipoproteinemia is associated with HDL, which is less in esterified form than normal. Phospholipid distribution related to HDL is also abnormal in this disease. Heterozygotes, as in our family, are asymptomatic, with normal cholesterol, triglyceride level and lipid electrophoresis, which allows this condition to be differentiated from familial hypobetalipoproteinemia[3].

Since betalipoproteins are formed neither in the intestine nor in the liver in this disease, chylomicrons and VLDL are absent and phospholipid concentrations are decreased by about 75%, with a greater decrease in the phosphatidyl choline level than in sphingomyelin concentration in the plasma. Although a very low plasma cholesterol level (<40 mg/dl) is characteristic of this disease, it was not very low in our patient, but even low normal plasma cholesterol levels have been recorded in some patients with this disease[4-8]. Actually whole body cholesterol synthesis is probably increased in abetalipoproteinemia, but because of dietary malabsorption and poor synthesis in the plasma, the cholesterol plasma level is low. Cholestanol levels have not been determined in abetalipoproteinemia cases. Since the symptoms of cerebrotendinous xanthomatosis[9], in which cholesterol synthesis is augmented, resemble those of abetalipoproteinemia, intracellular cholestanol should also be determined in abetalipoproteinemia.

Although anemia is not a constant feature in abetalipoproteinemia cases, it is rather common in young children, with hemoglobin levels as low as 4 to 8 g/dl as in our case[6,10-12]. Shortened erythrocyte survival has been reported in at least three patients[6,10,11]. Acanthocytes are not found in the bone marrow of these patients; therefore membrane distortion is presumed to be acquired in the peripheral circulation, most likely due to changes in the membrane phosphatidyl choline-sphingomyelin ratio, which is parallel to the ratio in plasma. Our finding of generalized, non-specific aminoaciduria is not frequently seen in this syndrome, but it has been reported previously by Becroft et al[1].

Gross hepatic enlargement has also been described in one child with abetalipoproteinemia[13], with slight elevation of transaminase levels[13,14] and with hypoalbuminemia[15] like in our case. Our patient showed malabsorption, marked growth retardation[16], hypoproteinemia and acanthocytosis. She was too young to have developed ocular, neurologic and neuromuscular manifestations. She died because of severe emaciation although she was given very high doses of vitamin E in addition to other vitamins[2].

The diagnosis of abetalipoproteinemia in this case was reached after noting multiple acanthocytes on the peripheral smear. When the low cholesterol level was seen, lipoprotein electrophoresis was obtained, which confirmed the diagnosis. The high alpha fetoprotein level (195 ng/ml) obtained in the referring hospital had not been reported previously.

Summary

A six-month-old girl, with abetalipoproteinemia is presented here, the first report of this syndrome from Turkey. She was the child of first cousins, and was referred to Hacettepe Children's Hospital with hemolytic anemia with severe acanthocytosis, severe malnutrition and hepatomegaly. Diagnosis was made by lipid electrophoresis studies in the patient and in both parents. Only high density lipoproteins were seen in the patient's electrophoresis results, but with both parents the findings were normal.

Acknowledgements

This patient was referred to us by Dr. Ayfer Gür-Güven. Miss Ülkü Çayır's help in typing is much appreciated.

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