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Case Report

An infant with hypertriglyceridemia presenting as failure to thrive: a case report

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ABSTRACT

Familial hypertriglyceridemia is rare in infancy. Diagnosis in infancy is very difficult and is usually diagnosed when acute pancreatitis sets in. Early diagnosis is important as it can prevent the complications associated with acute pancreatitis and pancreatic necrosis. Here is a case familial hypertriglyceridemia in an infant who presented to us with failure to thrive but was diagnosed early due to presence of highly viscous and milky blood. This holds importance as early treatment can reduce the complications and morbidity associated with familial hypertriglyceridemia.

Keywords: Familial hypertriglyceridemia, Milky serum, Failure to thrive

INTRODUCTION

Familial hypertriglyceridemia is a rare condition occurring 1 in 1000 pediatric population.[1] Hypertriglyceridemia is defined as plasma or serum triglyceride concentration above 150 mg/dl in a fasting state, or it refers to a fasting plasma triglyceride measurement that is increased, typically above the 95th percentile for age and sex, although additional quantitative or qualitative lipoprotein abnormalities can also be present.[2] Elevated plasma triglyceride concentrations contribute to increased risk of cardiovascular disease. The two main sources of plasma triglycerides (also known as triacylglycerol) are exogenous (i.e. from dietary fat) and carried in chylomicrons, and endogenous (from the liver) and carried in very-low-density lipoprotein (VLDL) particles. After a meal, over 90% of the circulating triglycerides originate in the intestine and are secreted in chylomicrons, whereas during periods of fasting, endogenous triglycerides secreted by the liver as VLDL predominate. The increase in plasma of triglyceride-rich lipoproteins results from increased production from the liver and intestine (by means of upregulated synthetic and secretory pathways) or through decreased peripheral catabolism (mainly from reduced lipoprotein lipase activity).

CASE REPORT

A 3 month old male child was admitted with complaints of failure to gain weight and decreased oral acceptance (Figure 1). The baby was born at term by normal vaginal delivery at home and was 1.8 kg weight at birth. Antenatal and postnatal periods were uneventful and was born from non-consanguineous marriage.

Baby had multiple hospital visits in past with similar complaints for which complete blood count (CBC) was done and found to have normocytic normochromic anemia with haemoglobin (Hb) of 9.9 mg/dl and normal renal and liver function test and serum calcium, for which he was given outpatient department (OPD) based treatment and exclusive breast feeding was advised. But baby came back with similar complaints after 25 days, when he was investigated, he was found have milky serum (Figure 2). Patient was admitted and investigated for lipid disorders.

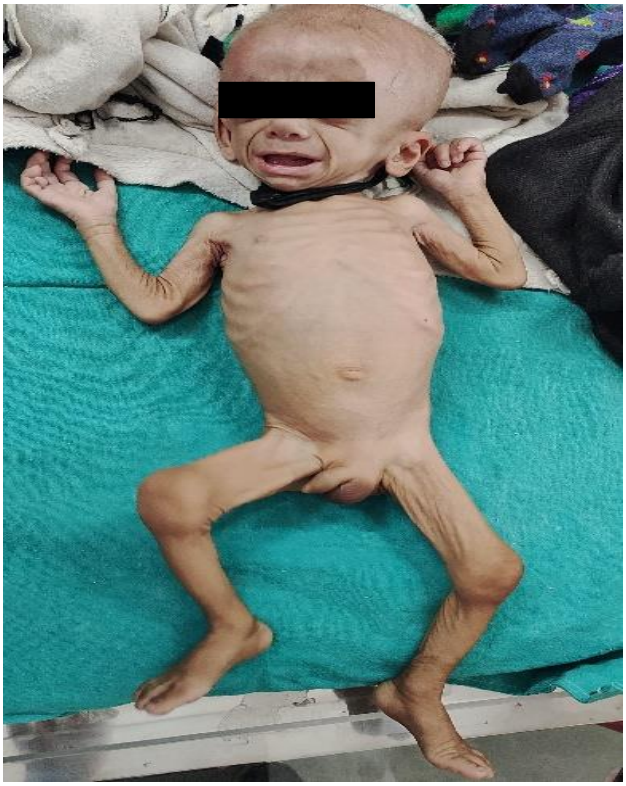

Figure 1: Poor nutritional status of infant.

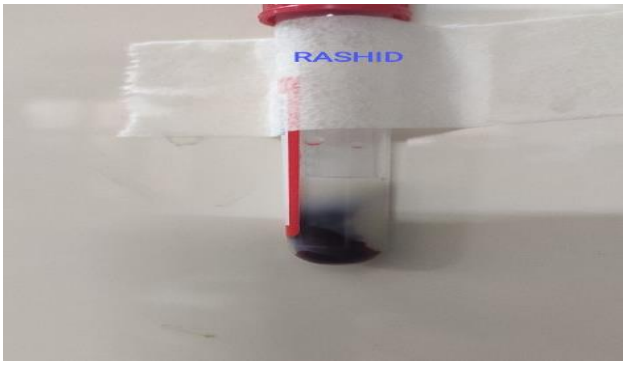

Figure 2: Blood sample of infant with milky serum.

The child was active and vitally stable with normal blood sugar levels and had no hepatosplenomegaly or xanthomas. Anthropometric measurements being weight: 2.2 kg (W/A<-3SD), length: 51 cm (L/A<-3SD) (W/H<-3 SD), head circumference: 37.5 cm (<3rd centile), chest circumference: 29 cm. Ophthalmological examination was normal. The baby had normal thyroid, renal and liver function test along with normal ultrasonography (USG) abdomen and brain. Urine and blood cultures were sterile.

Serum was analysed by immunoturbidimetry for apolipoproteins and results were obtained, apolipoprotein A1 was 75 mg/dl (105-175 mg/dl), apolipoprotein B 84 mg/dl (60-140 mg/dl), apo B/apo A1 was 1.12 (0.35-0.98). Spectrophotometry and agarose gel electrophoresis was done for lipid profile (Figure 3) and results are total cholesterol 175 mg/dl, triglycerides 1917 mg/dl. HDL cholesterol 26 mg/dl, LDL cholesterol 97 mg/dl. VLDL cholesterol could not be reported in the sample as triglyceride levels were high. Lipoprotein electrophoresis revealed HDL 22%, LDL 34%, VLDL 44%, absent chylomicrons. Blood sugar was normal throughout hospital stay. Parent's lipid profile was normal with no history of xanthoma, pancreatitis or premature death in the family. Based on the above finding the patient was diagnosed to have Fredrickson type IV dyslipidemia. Patient triglyceride levels were>1000 mg/dl hence was started on omega 3 fatty acids, fenofibrate and niacin. Exclusive breast feeding was advised till 6 months.

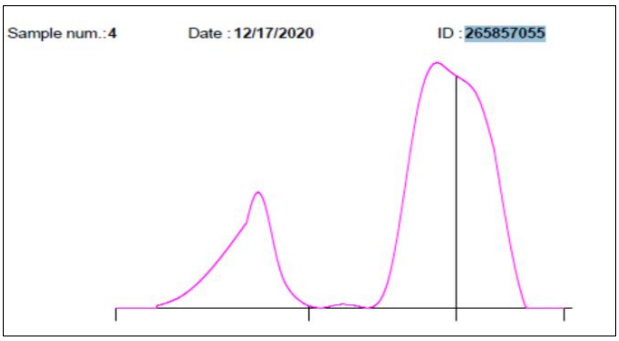

Figure 3: Lipid electrophoresis pattern suggestive of type IV familial hypertriglyceridemia.

DISCUSSION

The major classes of dyslipidemia have been conventionally classified according to the Fredrickson phenotype. A variety of defects, some of which are familial, can produce these disorders.[3] The present case was found to be Fredrickson type IV as triglyceride levels were high and low HDL concentration. Fredrickson phenotype IV is defined as serum concentrations of VLDL elevated; total cholesterol may be >90th percentile and may also see triglyceride concentrations >90th percentile or low high-density lipoprotein.

Most children with hypertriglyceridemia have no symptoms or signs associated with the biochemical abnormality. The following are exceptions: in patients with hereditary disorders, skin lesions such as eruptive xanthomas and xanthelasmas may be present, they also may exhibit lipemia retinalis or hepatosplenomegaly; and in patients with very high triglyceride levels (above 1000 mg/dl [11.3 mmol/l]), pancreatitis may develop.[4]

Children and adolescents with persistent moderate to high levels of TG maybe at increased risk for premature cardiovascular disease during adulthood. However, the extent to which HTG independently contributes to CVD has long been debated and remains unknown.[5,6]

The serum is opalescent in these cases due to increase in VLDL. Lipid disorders occurs either as primary event or secondary to an underlying disease. Primary causes of hypertriglyceridemia; its molecular basis is still largely

unknown but is likely to be multifactorial or polygenic with complex genetic susceptibility, including : Accumulated common small-effect TG-raising polymorphisms (e.g. numerous GWAS loci including APOA1-C3-A4 A5; TRIB1, LPL, MLXIPL, GCKR, FADS1-2-3, NCAN, APOB, PLTP, ANGPTL3) and transient infantile HTG (glycerol-3-phosphate dehydrogenase 1 deficiency) from bi-allelic GPD1 gene mutation.[7] Secondary causes of hypertriglyceridemia include Metabolic syndrome with triglyceride levels > 1.7 mmol/l, a diet with a positive energy-intake balance and a high fat or high glycemic index content, renal disease, especially uraemia or glomerulonephritis, hypothyroidism, an autoimmune disorder, such as a paraproteinemia or systemic lupus erythematosus, several types of medications, including corticosteroids, antihypertensives: e.g. non-cardio selective β-blockers, thiazides, bile-acid–binding resins, cyclophosphamide, antiretroviral regimens, especially for HIV infections, phenothiazines, second-generation antipsychotics.[8]

Familial hypertriglyceridemia (type IV hyperlipidaemia), an autosomal dominant disorder occurring in approximately 1 in 500 individuals is characterized by elevation of plasma triglycerides >90th percentile (250-1,000 mg/dl range), often accompanied by slight elevation in plasma cholesterol and low HDL. The disease usually presents during childhood with acute pancreatitis. Severe hypertriglyceridemia accounts for 1 to 10 percent cases of acute pancreatitis.[9] The patients with type I hyperlipidemia often develop eruptive xanthomas in adulthood more compared to type IV hypertriglyceridemia individuals. Our patient didn't present with any of the above complaints, rather presented with failure to thrive. Parents had a normal lipid profile and secondary causes being ruled out, the genetic workup could not be done as they were not affordable for a genetic testing. The patient was managed based on the lines of isolated hypertriglyceridemia.

The most effective treatment modality is dietary triglyceride restriction by restriction of fat, carbohydrates, especially high-glycemic and high fructose foods. Dietary fat is not a primary source for liver TG, and higher fat diet do not raise fasting plasma TG levels. Nevertheless, a change in the type of fat (i.e. saturated versus poly- and monounsaturated fats) is recommended.[10] Exclusive breast feeding is advised till 6 months. Sugar sweetened beverages are avoided. Water intake is encouraged.[11] Niacin in hypertriglyceridemia is not recommended in infants as it is associated with toxicities including liver disease. However, few guidelines for niacin dosing is available and an effective dose must be balanced against the toxicities. HMG-CoA reductase inhibitors are variably effective in lowering triglyceride levels. Fibric acid derivatives safety and efficacy data in children is limited. Their use is reserved for persistent hypertriglyceridemia with regular ALT level monitoring.[12] Marine omega-3 fatty acids that contain omega-3-acid ethyl esters reduce VLDL production and serum triglyceride concentration as much as 50 percent or more.[13,14]

CONCLUSION

Early diagnosis of Familial hypertriglyceridemia and medical intervention by lipid-lowering agents and dietary modification, at the time of diagnosis, can improve the prognosis and maintain a near normal lifestyle for affected children, as triglyceride induced pancreatitis occur at plasma levels >2000 mg/dl. Recommended triglyceride levels <1000 mg/dl can be used as a threshold. It also prevents complications like atherosclerosis, pancreatic necrosis and the frequency of hospital admissions is significantly reduced. Children tolerate these agents well and show no serious side effects. Long-term studies are still needed to ensure the safety and effectiveness of these agents in children. Genetic studies in the initial visits itself will guide the treatment and prognosis of disease.

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