An Infant with Milky Blood : An Unusual but Treatable Case of Familial Hyperlipidemia

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Abstract Hyperlipidemia is increasing prevalent risk factor in children, concomitant with worldwide epidemic of obesity. Lipid disorder can occur either as primary event or secondary to an underlying disease. The primary dyslipidemia are associated with overproductions/or impaired removal of lipoprotein. The latter defect can be induced by an abnormality in either the lipoprotein itself or in the lipoprotein receptor. A 2 month old male baby was found to have highly viscous and milky serum. S. Cholesterol was 2,200 mg/dl and triglycerides 13,292 mg%. There was no dysmorphic feature. Child was anemic and had hepatosplenomegaly and xanthomas. There was positive history of hyperlipidemia in first maternal cousin. Parents of index case had normal lipid profile. The child was put on lipid lowering agents, Iron drops, medium chain fatty acid.

Keywords Hypertriglyceridemia · Xanthoma · Milky serum

Case Report

A 2 month old male baby was admitted in emergency with excessive cry and abdominal distention. The baby was younger of two siblings, born at term by normal vaginal delivery with birth weight of 3 kg with uneventful antenatal and postnatal periods. The child was on exclusively breast feeding since birth.

During sampling, his blood was found to be highly viscous and milky (Fig. 1). The child was active and had hepatosplenomegaly and xanthomas (Fig. 2) without dysmorphic features. The child has normal Liver and kidney function test with sterile urine and blood cultures. Ultrasonography showed hepatosplenomegaly with normal liver texture. Electrocardiography and echocardiography results were within normal limits. Ophthalmological examination revealed lipemia retinalis (Fig. 3).

Serum was analyzed by using Becman Coulter USA in which LDL, VLDL, HDL done by electrophoresis, TG and S. Cholesterol by Spectrophotometry and Apo A, Apo B S. lipase by immunoturbidimetric technique. Results are obtained as S. cholesterol 2,200 mg/dl (<170 mg/dl), S. triglycerides 13,292 mg% (<150 mg/dl), HDL 94 mg/dl (40–60 mg/dl), VLDL 426 mg/dl (<30 mg/dl), LDL 463.5 mg/dl (<110 mg/dl). Other investigations are Apo B 163 mg/dl (55–140 mg/dl), Apo A 175 mg/dl (110–225 mg/dl), S. lipase 163 mg/dl (0–8 mg/dl), S. amylase 13 U/l, T3 10.8 ng/ml, T4 10.4 µg/dl, TSH 2.4 µIU/ml, S. ca 9.8 mg/dl, S. Phosphorus 3.50 mg/dl, S. Uric acid 5.0 mg/dl, ALP 743 U/l. Routine blood counts revealed Hb < 8 g/dl.

Other sibling and both parents of index case had normal lipid profiles. No history of convulsion, jaundice, bleeding manifestation, skin rash, any premature sudden death or any known case of hyperlipidemia in family members. Developmental milestones were achieved at appropriate age.

The child was put on lipid lowering agents, medium chain fatty acid formula, intravenous fluid and blood transfusion given. Lipid profile was repeated after 15 days which showed blood red in color (Fig. 4) with lowering lipid contents as S. cholesterol 984 mg% (normal < 170 mg%), S. triglycerides 7,828 mg% (normal < 150 mg%), HDL 94 mg% (normal range 40–60 mg%), VLDL 126 mg% (<30 mg%), LDL 226 mg% (normal < 110 mg%), apoB-120 mg%

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Fig. 1 White milky blood

Fig. 2 Infant with xanthomas

Fig. 3 Lipemia retinalis

(normal range 55–140 mg%), apo A 112 mg% (normal 110–205 mg%).

Discussion

Hyperlipidemia is increasing prevalent risk factor in children, concomitant with worldwide epidemic of obesity (1). FCS usually manifests in childhood, but 25 % of cases manifested during infancy [1] and are rarely manifest in the newborn period, as in this case, who was diagnosed in 2 months of life. In India, several cases have been reported in very young children aged between 20 and 60 days. Some presented with features of sepsis with systemic complications and acute renal failure with complete recovery [2]. The diagnosis was clinical and genetic testing was not available. Lipid disorder can occur either as primary event or secondary to an underlying disease. The primary dyslipidemia are associated with overproductions/or impaired removal of lipoprotein. The latter defect can be induced by an abnormality in either the lipoprotein itself or in the lipoprotein receptor [3]. Monogenic disorders that cause abnormal levels of plasma cholesterol and triglycerides have received much attention due to their role in metabolic dysfunction and cardiovascular disease. While these disorders often present clinically during adulthood, some present in the pediatric population and can have serious consequences if misdiagnosed or untreated [4]. Hypertriglyceridemia is defined as having plasma triglyceride above the 95th percentile for age and sex [3]. It is a rare disorder in childhood. According to the National Cholesterol Education Program (NCEP), normal triglyceride level

Fig. 4 Sample of blood after treatment

is < 150 mg/dl (< 1.7 mmol/l) [2]. Primary hypertriglyceridemia is the result of various genetic defects leading to disordered triglyceride metabolism. Secondary causes are acquired and may include a high-fat diet, obesity, diabetes, hypothyroidism, and certain medications (e.g., estrogen and tamoxifen) [5].

Familial chylomicronemia syndrome is disorder of lipoprotein metabolic due to familial lipoprotein lipase or apo C deficient or presence of inhibition to lipoprotein lipase. It is very rare syndrome with prevalence of 1 in 1 million for homozygotes and 1 in 500 for heterozygote [6–8]. FCS is characterized by severe hypertriglyceridemia with episodes of abdominal pain, recurrent acute pancreatitis, eruptive cutaneous xanthomata, hepatosplenomegaly, and lipemia retinalis. However, evidence suggests that presentation during infancy can be heterogeneous and may include other signs such as pallor, anemia, jaundice, irritability, and diarrhea. These manifestations are variable in the time and severity of presentation [4]. One study conducted in Quebec, Canada, in which LPL deficiency was demonstrated in 16 infants who presented with heterogeneous features, irritability, pallor, anemia, and gastrointestinal bleed, while others presented with splenomegaly and positive family history. This is also demonstrated in case one, he was accidentally found to have severe hypertriglyceridemia when he was evaluated for pallor and jaundice [8].

Diagnosis is based on lipemic appearance of serum caking of chylomicrons on serum on refrigeration, serum triglycerides in excess of 10,00 mg/dl. [5]. Early diagnosis is important to prevent complications such as acute and chronic pancreatitis and pancreatic necrosis, although pancreatic function often deteriorates very slowly [4, 9]. Cardiovascular risk may also be increased in these patients, though evidence has been inconclusive [4]. Unfortunately, FCS resulting from deficiency in LPL or apo C-II is very difficult to treat with existing pharmacologic agents. The most effective treatment modality is severe dietary triglyceride restriction. The recommended targets vary from less than 50 g/day, or under 25 % of total daily caloric intake, to less than 20 g/day, or under 15 % [3, 10]. But a significantly persistent high triglyceride level necessitates pharmacological intervention. There has been a general reluctance to use drug therapy to treat lipid abnormalities in children; however, increasing evidence suggests effectiveness and short-term safety similar to those in adults [1, 11]. Recently, the American Heart Association provides general recommendations for pharmacological management of high-risk lipid abnormalities in children and adolescents.

They defined high-risk lipid abnormalities as primary and secondary conditions associated with extreme lipid abnormalities or conditions underlying high risk of cardiovascular disease whereby the presence and severity of lipid abnormalities may further exacerbate that risk [11].

The drugs studied and recommended for treating hypertriglyceridemia are fibric acid derivatives (e.g., Gemfibrozil, Fenofibrate). These have the effect of both raising HDL and lowering triglycerides. Main adverse effects observed were gastrointestinal upset together with an increased predisposition to cholelithiasis. Elevated liver transaminases and creatine kinase are transient. There is risk of myopathy and rhabdomyolysis-especially if used with other agents, particularly statins. Wheeler and colleagues performed a 6-month randomized cross-over trial of Bezafibrate in 14 children with familial hypercholesterolemia [11, 12]. One patient had transient elevation in liver transaminase and one patient had elevation of alkaline phosphatase. The medication was well tolerated with no impact on growth or development. Other drugs, such as statins, were also studied and found to be effective in treating familial hypercholesterolemia but did not have much effect in lowering triglyceride level [11]. Niacin is not recommended because of poor tolerance, serious adverse effects, and limited available data [11, 13, 14].

Our study noted that the hemoglobin (Hb) was low when the triglyceride level was high. His Hb was very low at 6.7 g/dl (normal 13.6–19.6 g/dl), with no evidence of hemolysis. The Hb level improved with his improving triglyceride level. The baby was accidentally discovered to have hyperchylomicronemia, hepatosplenomegaly, raised serum cholesterol, raised serum triglycerides and lipemia retinalis. Lipid lowering drug and low fat formula dramatically improve lipid parameter and prevent premature death.

Conclusion

Familial chylomicronemia syndrome (FCS) is a disease of late childhood and adolescence; however, cases have been reported in infants and neonates. The syndrome presentation is heterogeneous in a very young age group. Early diagnosis 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 the risk of pancreatitis and 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.

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