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A rare case of familial chylomicronemia in a two and half month old boy

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Abstract: *Familial chylomicronemia syndrome is a group of very rare genetic disorders characterized by deficient activity of an enzyme lipoprotein lipase(LPL) or apo-protein C-II, resulting into severe fasting hypertriglyceridemia and massive accumulations of chylomicrons in plasma. LPL deficiency typically presents in childhood with failure to thrive, colicky abdominal pain, eruptive xanthomas, lipemia retinalis, and pancreatitis,hepatomegaly. It is Inherited as autosomal recessive disorder. Its estimated incidence is 1 in 10,00,000 population [1]. We report a rare case of familial chylomicronemia in a 2.5 months old infant who was diagnosed after his plasma incidentally found to be milky. Lipid profile revealed familial chylomicronemia. The infant was started fat restricted diet and advised a regular follow up.*

Keywords: *Familial chylomicronemia , Lipemic plasma , Eruptive xanthoma*

I. Introduction

Lipid disorder refers to elevation of plasma cholesterol &/or triglyceride or low HDL level that contributes to the development of atherosclerosis and they can be primary or secondary[2].Primary disorders are transmitted genetically and usually manifests from childhood[3]. Secondary disorders contribute to the most cases of dyslipidemia in adults which are due to sedentary lifestyle with excessive intake of saturated fats, cholesterol and transfatty acids. These secondary causes may include diabetes, hypothyroidism, alcohol, oral estrogens, renal disease, diuretics and B blockers, retinoic acid drugs, and atypical antipsychotics [4] . Dyslipidemia itself causes no symptoms but can lead to coronary artery disease and peripheral vascular arterial disease.

Primary genetic dyslipidemias are rare defects of lipid metabolism; familial chylomicronemia syndrome (FCS) (Type I hyperlipoproteinemia) is inherited as an autosomal recessive disease. Its estimated incidence is 1 in 10,00,000 population [1]. It is caused by deficiency of extrahepatic lipoprotein lipase (LPL) or its cofactor apoprotein-CII (apo- CII). LPL enzyme is responsible for hydrolysis and removal of chylomicrons and very low density lipoprotein (VLDL) triglycerides (Tg) from circulation. Without effective clearance of triglycerides, striking elevation of chylomicrons and VLDL does occur [5].

We report a rare case of familial chylomicronemia in a 2.5 month old infant.

II. Case Report

A 2.5 months old immunized boy born of third degree consanguineous marriage weighing 4.5kg attended to our OPD with the complaints of black tarry stool for last 3-4 days with pallor and gradual distension of abdomen. Birth history was unremarkable and he had been on exclusive breastfedding. For investigation and management child was admitted in our inpatient department. When blood was drawn for laboratory tests it appeared milky in colour (Fig:2). On examination baby was active, playful and multiple xanthomatous eruption (Fig:1) seen over knees and extensor aspect of the limbs with moderate hepatospleenomegaly. Blood reports showed Hb 6.9gm/dl, TLC 13100/cumm, N50,L42,E5,M3,B0 Platelet count 1.38lacks/cumm ,ESR 46mm ,Reticulocyte count 2.8% with hypocromia and anisocytosis in peripheral blood smear. LFT showed serum total Bilirubin 1.9mg/dl, direct 0.6mg/dl, indirect 1.3 mg/dl, serum total protein 6.3g/dl with albumin 2.9gm/dl, globulin 3.4gm/dl, SGOT 97U/L, SGPT 102U/L .Prothombin time test was 28sec, INR 2.1 ,APTT 46sec ;control 33 sec . TSH & Bone marrow study of the baby were within normal limits.

Lipid profile report showed grossly lipemia- triglyceride (TG) 28980 mg/dl, total cholesterol 3820 mg/dl. Increased TG interferes the assay of other factors. USG abdomen showed parenchymal echogenicity of liver and not clearly visible pancreas. Opthalmoscopy showed lipemic retinitis. High perfusion liquid chromatography of hemoglobin studies of both parents were normal. Lipid profile of mother was normal but father had increased Triglyceride (230mg/dl) and low HDL cholesterol (38mg/dl). Initially child was managed with inj vitamin K1 and blood transfusion . As age of our child was 2.5 months, we continued breastmilk and added simyl MCT (medium chain triglyceride) and fat soluble vitamin supplement. Statin group of drug could not be started as we could not found any recommendation of its use below three months of age.

On his last follow up child was clinically improved and triglycerides were also decreasing.

III. Discussion

Familial chylomiconemia is a very rare autosomal recessive (AR) disorder. It is caused by deficiency of extrahepatic lipoprotein lipase (LPL) or its cofactor apoprotein-CII (apo- CII). ApoCII deficiency typically has a later onset of symptoms and is often milder in appearance[4]. In comparison with patients with deficiency of apoC- II, patients with LPL deficiency present at an earlier age with more severe hypertriglyceridemia and lower tolerance to dietary fat[6] . Our case was probably due to LPL deficiency as it manifested at 2 months of age and triglycerides was markedly high.

In the present report, we describe an infant with FCS who presented to us for some other reason like hemorrhagic disease of newborn (most probably). Diagnosis of FCS was based on lipemic appearance of serum ,caking of chylomicrons on serum on refrigeration, serum triglycerides in excess of 1,000 mg/dl. [7]

FCS arises from deficiency of LPL/ apo-CII. LPL is located on chromosome 8. More than 30 structural defects have been reported to result in LPL deficiency. Diagnosis is usually made by measurement of LPL immunoreactive mass in postheparin plasma and apo-CII levels by gel electrophoresis [8] . We could not do these tests in our patient as these tests were not available in our setting .But clinical and biochemical picture pointed towards LPL deficiency.

Familial lipoprotein lipase deficiency usually mentioned by 10 yrs of age, and in 25% occurs in infancy. Often this condition is silent and the initial clue to diagnosis is the presence of lipemic plasma as it happened in our case. It manifests during childhood with lipemic retinitis, hepatospleenomegaly, irritability and recurrent epigastric pain with increased risk of pancreatitis. It is characterized by the pathologic presence of chylomicron after a 12-14 hours period of fasting[9].

Patients with triglyceride levels above 2,000 mg/dl are more likely to present with xanthomas, and those with levels above 4,000 mg/dl may present with lipemia retinalis[1] (pale pink color to the retinal arterioles and venules due to light scattering of the large chylomicrons)[4]

Eruptive Xanthomas present as asymptomatic, evanescent, yellowish papules over buttocks, shoulders, & extensors of limbs when serum triglycerides exceed 2000mg/dl.[1]. In our case TG was 28980mg/dl. There was no family history of triglyceridemia .Lipid profile of father only showed borderline increase TG and decrease HDL. Phagocytosis of chylomicrons by macrophages in the skin results in the formation of eruptive xanthomas (Fig. l). Skin xanthomas usually regress within a few weeks to months after the lowering of plasma triglycerides[6].

Hepatosplenomegaly in our patient is due to ingestion of chylomicrons by reticuloendothelial cells [10].

The treatment is aimed at normalizing triglycerides (Tg) levels. Lipid abnormalities as primary and secondary conditions are usually associated with risk of development of cardiovascular diseases [11]. Dietary recommendations vary from Tg restriction to <50 gm/day or under 25 % of total daily calorie intake to <20 gm/day of triglycerides or under 15 % of total daily calorie intake[12]. Intake of saturated fats and trans fats should be reduced and should be replaced by polyunsaturated and monounsaturated fats[13]. Medium chain triglyceride are preferred source of dietery fat. Other options include a diet rich carnitine, vitamin C, plasmapheresis. Studies have evaluated the safety and efficacy of benzafibrate and statins in older children [14].

Medium chain TGs (MCTs), for example, chain length of 10 and 12 carbons, can be considered for cases of familial chylomicronemia syndrome. MCTs can be either added to infant formula or given as an oral solution to supplement fat calories. Dietary MCTs are directly absorbed into the portal vein and do not require transport on chylomicrons. Therefore, no increase in TG concentrations is seen. Rouis et al[15] described a unique patient with clinical features of LPL deficiency with a complete resolution of clinical symptoms with MCT oil and omega 3 fattyacid therapy.We also prescribed MCT.

Early diagnosis is important to prevent complications such as acute and chronic pancreatitis and pancreatic necrosis, although pancreatic function often deteriorates very slowly [16].The complication in these children is due to increased amount of fat intake which causes recurrent bout of illness leading to formation of cysts, hemorrhage and death. Lipid level should be monitored after starting treatment. Dietery and genetic counselling of the family were advised .

Pharmacologic management is sometimes needed in primary triglycerides to prevent pancreatitis and/or reduce the risk of CVD. Medications commonly used for TG lowering are fibric acid derivatives (e.g., Gemfibrozil, Fenofibrate) Niacin,omega 3 fatty. But, none are U S Food and Drug Administration approved for use in children and adolescents (<18 years of age)[17] . Recommendation for their use in children for this particular group of disease needs further studies. As the use of pharmacological agents was never recommended for infants, we did not use them in our case. We only advised for dietary modification with use of Simyl MCT.

Literature and case reports on Familial chylomicronemia in infantile age group are scanty and there is no specific treatment guidelines in these age group. Therefore there is a need for consensus on the management of these children.

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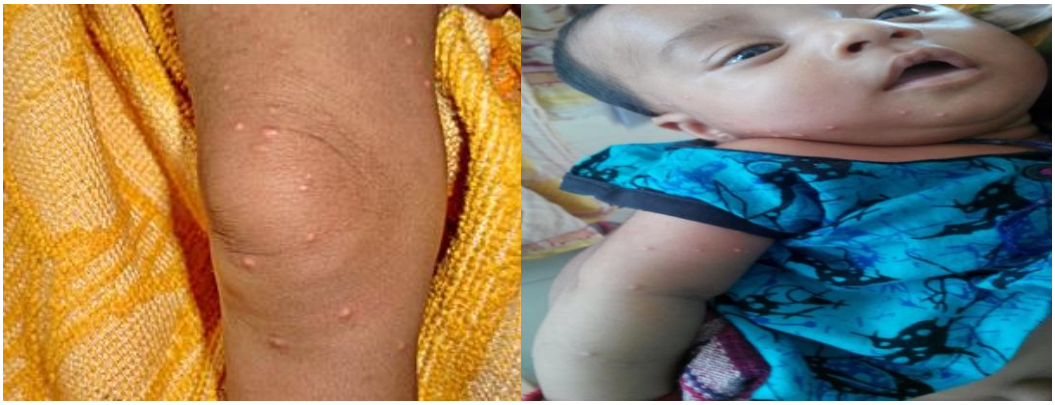

Figure 1: Xanthomatous eruption over knee joints, face and upper limb

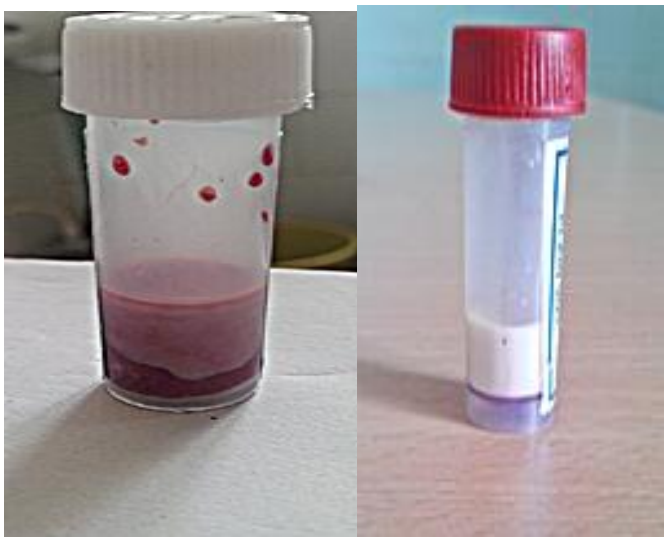

Fig 2 : Lipemic plasma after 15min & 6hour(milky) storage of blood sample