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Case Report (Pages: 449-453)

Familial Chylomicronemia Syndrome (FCS) in a 10- Day- Old Neonate: A Case Report

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Abstract

There are no adequate data that evaluate the safety and effectiveness of lowering triglyceride levels in infants. The authors report a neonate affected by Familial hyperchylomicronemia syndrome, while being investigated for sepsis the serum sample obtained for blood counts was discovered to be lipaemic and the case was subsequently investigated for dyslipidemia. Based on this very abnormal lipid profile compared to her age, we started her on statins. The parents were referred to a dietitian vigorous dietary fat restriction supplemented by fat-soluble vitamins including mixing food with olive oil and giving skimmed dairy products as she is growing. Follow up is ongoing.

Key Words: Apolipoprotein C-II deficiency, Familial chylomicronemia syndrome, Familial lipoprotein lipase deficiency, LPL.

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Introduction

Familial chylomicronemia syndrome (FCS) is disorder of lipoprotein metabolism due to familial Lipoprotein Lipase (LPL) or apolipoprotein C-II deficiency (Apo C-II) or the presence of inhibitors to lipoprotein lipase (1). It is a very rare syndrome with prevalence of approximately 1 in 1 million for homozygotes. It is relatively common for heterozygotes, approximately 1 in 500 (2). The disease has been described in all races. To date, several hundred patients with LPL deficiency have been described (3-5).

FCS is the most dramatic example of severe hypertriglyceridemia. Almost all patients with fasting triglyceride levels in excess of 1000 mg/dl (11.36 mmol/L) have FCS (6). It manifests as eruptive xanthomas, acute pancreatitis, hepatomegaly, splenomegaly, foam cell infiltration of bone marrow, and lipemia retinalis. These patients usually have lipemic plasma due to marked elevation of triglyceride and chylomicron levels (7).

Several mutations in the LPL gene located on chromosome 8p22 have been identified with familial LPL deficiency (8). More than 50 missense and nonsense mutations have been identified. The majority of mutations are located on exons 3, 5, and 6 which are responsible for the catalytic coding region of the gene (2). Apo C-II gene mutation has also been identified (9). Other extremely rare genetic disorders can present with chylomicronemia with severe hypertriglyceridemia. Examples of these are familial apoAV deficiency, familial Lipase Maturation Factor 1 (LMF1) deficiency, and familial GPIHDLBP1 deficiency (10).

Case Report

Aleena 10 - day- old female 2nd in birth order full-term, born at lal ded a teritiary care hospital by Lower Segment Cesarian Section (LSCS) an uneventful pregnancy presented with complaints of refusal of feeds and irritability from last 24 hrs. While being investigated for sepsis the serum sample obtained for blood counts was discovered to be lipaemic and the case was subsequently investigated for dyslipidemia. She was discovered to have very high cholesterol 1236mg/dl(nr<170) and triglycerides(2132).

Hb 16.gms% total leucocyte count of 8400/cmm Plts 2.5 lakhs/cmm,Blood Sugar of 97mg/dl . Lipid profile performed next day showed serum cholesterol 410 (normal <170mg/dl), high density lipoprotein (HDL) 54(normal 40-60mg/dl), and triglyceride (TG) 1550mg/dl (normal <150mg/dl).low density lipoprotein(LDL)46(normal<110mg/dl)VLDL 310(normal<30mg/dl).Thyroid Profile T3-210uIU/ml (79-200) T4-10.8 uIU/ml (4-11)TSH -1.202 uIU/ml (1.7-9.1) Based on this very abnormal lipid profile compared to her age, we started her on statins.

Further history revealed that aleena is the 2nd child born to a 3degree consanguineous parents with positive family history of hyperlipidemia, in father and mother.There is no history of sudden death, premature cardiovascular disease, or recurrent pancreatitis in the family. Maternal history of hypothyroidism and diabetes on treatment. Elder sibling of the patient who is 22 month old male child had normal lipid profile.

Examination revealed an active, but not dysmorphic baby. Systemic examination revealed hepatosplenomegaly. No skin manifestation. Examination of the cardiovascular system was normal, including blood pressure. Eye examination was normal..liver function tests and kidney function tests were normal . Baseline ultrasound of abdomen showed hepato-

spleenomegaly , ECG, and Echo were normal.

The parents were referred to a dietitian vigorous dietary fat restriction supplemented by fat-soluble vitamins. Medium-chain triglycerides were recommended, including mixing food with olive oil and giving skimmed dairy products as he is growing. Follow up is ongoing.

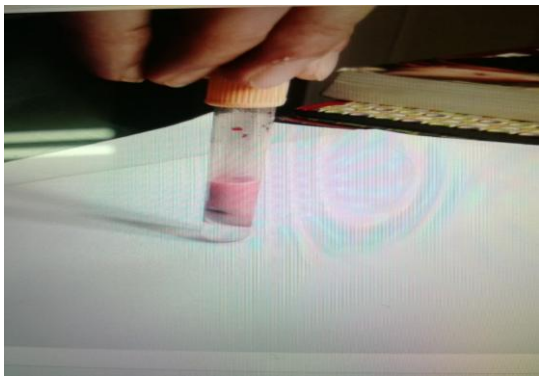

Fig.1:Thick viscous milky blood sample of patient

Discussion

FCS usually manifests in childhood, but 25% of cases manifested during infancy (11) and are rarely manifest in the newborn period, as in our case, who was diagnosed in day 21st of life. In India, several cases have been reported in infants aged between 20 and 60 days. Some presented with features of sepsis with systemic complications and acute renal failure with complete recovery (12). As mentioned above, the genetic diagnosis for FCS is available but only for limited laboratories. For our cases, the diagnosis was clinical and genetic testing was not available.

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 (13). 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 accidently found to have severe hypertiglyceridemia when he was evaluated for pallor and jaundice (14).

This syndrome is autosomal recessive, and a positive family history (e.g., a child in a family) will necessitate screening of other family members (parents and siblings). Even if the lipid profile is normal, close follow up with lipid profile is indicated.

The most dramatic manifestation of FCS is acute pancreatitis. It is responsible for up to 7% of all cases of pancreatitis. Failure to consider and investigate chylomicronemia as a cause of pancreatitis may lead to an underestimation of incidence. Hyperchylomicronemia-induced pancreatitis rarely occurs unless triglyceride levels exceed 20 mmo/L (1760 mg/dL). Acute pancreatitis, due to any cause, is an emergency and necessitates an urgent intervention. However, in patients with hyperchylomicronemia, further management of hyperlipidemia to prevent future attacks is recommended (15-17).

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 per day, or under 25% of total daily caloric intake, to less than 20 g per day, or under 15% (18-20). 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 (21, 22). 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 (21).

Conflict of interests: None

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