Case Report

Milky Blood and Bloody Stools: A Twist Of Fate Spotting Of Neonatal Hyperlipoproteinemia

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ABSTRACT

Hyperlipoproteinemia is a very rare condition in a neonate and its mechanism includes lipoprotein molecular defect, lipoprotein lipase deficiency, or lipoprotein receptor defect. The common ones are familial combined hyperlipidemias, familial & polygenic hypercholesterolemia and familial hypertriglyceridemia. Usually, the detection is by accidental observation of milky blood while sampling for non-specific symptoms. Hyperlipoproteinemia can cause acute pancreatitis and early-onset cardiovascular disease if left untreated. Here we are reporting the case of a 25-day-old baby who presented with blood in stools. Physical examination was normal. Incidentally, it was found that the blood was highly viscous and milky. Complete lipid profile done suggested familial combined hyperlipidemia. The baby was started on Gemfibrozil (20 mg/kg twice daily) and continued on exclusive breast feeds along with the addition of medium chain triglyceride oil and multivitamins. Lipoprotein levels normalized within 5 months. This condition requires lifelong follow up.

Key words: Familial combined hyperlipidemia, Gemfibrozil, neonatal, milky blood

Hyperlipoproteinemia is characterized by markedly elevated blood cholesterol and triglyceride levels. This can lead to early-onset cardiovascular diseases, pancreatitis, pancreatic necrosis or persistent multiple organ failure if left untreated. It can occur either as a primary event or secondary to an underlying disease. The treatment of primary hyperlipoproteinemia is confusing in neonates and there is no uniform protocol. While some cases have been managed with continuation of breast feeding and pharmacological drugs, there are reports of cases managed with breast milk restriction and parenteral nutrition along with skimmed milk supplementation. Here we are reporting the experience on managing a neonate with accidental detection of hyperlipoproteinemia.

CASE REPORT

A 25-day-old term male infant with a birth weight of 2.88 kg, born to a primigravida mother from a nonconsanguineous marriage, was admitted to the neonatal intensive care unit with complaints of passing blood in stools. The blood was fresh and mixed with stool. Baby was exclusively breastfed. There was no history of vomiting, watery stools, abdominal distension, intake of prelacteal feeds or intake of ayurvedic medicines by the mother. There was no urticaria or excess irritability. On examination, baby was active with normal vitals and growth parameters. There was no hepatosplenomegaly or guarding of the abdomen. Respiratory, cardiac, and neurological examinations were also normal. A working diagnosis of invasive diarrhoea was made. A possibility of cow's milk protein allergy or probable late onset sepsis with necrotising enterocolitis were also considered. Baby was incidentally found to have pink coloured viscous blood while sampling for the lab workup (Figure 1).

The serum turned milky whitish on standing (Figure 2). Hence hyperlipidemia was suspected. There were no external features of hyperlipoproteinemias like xanthomas.There was no history of dyslipidemia, recurrent pancreatitis, premature cardiovascular disease, or sudden death in either of the maternal or paternal family members. There was no blood in stool after admission. Laboratory parameters for sepsis including CRP and blood culture were negative. Kidney function, liver function, blood sugar, and thyroid function tests were normal. Lipid profile showed very high-serum triglycerides (2369 mg/dL), very high LDL (1593mg/dl), high VLDL (752.6 mg/dl) and low HDL (22.8mg/dl). Serum amylase and lipase levels and abdominal ultrasonography were normal. Lipid profile of father

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showed mildly deranged total cholesterol and LDL levels whereas the mother's lipid profile was within normal range (Table I).

As both triglycerides and VLDL were elevated, Familial combined hyperlipidemia (FCHL) was suspected. In view of financial constraints, genetic study was not done. Breastfeeding was continued. He was started on Gemfibrozil (20 mg/kg twice day) after consulting with the paediatric cardiologist.Medium chain triglyceride (MCT) oil and multivitamins were started. Serial lipid profile done showed normalisation of the levels (Table II). Drug therapy was stopped at 5th month when TG levels started to normalise and LDL became normal. The TG level was 208 mg/dL during the 9-month follow-up. Growth centiles were normal. There was no lipemia retinalis.

DISCUSSION

Lipoproteins are soluble lipid-protein complexes that influence the movement of fat (cholesterol or triglycerides) that is either produced by the liver and adipose tissue or absorbed from the diet for use and storage. They are chylomicrons, HDL, LDL, VLDL, and IDL. The constituent proteins, known as apolipoproteins, mediate the binding of lipoproteins to receptors on the cell surface. There are two possible reasons for lipid disorders: primary and secondary. Overproduction or poor lipoprotein clearance are linked to primary dyslipidemias. An anomaly in either the lipoprotein or the lipoprotein receptor itself may cause the latter problem [1].

Genetic causes of hyperlipoproteinemias are uncommon, particularly in neonates, and include defects in the lipoprotein receptor, lipoprotein lipase, or lipoprotein molecular defects. Some are autosomal dominant and others, recessive. The common ones are familial hypercholesterolemia, familial defective ApoB-100 (elevated LDL, tendon xanthomas and high risk for coronary heart disease), familial combined hyperlipidemia (FCHL) (both LDL &TG are elevated) & familial hypertriglyceridemia (Frederickson type IV). Familial combined hyperlipidemia have an incidence of 1 in 200. Rare types are with an incidence of less than 1 in 10 lakhs [2].

The presentation throughout infancy might vary in severity and time, and it can be heterogeneous. Abdominal pain episodes, recurrent acute pancreatitis, eruptive cutaneous xanthomata, hepatosplenomegaly, lipemia retinalis, pallor, anaemia, jaundice, aggression, diarrhoea, gastrointestinal bleeding, splenomegaly, and a positive family history are among the symptoms [3, 4]. Acute renal failure followed by full recovery and sepsis with systemic consequences can be two manifestations of familial chylomicronemia syndrome (FCS) [5]. The other reported symptoms in the literature includes fever, vomiting, hemoptysis [6]. Hyperlipidemia increases the risk of arterial blockage and this can lead onto stroke like features and mesenteric ischemia. This may be the reason for blood in stools in this case.

FCHL is the most prevalent type of heritable lipid disease, with an estimated frequency of 10% to 20% in myocardial infarction survivors and 1.0% to 2.0% in the general population. Its inheritance pattern is autosomal dominant, and the lipid phenotype varies [7]. The term "multiple-type hyperlipidaemia" refers to hyperlipidaemia, which is defined by increases in the concentrations of LDL, plasma total cholesterol (TC), and/or triglycerides (TG). This lipid profile is characterised by an adverse drop in HDL cholesterol (HDL-C) concentration, an increase in apoB concentration, and a prevalence of atherogenic tiny dense LDL particles.

Hepatic overproduction of lipoprotein particles (i.e., VLDL and LDL) containing apoB-100 is believed to be the pathophysiological mechanism behind FCHL. This manifests as elevated levels of apoB, triglycerides, and total cholesterol in plasma. Additionally, patients with FCHL have been found to have higher levels of residual lipoprotein particles and tiny dense LDL and HDL cholesterol.The symptoms of FCHL can include stroke-like features, calves cramping, toe sores, and chest pain. It increases the chance of developing CVD in the future. The aetiologies of several syndromes, including familial dyslipidemic hypertension, syndrome X, hyperapobetalipoproteinemia, and the atherogenic lipoprotein phenotype, seem to overlap with FCHL [8].

FCHL is diagnosed when one other family member has hyperlipidaemia and the proband and affected parent have LDL-C, triglyceride, or both values that are greater than the 90th percentile. The formal diagnosis of premature heart disease requires that at least two first-degree relatives have evidence of one of three variants of dyslipidaemia: i. > 90th percentile plasma LDL cholesterol; ii. > 90th percentile plasma LDL cholesterol and triglycerides; and iii. >90th percentile triglycerides. Premature heart disease is usually associated with a positive family history. Xanthomas are not one of its characteristics. The diagnosis is supported by elevated plasma apoB levels along with an increase in tiny, dense LDL particles.

The diagnosis of FCHL or its potential variant hyperapobetalipoproteinemia necessitates family data due to the disorder's phenotypical heterogeneity and the potential for total cholesterol and triglyceride levels to fluctuate over time within an affected individual. If the LDL-to-apoB ratio is less than 1.2 (normal value >1.4), one of these two problems may be present. Many characteristics of the metabolic syndrome are shared by type II diabetes and FCHL, indicating that they are not as different as formerly believed [9].

Management includes drug therapy with lifestyle modification with severe dietary triglyceride restriction. Diet should be low in saturated fats, trans fats and cholesterol, as well as reduced consumption of simple sugars. Increase fruits and vegetables and enure an hour of moderate physical activity daily. Drug therapy includes statins and fibrates in the neonatal age group. Pharmacological intervention is required when a high triglyceride level is noticeably persistent. Drug therapy is

necessary if the LDL cholesterol level is greater than 160 mg/dl [9]. Although there has been widespread resistance to using medication therapy to treat lipid problems in children, there is growing evidence that it can be just as effective and safe in the short term as it is for adults [10, 11].

The American Heart Association recently released broad guidelines for the pharmaceutical treatment of children's and adolescents' high-risk lipid disorders. Primary and secondary conditions linked to severe lipid abnormalities or conditions underlying a high risk of cardiovascular disease, where the existence and severity of lipid abnormalities may further increase that risk, were designated as high-risk lipid abnormalities [11]. Fibric acid derivatives, such as Gemfibrozil and Fenofibrate, are the medications that have been researched and suggested for the treatment of hypertriglyceridemia. These have the dual impact of reducing triglycerides and increasing HDL. A higher risk of cholelithiasis and gastrointestinal distress were the main side effects noted. Creatine kinase and hepatic transaminases are temporarily elevated. Using it with other medications, notably statins, increases the risk of myopathy and rhabdomyolysis. Statins and other medications were shown to be useful in treating familial hypercholesterolaemia, but they had no effect on lowering triglyceride levels [11]. Given its low tolerance, severe side effects, and paucity of data, niacin is not advised [11, 12, 13].

CONCLUSIONS

Hyperlipoproteinemia may be an incidental finding in newborn with non specific symptoms. But pharmacotherapy should be considered in the immediate neonatal period and long term follow up is needed to watch for complications.

Table 1: Fasting Lipid profile of the parents

Parameter (mg/dl)	Mother	Father
Total cholesterol(<200)	178	**235**
Triglyceride(<150)	68.6	76.3
HDL(40-60)	61.3	52.1
LDL (70-130)	102	**167.5**

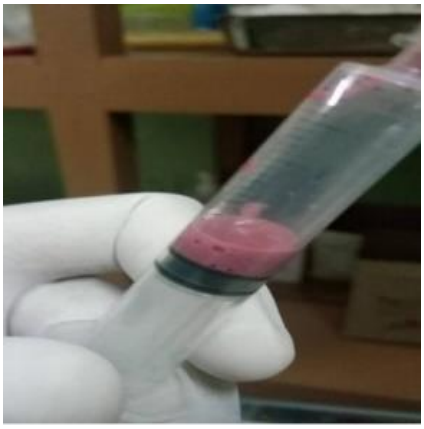

Figure 1: Pink coloured blood

Table 2: Serial lipid profile of the baby

Parameters (mg/dl)	1 month	2 month	3 month	5 month	9 month
Triglyceride (<150 mg/dl)	3763	1441	385	235	208
HDL (40–60 mg/dl)	22.8	38	43	15	14
LDL (<110 mg/dl)	1593.6	697	254	130	66
VLDL (<30 mg/dl)	752.6	567	321	301	421
Total Cholesterol (<170 mg/dl)	2369	1182	458	97	94

Figure 2: Lipemic serum

REFERENCES

1. Brunzell JD, Miller NE, Alaupovic P. Familial chylomicronemia due to a circulating inhibitor of lipoprotein lipase activity. J Lipid Res. 1983; 24(1):12–19.
2. Ramakrishnan S, Hegde V, Naik DM, *et al*. Familial chylomicronemia syndrome: a case report. *J Med Case Rep.* 2020; 14(1):207. doi:10.1186/s13256-020-02609-0.
3. Yuan G, Al-Shali KJ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. *Can Med Assoc J.* 2007; 176(8):1113–20.
4. Nagar R, Arora U. An unusual case of familial hyperlipidaemia. *Indian J Clin Biochem.* 2008; 23(3):302–4.
5. Feoli-Fonseca JC, Levy E, Godard M, *et al*. Familial lipoprotein lipase deficiency in infancy: clinical, biochemical, and molecular study. *J Pediatr.* 1998; 133(3):417–23.
6. Liu S, Wang Z, Zheng X, *et al*. Case report: successful management of a 29-day-old infant with severe hyperlipidemia from a novel homozygous variant of *GPIHBP1* gene. *Front Pediatr.* 2022; 10:792574.
7. Alves AC, Medeiros AM, Soutar AK, *et al*. Genetics of familial combined hyperlipidemia: an update. *Clin Lipidol.* 2018; 13(2):1–15. doi: 10.2217/clp-2018-0014.
8. Bello-Chavolla OY, Kuri-García A, Ríos-Ríos M, *et al*. Familial combined hyperlipidemia: current knowledge, perspectives, and controversies. *Rev Invest Clin.* 2018; 70(5):224–36. doi:10.24875/ric.18002575.

9. Kliegman RM, St Geme JW, Blum NJ, *et al*. Nelson Textbook of Pediatrics. 21st ed. Philadelphia: Elsevier; 2020. Chapter 544, Disorders of lipoprotein metabolism.
10. Santamarina-Fojo S. The familial chylomicronemia syndrome. *Endocrinol Metab Clin North Am.* 1998; 27(3):551–67.
11. Ben-Avram CM, Ben-Zeev O, Lee TD. Homology of lipoprotein lipase to pancreatic lipase. *Proc Natl Acad Sci USA.* 1986; 83(12):4185–9.
12. McCrindle BW. Hyperlipidemia in children. *Thromb Res.* 2006; 118(1):49–58.
13. Colletti RB, Neufeld EJ, Roff NK, *et al*. Niacin treatment of hypercholesterolemia in children. *Pediatrics.* 1993; 92(1):78–82.

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