

Case Report

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A case report of 5 y/o girl with familial chylomicronemia

Abstract

Background: Familial chylomicronemia syndrome is a rare disorder of lipoprotein metabolism due to familial lipoprotein lipase or apolipoprotein C-II deficiency or the presence of inhibitors to lipoprotein lipase. It manifests as eruptive xanthomas, acute pancreatitis, and lipaemic plasma due to marked elevation of triglyceride and chylomicrons levels.

Case presentation: We report a rare case of familial chylomicronemia in a 5 year old girl who was diagnosed after her plasma was incidentally found to be milky. Lipid profile showed familial chylomicronemia. The girl was advised on a low fat diet and a regular follow up check up.

Conclusion: Pediatricians should be alerted for the possibility of familial hyperchylomicronemia due to apolipoprotein CII deficiency and initiate appropriate treatment.

Key words: Familial chylomicronemia , lipoprotein lipase, apolipoprotein CII deficiency.

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Dyslipidemia refers to the elevation of plasma cholesterol and/ or triglycerides or a low HDL level that contributes to the development of atherosclerosis and they can be primary or secondary (1). Primary disorders are genetically transmitted and are the common causes of diseases in children. Secondary disorders contribute to most cases of dyslipidemia in adults which are due to sedentary lifestyle with excessive intake of saturated fats, cholesterol and trans fatty acids (2). Dyslipidemia itself causes no symptoms but can lead to coronary artery disease and peripheral arterial disease. Familial chylomicronemia is a rare autosomal recessive genetic disorder of lipoprotein metabolism with an incidence of one per million in the general population. Clinically, this condition can be silent and be discovered incidentally owing to the lipemic appearance of the blood (3). Familial chylomicronemia syndrome, characterized by severe fasting hypertriglyceridemia and massive accumulation of chylomicrons is due to impaired hydrolysis. Affected individuals often present in infancy or childhood recurrent episodes of abdominal pain and pancreatitis, as well as eruptive xanthomas, and lipemia retinalis (4). The diagnosis of LPL deficiency is established by the absence of LPL enzyme activity, assayed in the presence of an exogenous source of apoC-II, in adipose tissue or postheparin plasma (4-6). In this study, we report a rare case of familial chylomicronemia in a 5 year old girl to describe the different features of this syndrome and increase the knowledge of physicians about this syndrome.

Case presentation

A 5 y/o girl was admitted with chief complaint of abdominal pain vomiting, low grade fever and anorexia. Her pain was epigastric that progressed in a bending position and after persistent vomiting she vomited biliary liquid.

In her medical history, three years ago she was suffering from hypelipideneia without any follow up. According to her family history, the patient's grandmother had hyperlipidemia too. During the examination she was ill but not toxic. In a sitting position she had abdominal pain and vomiting. Her vital signs showed low fever, normal BP and tachycardia. Her abdominal examination indicated epigastric and rebound tenderness. In the course of blood sampling, after blood centrifuging, the serum color was milky and in paraclinic findings she had triglyceride of 2040 mg/dl and high level of amylase (1014) ipase (250), high leukocytes with neutrophilic dominancy, high ESR (79), high CRP levels, SGOT and SGPT, high PT were mildly elevated and high PTT 120 (Fig. 1).

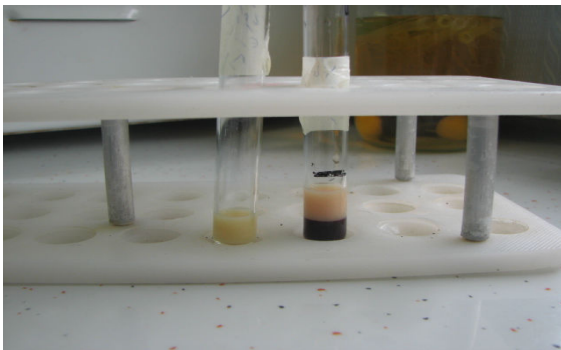


Fig 1. Chilomicrone cake, Lipemic plasma.

After the abdominal sonography, the radiologist reported large dilated and inflammated pancreas with peritoneal free liquid most probably of acute pancreatitis. Because of her family history of hypelipidemia and high triglyceride, lipid profiles were done for her brother, mother (her father died due to a car accident), grandfather grandmother, aunts and uncles but genetic study for lipoprotein lipase gene was not done.

This lab data detested high triglyceride lipid in her brother which was more than 1805mg/dl, her mother had more than 2300 mg/dl and her paternal grandmother with triglyceride more than 2150 mg/dl. The levels of cholesterol in these four people were low between 150 to 280 mg/dl and other lab findings such as blood sugar, calcium, phosphorus and electrolytes were in normal ranges (Table 1).

Table 1. Lipid profile of the patient and relative.

Variant	patient	brother	mother	grandmother
Triglyceride	2040	1805	2300	2150 mg/dl
Cholesterol	280	210	150	197 mg/dl

The patient was diagnosed of pancreatitis with underlying disease of familial hypertriglyceridemia (patient, her brother, her mother and her parental grand mother). The pattern of genetic inheritance for this patient and her brother was autosomal recessive (fig 2). The patients mother had hypertriglyceridemia whose parents and brothers had normal lipid profile with inheritance more likely to be autosomal recessive. The patient was treated with hydration and antibiotic for treatment of acute pancreatitis but because of failure to resolve, infusion of fresh frozen plasma was started. Then, restriction of total dietary fat and use of medium chain fatty acid was prescribed. This patient is a new diagnosed case that is under a follow up for 7 months. Her abdominal pain and pancreatitis improved and her triglyceride level decreased to 1000 mg/dl.

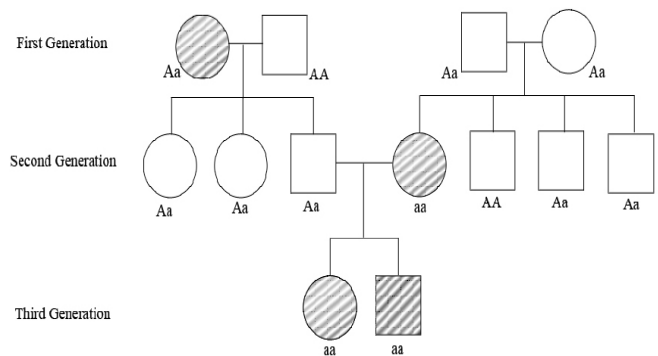


Fig. 2. Patient's pedigree

Also her family was treated with low dietary fat and medium chain fatty acid.

Discussion

Our patient had typical findings of familial chylomicronemia with acute pancreatitis and high level of triglyceride (2040 mg/dl), hypertriglyceridemia in her brother (1805 mg/dl), mother (2300 mg/dl) and paternal grand mother (2150 mg/dl). Familial chylomicronemia syndrome is a rare autosomal recessive disorder resulting from LPL or apolipoprotein CII deficiency or due to the presence of an inhibitor of LPL (7). Familial LPL deficiency usually manifests at 10 years of age, and 25%, occurs during infancy. Often this condition is silent and the initial clue to its diagnosis is the presence of lipemic plasma (8).

Acute relapsing pancreatitis is the most significant and often life-threatening complication. Eruptive xanthomas occur when serum triglyceride level exceeds to 2000 mg/dL

and present as asymptomatic, evanescent, yellowish, grouped papules over the buttocks, shoulders, and extensors of limbs (9).

In our patient, eruptive xanthoma lesions resembled lichen nitidus in their glistening appearance and only faint erythema. However, their evanescent nature, yellowish waxy hue and a few lesions with an erythematous base, typical distribution (lichen nitidus occurs on flexor aspect of arms and wrist, lower abdomen, glans, and shaft of penis) and histopathology ruled lichen nitidus out (10). Another characteristic finding is lipemia retinalis, in which the retinal arterioles and venules become distended and creamy white because of the scattering of light by the large chylomicrons. Secondary complications include diabetes mellitus, steatorrhea, and pancreatic calcification, which develop by middle age (11).

Other manifestations included lower intestinal bleeding, dementia, or depression. Accelerated atherosclerosis and increased risk of coronary artery disease is uncommon. Familial apolipoprotein CII deficiency is a rare autosomal recessive disorder with a generally later age of onset than LPL deficiency but with similar clinical features. The diagnosis of familial LPL deficiency is based on the demonstration of lipemic plasma with elevated chylomicron and triglyceride levels and a reduced to normal VLDL level, and is confirmed by assessment of LPL activity in plasma (12). Familial apolipoprotein CII deficiency shows a raised VLDL level in addition to the derangements as seen in LPL deficiency. Apolipoprotein CII level, as assessed by gel electrophoresis, is also reduced. In our patients, the exact cause of familial hyperchylomicronemia could not be ascertained as LPL assay and apolipoprotein CII estimation were not performed. But after FFP infusion significant drop in TG level from 2040 mg/dl to 400 mg / dl confirmed the diagnosis of apolipoprotein CII deficiency. As yet three patients with this syndrome including one with confirmed LPL deficiency have been reported from India (11-13).

Dietary modification plays a key role in the management of this disease. Dietary fat should be restricted to <20 g/day and <15% of the total caloric intake so that triglyceride levels are maintained below 1500 mg/dL. Medium-chain triglycerides are the preferred source of dietary fat. Avoidance of alcohol, estrogen, and drugs that increase triglyceride levels, supplementation with fat soluble vitamins, antioxidant therapy, plasmapheresis, and surgical management (modified Scopinaro's bilopancreatic diversion) are the various modalities in LPL deficiency. Familial

apolipoprotein CII deficiency is also treated with fat restricted diet and by plasma or synthetic apolipoprotein CII infusion (14).

The complications are due to an increase intake in the amount of fat, which causes recurrent bouts of illness leading to formation of cysts, hemorrhage and death. In the follow-up of these children, lipid levels should be monitored periodically after starting treatment. The family was advised of diet and genetic counselling (7, 10). Literature and case reports on hypertriglyceridemia in pediatric age group are very scarce and there are a few specific treatment guidelines in children. Therefore, here is a need for consensus suggestions on the management of these children. Our patients were put under dietary restriction, with the use of coconut oil as the cooking medium.

Pediatricians should be alerted for the possibility of familial hyperchylomicronemia due to apolipoprotein CII deficiency in such patients, attack of acute pancreatitis that fails to resolve can be treated with infusion of fresh frozen plasma to provide an exogenous source of apolipoprotein CII in an attempt to clear severe hypertriglyceridemia and resolution of the pancreatitis.

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References

1. Sugandhan S, Khandpur S, Sharma VK. Familial chylomicronemia syndrome. *Pediatr Dermatol* 2007; 24: 323-5.
2. Mustafa G, Khan PA, Azam MK, Rabbani W, Ali Q. Hypertriglyceridemia in pediatrics J. *Coll Physicians Surg Pak* 2003; 13: 57-8.
3. Yuan G, Al-Shali KZ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. *CMAJ* 2007; 176: 1113-20.
4. Santamarina-Fojo S, Brewer HB JR. The familial hyperchylomicronemia syndrome. New insights into underlying genetic defects. *JAMA* 1991; 265: 904-8.
5. Brunzell JD. Familial lipoprotein lipase deficiency and other causes of the chylomicronemia syndrome. In: C.R Scriver, A.L Beaudet, W.S Sly, D Valle, Editors: *The metabolic bases of inherited disease*. 7th ed. McGraw-Hill, New York .1995; pp: 1913-32.

6. Kwiterovich PO, Diagnosis and management of familial dyslipoproteinemia in children and adolescents. *Pediatr Clin North Am* 1990; 37: 1489-523.
7. Feoli-Fonseca JC, Levy E, Godard M, Lambert M. Familial lipoprotein lipase deficiency in infancy: clinical, biochemical and molecular study. *J Pediatr* 1998; 133: 417-23.
8. American Academy of Pediatrics: committee on nutrition: indications for cholesterol testing in children. *Pediatrics* 1989; 83: 141-2.
9. Mohandas MK, Jemila J, Ajith Krishnan AS, George TT. Familial chylomicronemia syndrome. *Indian J Pediatr* 2005; 72: 181.
10. Fojo SS. The familial chylomicronemia syndrome. *Endocrinol Metab Clin North Am* 1998; 27: 551-67.
11. Thomas VT, Letha S. Lipemia retinalis. *Indian Pediatr* 2001; 38: 925.
12. Fojo SS, Brewer HB. Hypertriglyceridemia due to genetic defects in lipoprotein lipase and Apolipoprotein C-II. *J Intern Med* 1992; 231: 669-77.
13. Shankar KN, Bava HS, Shetty J, Joshi MK. Lipoprotein lipase deficiency. *J Postgrad Med* 1997; 43: 81-2.
14. Baggio G, Manzato E, Gabelli C, et al. Apolipoprotein C-II deficiency syndrome. Clinical features, lipoprotein characterization, lipase activity, and correction of hypertriglyceridemia after apolipoprotein CII administration in two affected patients. *J Clin Invest* 1986; 77: 520-7.