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Case Report

Primary hypertriglyceridemia in children with familial chylomicronemia syndrome

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Hypertriglyceridemia can be caused by primary (genetic) or secondary etiology. One of the primary causes is hyperlipoproteinemia type I or known as familial chylomicronemia syndrome. Familial chylomicronemia syndrome is a rare autosomal recessive disease that occurs in 1-2 per 1,000,000 people, with specific characteristic signs, namely severe increment of fasting plasma triglyceride up to 100 times the normal value (about 1500-15,000 mg/dL) caused by lipoprotein lipase (LPL) mutation. **[Paediatr Indones. 2024;64:281-6; DOI: 10.14238/pi64.3.2024.281-6**].

Keywords: *chylomicronemia; hypertriglyceridemia; medium-chain triglyceride; low-fat complementary food*

Lipoprotein lipase deficiency causes biochemical changes characterized by severe hypertriglyceridemia with clinical manifestations such as failure to thrive, eruptive xanthomas, hepatosplenomegaly, recurrent pancreatitis, and lipemia retinalis.[1-3] Hypertriglyceridemia treatments aim to prevent complications, such as pancreatitis in severe hypertriglyceridemia, and reduce the risk of cardiovascular diseases. The therapy is classified as non-pharmacological and pharmacological. Non-pharmacological means limiting fat and carbohydrate intake, while pharmacologically means giving medications such as fibrates, nicotinic acid, and omega-three fatty acids. Insulin, heparin, and plasmapheresis can be given in severe conditions.[4]

We observed an 11-month-old girl for 16 months (September 2019-January 2021) diagnosed with hyperlipoproteinemia type I (familial chylomicronemia syndrome) with a high level of serum triglyceride, leading to various complications. The primary outcome was triglyceride levels; secondary outcomes were complications caused by high triglyceride levels, nutritional status, and development due to diet management. Several interventions were given simultaneously, making it difficult to predict the causal relationship between the intervention and the outcome.

The case

An 11-month-old girl came to our clinic with a history of fever and milky blood on laboratory examination with no other symptoms. Laboratory

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examination revealed that triglycerides level was 1745 mg/dL, cholesterol level was 207 mg/dL, and triglyceride: total cholesterol ratio was 8.68 mg/dL (normal value: <5 mg/dL). Physical examination was within normal limits. She was hemodynamically stable, with no dysmorphic features or eruptive xanthoma, the abdomen was soft, not tender, and had no hepatomegaly. Abdominal ultrasound and funduscopic examination were normal.

The family history revealed asymptomatic dyslipidemia in other members (**Figure 1**). Her mother had high cholesterol level (226.1 mg/dL), normal triglyceride (99.7 mg/dL), HDL (27.3 mg/dL), and LDL (87.9 mg/dL). Her father had high triglyceride (179.6 mg/dL), normal cholesterol level (180 mg/dL), low HDL (27.3 mg/dL), and normal LDL (87.9 mg/dL). The child was exclusively breastfed, with the analysis result of breastmilk was a high-fat content of 10.8 g/100 mL (normal value: < 3.3 g/100 mL), thus the breastfeeding was stopped. Genetic analysis was not performed due to the limited financial background of the family. The final diagnosis was FCS based on very high triglyceride levels and significant familial history.

At the beginning of our observation, the child was asymptomatic, so it was essential to do regular monitoring to avoid complications. The variables were analyzed by comparing baseline data with the data after 16 months of follow-up, as shown in **Table 1**.

We treated the patient with fish oil supplementation and diet modification, including temporary discontinuation of breastfeeding, medium-chain triglyceride (MCT) formula, and complimentary low-fat food (<30%). Omega 3 was given after the child was diagnosed and was discontinued after three months because the child's triglyceride level was <300 mg/dL. Otherwise, the low-fat diet was continued until the end of the monitoring Lipid profile examination at the beginning of monitoring was planned to be checked every three months in the first six months and continued every six months, namely December 2019, March 2020, and September 2020. However, in September 2020, the patient did not visit our clinic due to the Covid-19 pandemic, so the examination was continued in January 2021. The results of the patient's triglyceride levels are described in **Figure 2**. At the end of our observation, the triglyceride level was finally decreased to

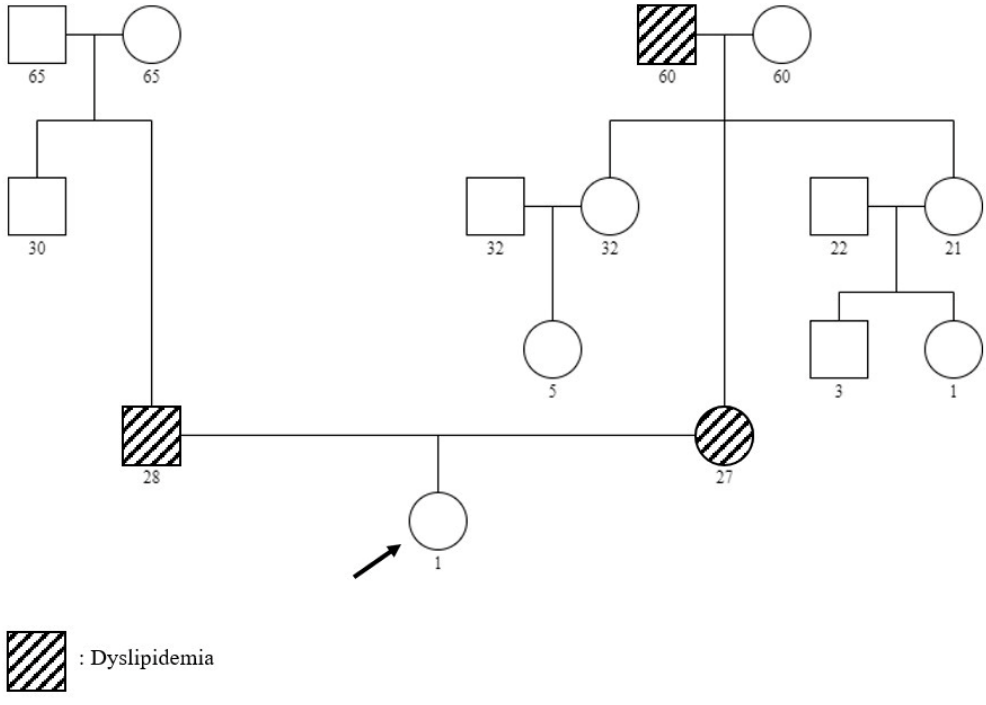

Figure 1. Family Genogram

Table 1. Summary of observation in a patient with type I hyperlipoproteinemia (chylomicronemia)

Measured output	Basic data before intervention and the expected result after intervention	Post-intervention data measured periodically
Lipid profile	September 2019 Total cholesterol: 1745 mg/dL Triglyceride (TG): 398.5 mg/dL HDL: 35.4 mg/dL LDL: 80.7 mg/dL Expected result: TG: <200 mg/dL Cholesterol total: <200 mg/dL LDL <100 mg/dL HDL> 40 mg/dL	January 2021 Total cholesterol: 196.6 mg/dL TG: 186.5 mg/dL HDL: 43.5 mg/dL LDL: 115.8 mg/dL
Lipemia retinalis	No retinal lipemia Expected result: no retinal lipemia by funduscopy	No retinal lipemia was found during 12 months of observation.
Pancreatitis	No symptoms of pancreatitis and abdominal ultrasound was within normal limit Expected result: no pancreatitis found	No signs and symptoms of pancreatitis during 12 months of observation.
Eruptive xanthoma	No eruptive xanthoma was found on physical examination Expected results: no eruptive xanthoma was found	No eruptive xanthoma was found during 12 months of observation.
Nutritional status	October 2019 (1st month) WAZ -0.54 SD (normal weight) HAZ +1.5 SD (normal height) WHZ -1.8 SD (nNormal nutritional status) Expected result: normal nutritional status, normal height	January 2021 WAZ - 0.21 SD (normal weight) HAZ -0.33 SD (normal height) WHZ -0.7 SD (Normal nutritional status)
Development (Denver II)	Normal development Expected result: normal development	January 2021: normal development

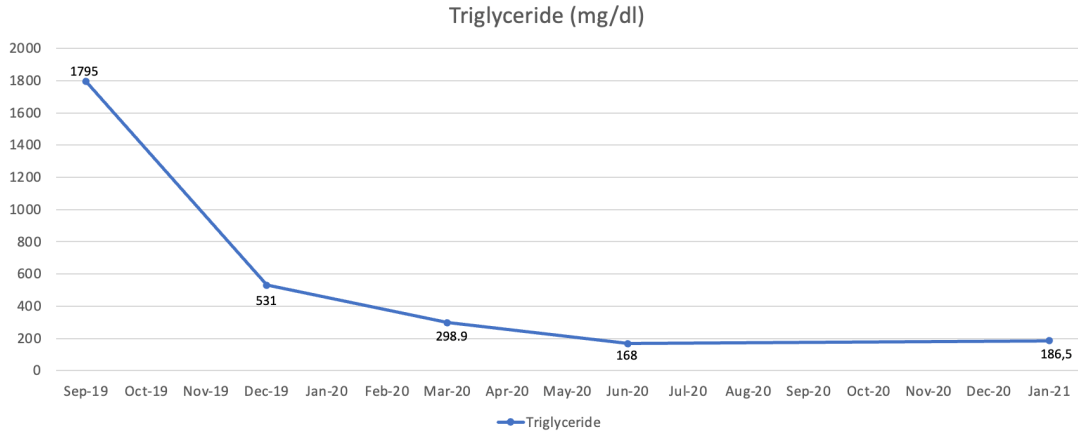

Figure 2. Triglyceride level trends

186.5 mg/dL (previously 1745 mg/dL at the first visit and 398.5 mg/dl at the beginning of observation in January 2020).

Lipemia retinalis is a retinal discoloration disorder due to lipid accumulation assessed by funduscopic examination. Funduscopic monitoring is performed to detect complications in patients with hypertriglyceridemia, namely lipemia retinalis. The examination was carried out at the beginning of the observation, and the result was normal. Evaluation at the 16th month of the intervention showed no retinal lipemia.

At the beginning of our observation, there were no signs of pancreatitis. Ultrasound examination was carried out to monitor signs of pancreatitis at the beginning of the observation and the 6th and 12th months of observation. In the 16th month of intervention, we found no abnormalities due to hypertriglyceridemia, such as hepatosplenomegaly or pancreatitis.

No xanthoma was found at the beginning of our observation. In the end, no xanthoma was found due to the stable triglyceride levels. At the beginning of the observation, the nutritional status was normal, with a weight of 9.0 kg, a height of 82.0 cm, WAZ -0.54 SD, HAZ 1.5 SD, and WHZ -1.8 SD. At the end of our observation, the nutritional status remained normal, with WAZ -0.21 SD, HAZ 0.33 SD, and WHZ -0.7 SD.

Discussion

Familial chylomicronemia syndrome is an autosomal recessive inherited disease resulting in LPL deficiency, Apo C-II lipoprotein deficiency, or other disorders of the LPL pathways.[2] Familial chylomicronemia syndrome is a condition resulting from the accumulation of chylomicrons in the plasma with one of the following manifestations: eruptive xanthoma, lipemia retinalis, abdominal findings of pain, pancreatitis, or hepatosplenomegaly. Other manifestations of this disease include blurred vision, memory disturbances, depression, and dyspnea.[1]

Severe hypertriglyceridemia can cause pink-colored blood, milky white supernatant, false elevated hemoglobin, and pseudohyponatremia.[5] Milky pink viscous blood is one of the characteristics of severe hypertriglyceridemia.[6] The pink color is due to the intermingling of the red blood corpuscles with the opaque white triglycerides containing very-low-density lipoprotein and chylomicrons.[5]

Familial chylomicronemia syndrome was diagnosed based on triglyceride levels above 750 mg/dL (8.5 mmol/L), which may be accompanied by a history of recurrent abdominal pain or pancreatitis and a family history of high plasma triglyceride levels. The diagnosis is confirmed by genetic testing to look for mutations in the gene encoding LPL or mutations in another gene that is essential for LPL to function properly. The most common mutations are at the LPL, apolipoprotein C2 (APOC2), lipase maturation factor 1 (LMF1), apolipoprotein A5 (APOA5), and glycosylphosphatidylinositol-anchored-high-density (HDL)-binding protein 1 (GP1HBP1).[2]

One of the complications in children with hypertriglyceridemia is lipemia retinalis (4-36%).[7] Pancreatitis is one of the complications that cause hospitalization in patients with hypertriglyceridemia and is the most common complication, which is 60-80%.[8] Observation at the 16th month of intervention showed no abnormalities due to hypertriglyceridemia, such as hepatosplenomegaly or pancreatitis. Previous studies stated that pancreatitis might occur when triglyceride levels were >1000-1500 mg/dL, although some cases of pancreatitis could occur at TG levels of 200-1000 mg/dL.[9,10]

Xanthomas associated with hyperlipidemia are thought to occur when serum lipoprotein levels increase and extravasate into the skin's capillaries.[11] Xanthoma manifested as papules around 1-5 mm in reddish-yellow color, mainly on the extensor surfaces of the buttocks and back. It often occurs in triglyceride levels above 1500-2000 mg/dL.[12]

Omega 3 (DHA) reduces serum triglyceride concentrations by several mechanisms, such as suppressing the expression of sterol regulators during lipogenesis, increasing oxidation of fatty acids, thereby reducing triglyceride substrates, and inhibiting triglyceride synthesis enzymes such as phosphatidic acid phosphatase and diacylglycerol acyltransferase which increase the expression of triglycerides. Omega 3 is more effective than bezafibrate to lower triglyceride levels.[8] A meta-analysis about the effect of omega 3 on lipid and lipoprotein levels showed that in 47 studies with 16,511 participants, participants who were given supplements had reduced TG levels by 14% without lowering total cholesterol, LDL, and HDL.[13] The same result was also described in A meta-analysis which is that administering high doses of EPA/DHA of about 3.25 grams per day will significantly reduce plasma TG levels by 15%. It will reduce total cholesterol, LDL, and HDL levels by about 5%, although studies in children were still limited.[14]

Dietary modification plays a key role in the management of this disease. Fat should be restricted to <30% of the total caloric intake to maintain

triglyceride level below 200 mg/dL. Medication was given if the triglyceride level was >300 mg/dL. Nowadays, the key point in treating this disease is to diagnose it early and limit the diet so that good results can be obtained.

Prospective observation and intervention for 12 months were carried out on a 15-month-old female with type I lipoproteinemia (familial hyperchylomicronemia). The intervention given was omega 3 (DHA) for 3 months of observation and a low-fat diet from the beginning until the end of the observation. The outcomes achieved were the decrement of triglyceride levels, although it still had not reached the target (<130 mg/dL). No other complications were found due to elevated triglyceride levels, such as pancreatitis, retinal lipemia, and xanthoma cutis, and the child's nutritional status was good.

Conflict of interest

None declared.

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