

Case Report



A 15 month - old Bangladeshi Baby With Very Severe Hypertriglyceridemia, Secondary to Glycogen Storage Disease

Sharmistha Ghosal ¹, Bodhrun Naher ¹, Morium Alam Noor ¹, Md. Shahidul Islam ¹,
Md Benzamin ², Md. Wahiduzzaman Mojumder ³.

Abstract

Hypertriglyceridemia is increasingly identified in children and adolescents, due to improved screening and higher prevalence of childhood obesity. The etiologic origin can be primary (genetic) or secondary, but it is often multifactorial. Management is challenging because of the interplay of genetic and secondary causes and lack of evidence-based guidelines. In this case report a fifteen month old boy was incidentally found with hypertriglyceridemia while finding the cause of his abdominal distension and was managed with oral and intravenous medications.

Key words: Hypertriglyceridemia, Glycogen storage disease

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Introduction

Hypertriglyceridemia (HTG) means increased triglyceride level in blood which usually remains asymptomatic. Most of times hypertriglyceridemia is diagnosed accidentally during routine screening of lipid profile test. If hypertriglyceridemia is associated with any pathology known as secondary hypertriglyceridemia, or if not associated with any other pathology known as primary hypertriglyceridemia.¹ In this present report we will discuss about hypertriglyceridemia in a 15 months old boy to increase the knowledge of physicians regarding management and follow up of such patients.

Case Summary

Our patient, a 15 months old child, third issue of non- consanguineous parents presented with gradual abdominal distension for last 4 months which was increasing day by day. He had history of recurrent RTI since birth and excessive sweating at night. He had no history of craving for food or early morning irritability, convulsion, jaundice, fever, abdominal pain, vomiting, joint pain, diarrhea, contact with TB patient, history of blood transfusion, bleeding manifestation, polyuria, polydipsia,

taking any offending drugs or sib death. He was breastfed up to 5 months of his age since then cow's milk, rice powder, formula feeding added along with breast feeding. Now he is on family diet. He was developmentally age appropriate. There is no family history of hyperlipidemia or cardiovascular disease. On examination, child was anicteric, mildly pale, vitally normal, skin survey revealed no evidence of coagulopathy or xanthoma, BCG mark present, no bony tenderness or edema, anthropometry revealed moderate underweight (8.5 kg), WLZ is on 5th -10th centile. Abdomen was soft, distended, non-tender abdomen with hepatomegaly (4 cm from right costal margin) and splenomegaly (8 cm along its long axis from left costal margin), ascites absent. Other systemic examinations revealed normal findings. We provisionally thought of TORCH infection, hemolytic anemia, portal hypertension, Glycogen storage disease (GSD). Investigations were sent and reports were listed on Table-1. During sample collection lipemic serum was found (Figure 1) that made us suspicious about having familial chylomicronemia and fasting lipid profile of both parents were sent which revealed normal.

1. Phase B, Resident, Department of Pediatric Gastroenterology & Nutrition, BSMMU, Dhaka, Bangladesh.
2. Registrar, Pediatric Gastroenterology & Nutrition, Sylhet M A G Osmani Medical College and Hospital, Sylhet, Bangladesh.
3. Associate Professor, Department of Pediatric Gastroenterology & Nutrition, BSMMU, Dhaka, Bangladesh.

Correspondence: Dr. Sharmistha Ghosal, Resident Phase B, Department of Pediatric Gastroenterology & Nutrition, BSMMU, Dhaka, Bangladesh. Email: sharmistha58@gmail.com , Cell Phone: 01716868645



Fig: Picture of the Patient



Figure - 1

Among all the reports marked abnormality was found on Triglyceride (TG) report which was 2705mg/dl. As patient has no jaundice or any feature of coagulopathy we started treatment of very severe HTG (>2000mg/dl) by keeping the child NPO with 10% Baby saline with Inj. Insulin with 0.1 unit/kg over 72 hours and monitored serum TG level after 3 days. There was dramatic response as it lowered to 396 mg/dl. Then we allowed oral feeding with low fat milk along with breast feeding and Gemfibrozil and Omega-3 fatty acid were added.

Table 1: Investigation reports

Name of Investigations	Patient	Normal value
Before treatment		
1. CBC	Hb-13.6 g/dl TC - 28,000/ mm ³ N-17%, L - 80% Platelet - 5,69,9000/mm ³	
2. Hb electrophoresis	Normal	
3. ALT	10 U/L	10-49U/L
4. Uric acid	2.7mg/dl	3.7 - 9.2mg/dl
5. FBS	8.4mg/dl	3.5- 6 mg/dl
6. Anti CMV IgM and IgG	Positive	
7. Liver biopsy	The hepatocytes are swollen and showed PAS positive glycogen granules within cytoplasm, portal area showed mild fibrosis	
8. Bone marrow study	Normal (No foam cell was found)	
9. USG of abdomen	Mild hepatosplenomegaly Kidney size normal	

But after 3 days, there was sharp rise of TG to 1210 mg/dl then we did TG every 3 days and it was in increasing trend 1242 mg/dl, 1280 mg/dl, 1564 mg/dl consecutively. Then Nicotinic acid and Ezetimib were added (4 days apart). During this journey the secondary causes of HTG were excluded. Liver biopsy which revealed Glycogen storage disease (GSD) and on TORCH panel –Anti CMV IgM and IgG were positive. The patient’s guardian was counseled regarding disease pathophysiology, its available treatment and the complications and dietary advice with low fat diet, MCT based oil, uncooked cornstarch 2-3 hourly specially at night to maintain euglycemic status and subsequently decrease dyslipidemia. Tab. Valgancyclovir was also started for CMV infection.

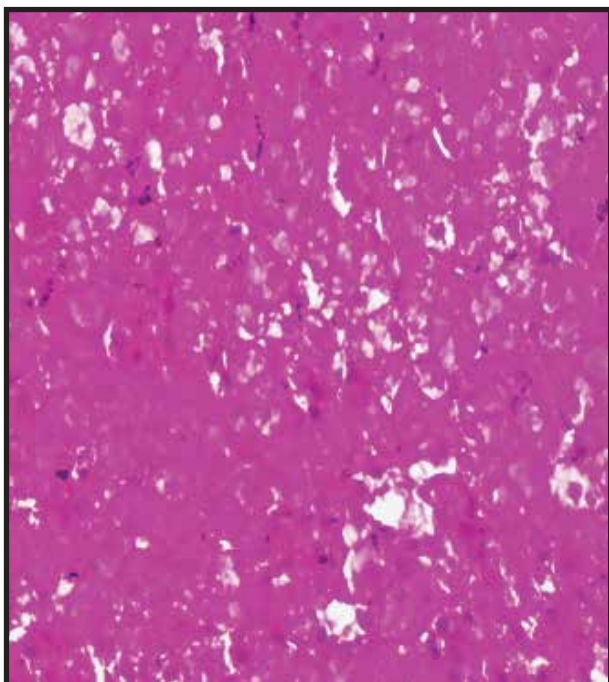


Fig 2: PAS positive liver tissue

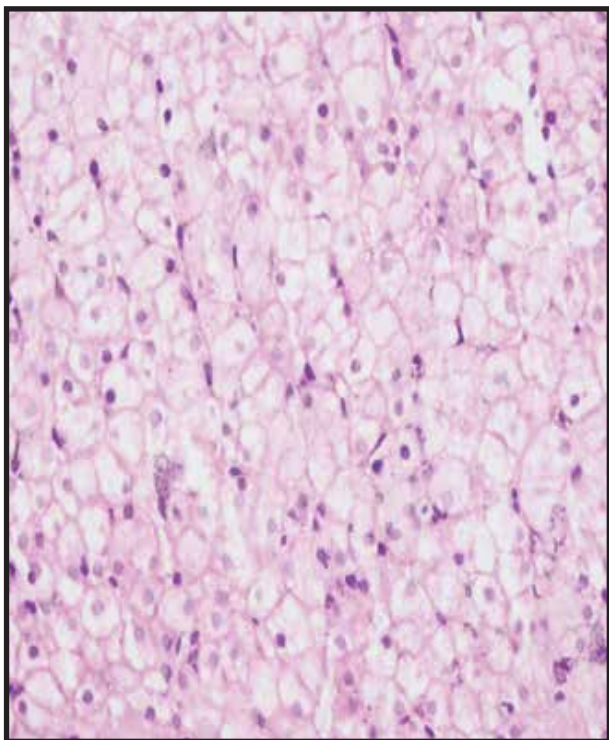


Fig 3: Diastase sensitive liver tissue

The patient was discharged with advising them to come after 1 month with fasting lipid profile and it showed the TG level is below 500mg/dl which will prevent the risk of pancreatitis. Patient party was advised to come according to follow up schedule.

Discussion

The term hypertriglyceridemia indicates an increased plasma fasting triglyceride (TG) concentration that is above the 95th percentile for age and sex.^{2,3} A TG level greater than or equal to 100 mg/dL (1.13 mmol/L) and a level greater than or equal to 130 mg/dL (1.47 mmol/L) are considered above the 95th percentile for children of ages 0 to 9 years and 10 to 19 years, respectively.^{4,6} An estimated 10% of US children and adolescents between 12 and 19 years of age have increased serum TG levels greater than 150 mg/dL (1.69 mmol/L).^{4,7,8} By extrapolating the adult guidelines, hypertriglyceridemia can be considered mild to borderline high (150–199 mg/dL), moderate to high (200–499 mg/dL), very high (500–999 mg/dL), severe (1000–1999 mg/dL), and very severe (>2,000 mg/dL).⁶⁻⁸ Hypertriglyceridemia in children parallels the increasing incidence in childhood obesity, metabolic syndrome, type 2 diabetes, sedentary lifestyle, high-fat and high-carbohydrate diet, and medication use.⁹ With increased universal lipid screening, the number of cases of hypertriglyceridemia identified will increase.

The prevalence of hypertriglyceridemia (HyperTG) defined as triglyceride (TG) concentration >150 mg/dL is estimated to be 10.7% among US children and adolescents aged 12 to 19 years.^{10,11} Secondary causes of high TG due to obesity and type II diabetes account for most cases of Hyper TG in children and adolescents.¹¹ TG concentration of >500 mg/dL is rare (0.2%) but when encountered prompt consideration of a defect in primary TG metabolism should be done. Severe hyper-TG in childhood is encountered in association with rare inherited disorders (for example GSD), which require treatment strategies based on their metabolic defect and predicted consequences. Hepatic GSD present as significant pediatric challenges because it's onset is at early age.^{12,13} Our patient was diagnosed as glycogen storage disease and we managed with oral anti lipid drug.

Type I GSD, caused by a recessively inherited defect in glucose-6-phosphatase, accounts for more than 60% of the GSD types involving the liver and results in the most excessive VLDL production. It presents during the first year of life with severe hypoglycemia and hepatomegaly caused by the accumulation of hepatic glycogen.¹³ Due to metabolic consequences of excessive anaerobic glycolysis and impaired glucose formation lead to lactic acidemia, hyperuricemia, and dyslipidemia. Our patient did not develop hyperuricemia yet. Impaired growth factor production and acidosis result in poor growth and delayed puberty. Treatment involves continuous complex carbohydrate feeding regimens prescribed as frequent meals and supplementation with corn-starch to reduce counter-hormonal stimulation of substrate supply for TG synthesis¹⁴ and needed to achieve blood glucose levels continuously above 75 mg/dL, especially at night.¹² This approach involves high carbohydrate intakes, which in the long-term may increase VLDL production resulting in requirement for lipid-lowering medications.¹³ Parents were counseled regarding the feeding management with corn starch accordingly.

Pharmacologic management is sometimes needed in primary HyperTG to prevent pancreatitis and/or reduce risk of CVD.

But There is a paucity of literature on pediatric hypertriglyceridemia and its management plan or any guidelines. Christian et al., described the use of dyslipidemic agents in children.¹¹

Very high levels that would increase the risk of pancreatitis is treated with a drug from the fibrate class. Fibrates can markedly lower triglyceride levels (40 to 60 %) and modestly raise HDL-C levels (15 to 25%).¹⁵ Niacin and omega-3 fatty acids as well as drugs from the statin class may be used in conjunction, with statins being the main drug treatment for moderate hypertriglyceridemia where reduction of cardiovascular risk is required.¹⁶ To prevent long term cardiovascular complication both Nicotinic acid and Omega 3 fatty acid were added. Niacin lowers triglyceride levels by 30 to 50 percent, raises HDL-C levels by 20 to 30 percent, and lowers LDL-C levels by 5 to 25 percent.^{15,17} Niacin is not as potent as fibrates for lowering triglyceride levels but is more effective at raising HDL-C levels. The use of niacin is limited because of the risk of vasomotor side effects and elevation of liver enzyme levels.¹⁷ Patients with high triglyceride levels (above 500 mg/dl) usually require drug therapy in addition to therapeutic lifestyle changes. Fibrates or niacin is a practical first-line drugs for these patients.¹⁸ These medications are helpful in preventing complications like acute pancreatitis, xanthomas, renal failure etc. Now the question is should we continue such treatment for lifetime? or should we stop that treatment? If we decided to stop that treatment the triglycerides level will increase & patient may suffer subsequent complications. Vice versa, if we continue such treatment, then the patient may suffer from drug complications. However we planned to continue his drug treatment.

Conclusion

Paediatricians should keep in mind that patients of this type of presentation (Hepatosplenomegaly) may have hypertriglyceridemia which needs immediate intervention to prevent catastrophe of pancreatitis. Paediatricians should also consider the risk-benefit ratio of dislipidemic drugs and exclude the secondary etiologies of hypertriglyceridemia and follow up these type of patients.

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