A CASE OF HYPERTRIGLYCERIDAEMIA (?TRANSIENT INFANTILE HYPERTRIGLYCERIDAEMIA) WITH ASSOCIATED HYPERGLYCINÆA AND CARNITINE DEFICIENCY

Prasad Torkadi, AK Bhute, UP Dhavale
Department of Biochemistry, Dr. PDM Medical College, Amravati, Maharashtra, India

Correspondence to: Prasad Torkadi (drptorkadi@gmail.com)

DOI: 10.5455/ijmsph.2013.170720131
Received Date: 21.06.2013
Accepted Date: 17.07.2013

ABSTRACT
Hypertriglyceridaemia is an emerging risk factor for atherosclerosis, coronary heart disease and pancreatitis in the developing countries like India. It can be familial or acquired. Hypertriglyceridaemia associated with hyperglycinæa and carnitine deficiency is rarely seen. We report a case of 3 months old infant with low birth weight admitted for failure to thrive and lower respiratory tract infection. He was screened for hypertriglyceridaemia and inborn error of metabolism. Serum was lipemic with triglyceride level -1236 mg%, Cholesterol-220 mg%, Amino acid Glycine (789 umol/L) was elevated, Fatty acids like Acetlylcarnitine (4.16 umol/L), Octadecanoyl carnitine (0.16 umol/L) were found to be decreased. There is no family history of hyperlipidaemia or consanguineous marriage. History, clinical examination and blood reports points towards transient infantile hypertriglyceridaemia. Reasons for high glycine level and carnitine deficiency could not be established. Further investigations like mass spectrometry and mutational screening for genetic defects are necessary for confirmatory diagnosis. Meanwhile infant was treated with lipid lowering agents, medium chain fatty acids and carnitine supplements.

Key-Words: Pancreatitits; Hypertriglyceridaemia; Hyperglycinæa; Lipemic; Spectrometry

Introduction
Hypertriglyceridaemia is an emerging risk factor for atherosclerosis, coronary heart disease and pancreatitis in the developing countries like India. It can be familial or acquired. The two main sources of plasma triglycerides (TG) are exogenous TG, absorbed in the gut and transported into the plasma as chylomicrons, and endogenous TG, synthesized in the liver and secreted as part of very-low-density lipoprotein (VLDL) particles. Elevated TG levels may represent primary hereditary disorders or be secondary to other conditions, particularly obesity and type 2 diabetes mellitus. Glycine is the simplest amino acid catabolised via glycine cleavage system. Increase in blood glycine level due to defective glycine cleavage system can lead to neurological manifestations. Carnitine is useful in fatty acid oxidation. So deficiency of carnitine leads to defective fatty acid oxidation, hypoglycemia etc.

Hypertriglyceridaemia associated with hyperglycinæa and carnitine deficiency has not been reported yet since it is rare to find. We report a case of transient infantile hypertriglyceridaemia with associated hyperglycinæa and carnitine deficiency.

Case Report
A 3 months old male infant admitted in paediatric ward with history of refusal to feed, fever and cough since 3days. Antenatal history was uneventful. It was a full term baby delivered by caesarean section. Developmental history was normal and the baby was immunized till date. There was no history of consanguineous marriage in parents. Family history of hyperlipidaemia was not significant.

On examination the baby was febrile, dysneic and pale. No xanthomas or lipemia retinalis were seen. Liver and spleen was not palpable. Bilateral crepits and wheezing were present on chest auscultation. Blood investigation reports: Hb-8.8gm%, TLC,DLC, ESR- normal, Random plasma glucose-80 mg%, Serum electrolytes- normal, ABG analysis on admission- Day 1: pH -7.18, pCO₂-116.3, pO₂-14.1; Day 4: pH -7.25, pCO₂-24.4, pO₂-102; Day 6: pH-7.28, pCO₂- 20.5, pO₂-76
A provisional diagnosis of Bronchiolitis with respiratory acidosis was made. Since the blood sample was lipaemic, the baby was screened for hyperlipidaemia.

Lipid Profile (mg%): Triglycerides-1236 (<170), Cholesterol-220 (<200), HDL-27 (35-50), LDL-102 (<130), VLDL subfraction elevated (by lipoprotein electrophoresis).

Simultaneously patient was also screened for inborn errors of metabolism (IEM). Glycine-789 (normal <505 µmol/L), levels of other amino acids like Alanine, Arginine, Citrulline, Leucine, Methionine, Ornithine, Phenylalanine, Tyrosine & Valine were normal. Acetylcarnitine-4.16 (normal 8-150 µmol/L), Octadecanoyl carnitine-0.16 (normal 0.6-3.5 µmol/L), Propionyl carnitine, Butyryl carnitine, Isovaleryl carnitine, Glutaryl carnitine were normal.

From the history, examination and investigations we diagnosed it as a case of an Inborn Error of Metabolism i.e. Transient infantile hypertriglyceridemia with associated hyperglycinemia and secondary carnitine deficiency. The patient was treated with antipyretics, antibiotics, IV fluids, nebulisation and blood transfusion, tablet Atorvastatin 10 mg half OD and Carnitine 75 mg/kg/day in divided doses. The parents were advised to bring the child for follow up after one month. But the parents did not come as the baby might have recovered from acute illness. Another reason may be that they were from remote place.

**Discussion**

The two main sources of plasma triglycerides (TG) are exogenous TG, absorbed in the gut and transported into the plasma as chylomicrons, and endogenous TG, synthesized in the liver and secreted as part of very-low-density lipoprotein (VLDL) particles.[1]

Elevated TG levels may represent primary hereditary disorders[2] or be secondary to other conditions, particularly obesity and type 2 diabetes mellitus.[3]

Several studies indicate that hypertriglyceridemia is an independent risk factor for coronary artery disease.[4] Extreme hypertriglyceridemia is also associated with an increased risk of acute pancreatitis.[5]

**Transient Infantile Hypertriglyceridemia:** One of the reason of hypertriglyceridemia can be a partial genetic deficiency in lipoprotein lipase.[6] Another reason may be mutation in GPD1 (glycerol-3-phosphate dehydrogenase) causing severe but transient hypertriglyceridemia, possibly by limiting the conversion of G3P to DHAP, and thus causing an increase in the amount of hepatic G3P available for TG synthesis.[7] On investigation fasting hypertriglyceridemia and mild elevation in cholesterol is seen. Transaminases are elevated but bilirubin and synthetic liver function (coagulation studies and albumin) remains normal. The condition is self-resolving in first few years of life.

From the above discussion we felt that the probable diagnosis of the child in our case would be Familial Hypertriglyceridemia (FTG) or Transient Infantile Hypertriglyceridemia. We are more inclined towards Transient Infantile Hypertriglyceridemia as this is expressed in infancy, compared to Familial Hypertriglyceridemia which has similar presentation but is expressed in late childhood or puberty. Moreover FTG is associated with obesity, hyperglycaemia, high insulin levels and a family history of hyperlipidaemia, which are not found in our case.

Nonketotic hyperglycinemia (NKH) is an autosomal recessive disorder caused by a deficient glycine cleavage system, and generally results in elevated glycine levels in urine, blood, and cerebrospinal fluid (CSF).[8] Infants with NKH are usually symptomatic within the first 48 hours, and after initial myoclonic or generalized seizure, rapid progression to coma occurs, often with apnoea. Most patients die during the neonatal period, despite intensive care.[9] Clinical trials with sodium benzoate, ketamine and dextromethorphan, have been tried but the outcome is usually poor.[9]

The child in our case presented with refusal to feed, fever and cough instead of typical features of NKH. It may be because the blood glycine level
was only mildly elevated. Hence it could not be labelled as a classic case of non-ketotic hyperglycinaemia. However the levels of different enzymes in glycine cleavage system may explain the rise in blood glycine.

Carnitine (3-hydroxy-4-trimethylaminobutyric acid) plays an essential role in the transfer of long-chain fatty acids into the mitochondria for beta-oxidation. Carnitine binds acyl residues and helps in their elimination. Biologic effects of low carnitine levels may not be clinically significant until they reach less than 10-20% of normal. Approximately half of the patients of Primary Carnitine Deficiency present around the age of 2 years (range: 3 months - 2.5 years) with metabolic decompensation characterized by episodes of hypoketotic hypoglycemia, hyperammonemia and hepatic encephalopathy (poor feeding, irritability, lethargy), triggered by fasting or common illnesses such as upper respiratory tract infections.[10]

In neonates, carnitine palmitoyltransferase deficiency is diagnosed in blood using mass spectrometry. In adults, the definitive diagnosis is based on acylcarnitine levels in serum, urine, and tissues (muscle and liver). Carnitine deficiency is treated by avoidance of fasting and strenuous exercise, l-carnitine 25 mg/kg orally six hourly, supplementation with medium-chain triglycerides and essential fatty acids (e.g., linoleic acid, linolenic acid). Patients with a fatty acid oxidation disorder require a high-carbohydrate, low-fat diet. A significant fall in acyl carnitine level (<10%-20%) manifests with above mentioned features. But minimal decrease in blood acyl carnitine levels in our case led to milder clinical presentation. This condition might be a result of secondary carnitine deficiency owing to defect in Carnitine Acyl Transferase-I, II or translocase enzyme, instead of primary carnitine deficiency which presents with severe form.

From the history, investigations and clinical presentation the infant can be said to be a case of inborn errors of metabolism of lipoproteins, glycine and carnitine. Further investigations like mutational screening, mass spectrometry, glycine breath test are advised which can help to diagnose this condition with certainty.

**Conclusion**

This case demands the attention of clinicians towards early diagnosis of hypertriglyceridaemia and related consequences like coronary artery disease and pancreatitis in an infant with lipemic sample. It also emphasizes the importance of early screening for inborn errors of metabolism in neonates by raising high degree of suspicion in clinicians.

**References**


**Cite this article as:** Torkadi PP, Bhute AK, Dhavale UP. A case of hypertriglyceridaemia (transient infantile hypertriglyceridaemia) with associated hyperglycemia and carnitine deficiency. Int J Med Sci Public Health 2013; 2:1120-1122.

**Source of Support:** Nil

**Conflict of interest:** None declared