

Case Report

Successful Management of Severe Hypertriglyceridemia in a Neonate with Apolipoprotein A Deficiency: A Case Report with Literature Review

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Abstract**Introduction**

Reports regarding severe neonatal hypertriglyceridemia are scarce, and there is no consensus regarding its management. This report describes the successful management of a neonatal case of hypertriglyceridemia managed successfully.

Case presentation

A 2-day-old male neonate born to consanguineous parents presented with yellow skin discoloration. The mother had moderate hypertriglyceridemia. While testing for jaundice, the neonate's blood was noticed to be milky. Blood lipid profile test showed highly elevated triglyceride (1,000-10,000 mg/dl), very-low-density lipoprotein level (1,800 mg/dl), and low-density lipoprotein (206 mg/dl) levels, and a low level of high-density lipoprotein (12 mg/dl). Further laboratory diagnosis revealed apolipoprotein A1 deficiency (39 mg/dl). The patient was put on a statin tablet of 0.25 mg twice daily and a formula diet (Monogen – Nutricia) low in triglycerides and rich in medium-chain triglycerides, and was given 1 ml Omega-3 syrup twice daily. After a dramatic decline in serum level, he was put on a 50% medium-chain-triglyceride formula and Gemfibrozil triglyceride-lowering agent.

Conclusion

Early diagnosis of severe hypertriglyceridemia in the neonatal period aids in the early initiation of treatment and prevention of severe complications. Conservative treatment via dietary modifications and supplementation can be associated with satisfactory outcomes.

1. Introduction

Severe hypertriglyceridemia (HTG) is defined as the elevation of serum triglyceride (TG) level to above 1,000 mg/dl in a fasting state (also referred to as chylomicronemia due to plasma accumulation of chylomicrons) [1]. However, according to some

authors, a level of more than 885 mg/dl, or even 500 mg/dl, can also be considered severe HTG [2,3]. Generally, there are two primary sources of serum TGs in the body; an endogenous source; in which TGs are produced in the liver and secreted as part of very-low-density lipoprotein molecules, and an

exogenous source; TGs are absorbed from diet in the gut and circulate as chylomicrons [4].

Severe HTG is considered an endocrine emergency and is one of the leading causes of acute pancreatitis (AP) and an independent risk factor for cardiovascular diseases [5]. Its occurrence in the first decade of life may indicate hereditary disorders, with a genetic basis of the illness only being found in less than 5% of the reported cases [4]. In the neonatal period, severe HTG is very rarely reported in the literature [2,6-11].

The diagnosis of severe neonatal HTG is quite challenging and is usually only made due to the onset of AP. Early diagnosis of the condition is crucial to prevent related complications, including pancreatic necrosis, AP and cardiovascular complications, especially when serum TG exceeds 2,000 mg/dl [2,12]. Usually, HTG in infants and neonates is monogenic and results from defects in genes involved in triglyceride metabolism [2]. There is currently no consensus on the management of severe HTG in the neonatal age group [9].

The present study describes the successful management of severe HTG in a 2-day-old neonate with apolipoprotein A deficiency using a formula diet with low TGs and rich in medium-chain TGs (MCT) and Omega-3 fatty acids (ω -3 FAs).

2. Case Presentation

2.1. Patient information and Clinical findings

A 2-day-old male neonate born to consanguineous parents presented with yellow skin discoloration. The mother had moderate hypertriglyceridemia. No other siblings had a history of any chronic diseases. There were no significant findings on general inspection.

2.2. Diagnostic assessment

The vital signs were within the normal range. Cardiac and chest examinations were also normal. While testing for jaundice, it was found that the yellow skin discoloration was from neonatal jaundice, which needed no treatment apart from follow-up. However, upon blood draw, his blood was noticed to be milky; hence, a blood lipid profile test was performed, which showed highly elevated triglyceride levels in multiple checkups (1,000-10,000 mg/dl), high very-low-density lipoprotein level (1,800 mg/dl), high level of low-density lipoprotein (206 mg/dl), and a low level of high-density lipoprotein (12 mg/dl). Further laboratory diagnosis revealed apolipoprotein A1 deficiency (39 mg/dl) and a normal level of apolipoprotein B (92 mg/dl).

2.3. Therapeutic intervention

The patient was kept under close monitoring. He was put on a statin tablet of 0.25 mg twice daily, and a formula diet (Monogen – Nutricia) with low triglycerides and rich in medium-chain triglycerides (MCT), and was given 1 ml Omega-3 syrup twice daily. After this, a dramatic response was noted as serum triglyceride dropped to 175 mg/dl. The patient was then put on a 50% MCT formula and Gemfibrozil (a triglyceride-lowering agent).

2.4. Follow-up

No symptoms were observed in the first two months of his life, apart from an upper respiratory tract flu-like illness. On a 9-month follow-up, the patient was normally thriving and had good feeding and typical developmental milestones.

3. Discussion

The initial presentation of severe neonatal HTG is often sudden in onset and unexpected, with recurrent attacks of AP [9]. An accidental diagnosis is uncommonly reported in the neonatal period, especially when TG levels are excessively high [11]. The current study presents an incidental finding of severe HTG in a 2-day-old male neonate with apolipoprotein A deficiency and describes the strategy used to treat the case.

In the pediatric population, HTG can be either monogenic, which is due to defects in a single gene that is involved in TG metabolism, or polygenic, which is an interplay between environmental, hormonal, and genetic factors, including metabolic syndrome, uncontrolled diabetes, obesity and medications [1]. In families with a high degree of consanguinity, novel genetic conditions can often occur due to the high probability of identical-by-descent disease-causing mutations because of the inheritance from a common ancestor [4].

Familial HTG is a rare version of the disease, with an estimated prevalence of nearly one per million [12]. However, it is probably more prevalent among populations with high consanguinity rates [9]. The condition occurs as a result of a genetic defect in the catabolic pathway of TG-rich lipoproteins, such as mutations in at least one of the genes encoding for these proteins; lipoprotein lipase (LPL), apolipoprotein CII (APOC2; the activator of LPL), apolipoprotein AV (APOAV; another LPL activator), glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (GPIHBP1; allows LPL interaction with TG-rich lipoproteins, APOAV, and APOC2), and lipase maturation factor 1 (LMF1; a tissue factor that allows the secretion of functional hepatic lipase and LPL) [7]. Among these, mutations in the LPL gene contribute to most of the genetic etiologic factors (95%) of severe familial HTG cases [12]. In a screening of the literature, El-koofy et al., reported that 45/62 (73%) of infantile/neonatal HTG cases were due to defects in the LPL gene, followed by the GPIHBP1 gene (10/62, 16%) [9]. The current study is limited by the fact that no genetic diagnosis has been carried out to determine the presence and type of a highly possible genetic defect in the patient, especially when the case was born to consanguineous parents.

In neonates, infants and very young children (<1 year), HTG can often be asymptomatic and pass undiagnosed until late childhood or even adulthood based on the phenotype's severity [9]. An incidental finding has been rarely made in neonates. All the reported studies of neonatal HTG, including this one, have reported an accidental diagnosis of the condition due to the observation of pink-colored or milky blood upon blood draw for routine laboratory testing, usually done due to the presence of clinical presentations not related to HTG [2,6-11]. This is crucial as it allows early initiation of a treatment plan and reduces the

possibility of complications associated with the condition [1]. When the disease manifests, it can include eruptive xanthomas, hepatosplenomegaly, failure to thrive, lipemia retinalis, episodes of AP and recurrent abdominal pain [11]. Pyrexia and respiratory distress were also reported in a 28-day-old male case by Bhatia et al. [2].

Decreasing serum TG levels in a relatively short period is somewhat difficult. In adult patients with HTG, plasmapheresis is reported to be effective in reducing TG levels and preventing life-threatening complications, particularly AP. However, being an extracorporeal approach, its use raises great concern in the pediatric age group, particularly the fear of adverse hemorrhagic events and hemodynamic effects related to the procedure [11]. The management of severe neonatal HTG with a genetic background is especially challenging due to the lack of an established guideline and is often a long-term persistent effort [1,9]. Despite this, multiple management approaches have been reported in the literature, represented by only a few cases [9]. Exchange blood transfusion has been considered a safer strategy to decrease serum TG levels in children than plasmapheresis [5,11]. In very young infants, plasma filtration has been preferred over plasma exchange since it needs a lower volume of extracorporeal circulation; however, it appears to be less effective in severe HTG, as due to the high molecular weight and large size of chylomicrons, they remain trapped in the plasma filter [13]. Lipid-lowering agents alone may not be particularly effective in cases of severe neonatal HTG [5].

A more conservative strategy has also been used in multiple case reports to treat severe neonatal HTG, such as using a dietary formula high in MCTs, ceasing breastfeeding, and restricting the consumption of other dietary fats after weaning to reduce chylomicron formation [1,9]. This strategy is sometimes used in conjunction with insulin therapy; however, it is inefficient for achieving a rapid decline in TG levels, and the risk of severe blood sugar depletion may outweigh the benefits in neonates [1,9]. In infants and neonates, a formula diet high in MCTs, which does not need pancreatic lipase and bile acids for absorption, can supply dietary calories without being transformed into chylomicrons. In the intestinal mucosa, MCTs are catabolized to MCT fatty acids that circulate via the portal vein and travel to the liver. However, compliance with a low-fat diet will be harder to attain as the child grows, especially in school-age children [1]. The use of MCTs in combination with other strategies for managing severe neonatal HTG has been reported in all the available case studies in the literature, including the current one [2,6-11].

Although some reports have used ω -3 FAs alongside dietary modifications to treat severe HTG, as they are known to exert positive effects on serum TG levels and can be safely used in combination with other medications, to date, no clinical trial has been conducted regarding the effectiveness of Omega-3 for the management of severe HTG in patients of the neonatal or infant age groups. It is not yet fully understood how Omega-3 helps to lower TG levels. It is postulated that it is able to disrupt TG synthesis by either reducing the activity of the enzymes involved in TG synthesis, decreasing substrate availability, or amplifying the synthesis of phospholipids [14].

4. Conclusion

The current study demonstrated the successful management of severe neonatal HTG via dietary fat restriction, a formula diet low in TGs and high in MCTs, and the administration of ω -3 FAs in a newborn with apolipoprotein A deficiency.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Patient consent (participation and publication): Consent has been obtained from the parents, and the parent gave consent for the publication of the report.

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