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CASE REPORT

CLINICAL CASE SERIES

Congenital Hyperlipidemia in Infants for Congenital Cardiac Surgery

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ABSTRACT

Infants with concurrent severe hypertriglyceridemia and complex congenital heart disease are a rare occurrence and can have life-threatening consequences when undergoing surgical intervention. This case series outlines two instances involving infants undergoing total anomalous pulmonary venous connection repair and surgical closure of a ventricular septal defect. The study explores troubleshooting the effects of hypertriglyceridemia on perioperative outcomes. (J Am Coll Cardiol Case Rep 2024;29:102368) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Hypertriglyceridemia, whether primary or secondary, is a rare familial genetic disorder in infants. Classified by Fredrickson in 1967, elevated lipoproteins manifest in 5 types, each requiring distinct management approaches.[1] Elevated hypertriglycerides can be life-threatening, potentially leading to acute pancreatitis. Limited data exist on hypertriglyceridemia in infants, particularly in the context of congenital cardiac surgery. This article explores hypertriglyceridemia, emphasizing its impact during cardiopulmonary bypass (CPB) in cardiac surgery and perioperative management, aiming to share crucial insights.

LEARNING OBJECTIVES

- To recognize the unique challenges and potential complications of severe hypertriglyceridemia in infants with congenital heart disease undergoing cardiac surgery on cardiopulmonary bypass.
- To understand essential perioperative strategies, including monitoring and surgical techniques to manage hypertriglyceridemia in this rare patient population, emphasizing the need for comprehensive care and early troubleshooting.

PATIENT 1

A 4-month-old infant (3.8 kg) presented with a cough, respiratory distress, and a recent respiratory tract infection. An abdominal examination revealed a soft abdomen with no organomegaly, room air SPo_2 80%. Chest X-ray showed cardiomegaly. Echocardiography revealed total anomalous pulmonary venous drainage of the coronary sinus type, restrictive atrial septal defect, severe pulmonary arterial hypertension

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ABBREVIATIONS AND ACRONYMS

ACT = activated clotting time

CPB = cardiopulmonary bypass

MCT = medium chain triglyceride

PAH = pulmonary arterial hypertension

VSD = ventricular septal defect

(PAH), and severe right ventricular dysfunction. Emergency surgical intervention was planned. During a routine surgical profile, preoperative milky serum (Figure 1) prompted lipid profiling, which showed elevated serum triglycerides 4,520 mg/dL (reference <150 mg/dL) and cholesterol 1,030 mg/dL (reference <170 mg/dL). High-density lipoprotein, low-density lipoprotein, and very-low-density lipoprotein were unmeasurable because of the high lipemic status. No family history of elevated lipid levels was available. Enzyme analysis and genetic testing were planned for further evaluation.

The decision was made to proceed with an emergency total anomalous pulmonary venous connection repair. An additional CPB pump was held in reserve as a precaution. Isolyte-p at 2 mL/kg/h was administered to pre-empt fasting-induced crises. Anesthesia induction included ketamine, fentanyl, and rocuronium, followed by maintenance with sevoflurane, dexmedetomidine, O_2, and air. Comprehensive monitoring included routine cardiac invasive monitoring, urine output assessment, temperature monitoring, near-infrared spectroscopy for cerebral perfusion, and pre- and post-membrane pressure monitoring on CPB. Temperature was meticulously lowered to 32 °C. Activated clotting time (ACT) during CPB was maintained for more than 480 seconds with heparin 4 mg/kg. Approximately 30 minutes into the procedure, a milky white sediment was observed over the recirculation cannula (Figure 2). Concurrently, post-membrane pressure rose from 20 to 45, with PO_2 remaining stable. Total anomalous pulmonary venous connection repair was executed with a brief clamp time (70 minutes) and a short CPB duration (115 minutes). Modified ultrafiltration included infusion of compatible fresh frozen plasma from the patient's side to have an advantage of partial exchange transfusion for elevated triglycerides. Upon cessation of CPB, support was initiated with adrenaline at 0.05 μg/kg/min and milrinone at 0.7 μg/kg/min, before the patient was transferred to the post-operative intensive care unit.

During the procedure, a milky precipitate was noted on the oxygenator, and postoperatively, upon dissecting the reservoir, a clot was discovered. The infant experienced hemolysis with reduced urine output, effectively managed with peritoneal dialysis and adequate measures. Within 4 to 6 hours, urine output improved, and discoloration of urine decreased. On the third day, the child exhibited features of encephalopathy, with restless limb movements and suspected seizure activity without any focal neurologic deficits. Decreased cerebral perfusion, attributed to the high lipemic status of blood during CPB in the intraoperative period, was initially suspected. A bedside neurosonogram revealed nothing significant. The child's sensorium levels were regularly monitored. Levitracetam (20 mg/kg/day)

FIGURE 1 Milky Serum

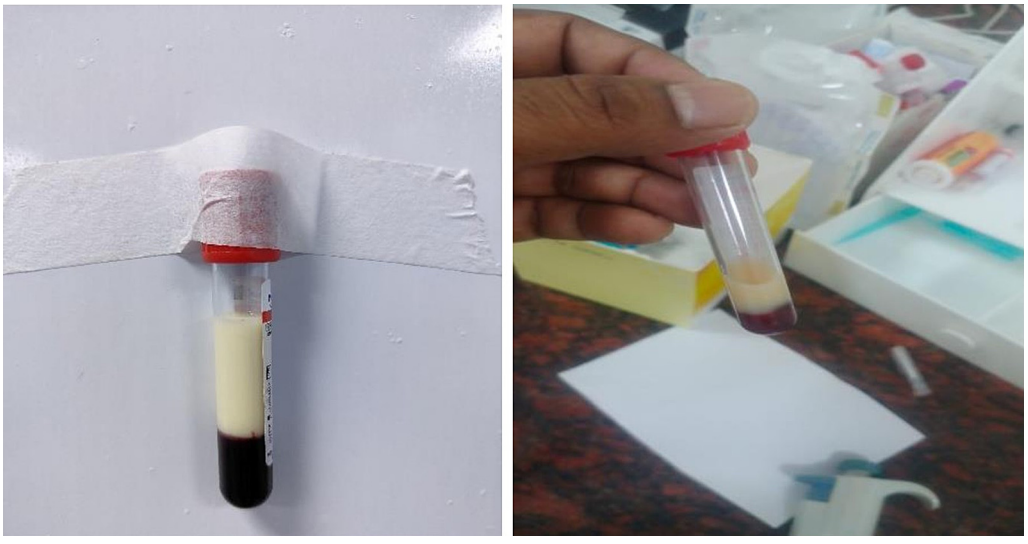
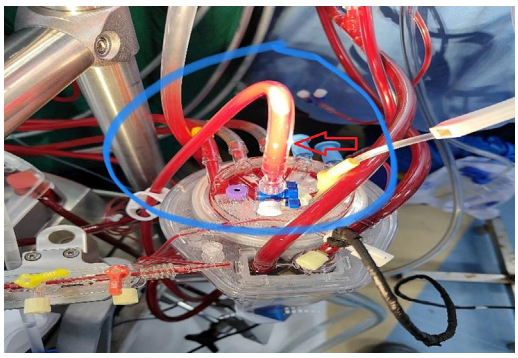


FIGURE 2 Recirculation Cannula Showing Milky Serum



and piracetam syrup (40 mg/kg/day) were administered, and neurostimulation was encouraged, leading to gradual improvement in sensorium.

After surgery, severe PAH, potentially influenced by preoperative obstructed pulmonary venous return and the high lipemic nature of the blood, was managed with multiple vasodilators, phenoxybenzamine infusion, oral sildenafil, and ambrisentan. Supportive measures maintained optimal hemoglobin, blood pH, and pain management, resulting in a gradual resolution of PAH. Table 1 shows the treatment timeline for Patient 1.

Severe PAH and central nervous system events extended the use of postoperative ventilation, underscoring their impact on mortality and morbidity. The infant was supported with mother-expressed breast milk, medium-chain triglyceride (MCT) oil, and nutritional assistance. The hypertriglyceridemia went untreated, given the uncertain safety of using statins and fibric acid derivatives in this age group.

TABLE 1 Timeline of Patient 1

Day	Event
0	Admission
1	Emergency surgery for right ventricular dysfunction, elevated pulmonary artery pressures, and decreased urine output. Treated with PD, diuretics, and fluid management.
3	Phenoxybenzamine infusion.
4	Attempted extubation; baby exhibited encephalopathy and seizure activity. Treated with levetiracetam and piracetam.
8	Second extubation trial failed.
11	Tracheostomy performed.
27	Weaned off to high-flow nasal cannula.
31	Oxygen support discontinued.
33	Shifted to the ward.
40	Discharged to home.

PATIENT 2

A 5-month-old infant was brought for treatment with respiratory distress, poor weight gain (4 kg), and a ventricular septal defect (VSD) of the perimembranous type. Elevated triglycerides, 1,200 mg/dL (reference <150 mg/dL) were observed during surgical profiling, despite no family history of elevated lipids. Early VSD surgical closure was scheduled. Meticulous precautions were taken to avoid dehydration. Invasive monitors, near-infrared spectroscopy, and ACT were maintained for >480 seconds. Pre- and post-pump oxygenator pressures were monitored, and temperature was maintained at 32 °C. VSD surgical closure, with a short clamp time (47 minutes) and CPB time (70 minutes), included modified ultrafiltration. After surgery, no reservoir clot was found, and the immediate postoperative period was uneventful. The baby received expressed breast milk and MCT oil, and was planned for follow-up care and further workup.

DISCUSSION

This study presents groundbreaking documentation of 2 infants with hypertriglyceridemia undergoing congenital cardiac surgery on CPB.

Hypertriglyceridemia can be primary, involving genetic factors, or secondary, resulting from various causes, such as metabolic issues and environmental factors.[2] Severe hypertriglyceridemia, commonly caused by lipoprotein lipase deficiency in infants, can lead to life-threatening complications. Elevated triglyceride levels, particularly >2,000 mg/dL, are associated with an increase of >20% in the incidence of acute pancreatitis and can have an impact on postoperative outcomes.[3] This study emphasizes that individuals with defective lipoprotein lipase activity, unable to hydrolyze triglycerides, accumulate chylomicrons rich in triglycerides, cholesterol, and phospholipids, resulting in lipemic blood with extremely high levels of serum triglycerides and cholesterol. The deleterious effects of hypertriglyceridemia include increased blood viscosity, raising the risk of acute pancreatitis, capillary leak, acute noncardiogenic pulmonary edema, hypoxic damage,[4] and acute kidney injury.[5] Specific consequences on organs include acute pancreatitis, hemolysis leading to acute kidney injury,[5] decreased blood flow to the gastrointestinal tract causing bowel necrosis,[6] PAH resulting in hypoxia further complicating the postoperative course in congenital cardiac surgery, and impaired cerebral circulation leading to silent strokes and poor neurologic outcomes.[7] The mechanism of

tissue hypoxia and organ injury is probably due to reduced capillary blood flow and impaired microvascular vasodilation.

Despite the lack of specific guidelines for CPB management in hypertriglyceridemic patients, this study highlights crucial considerations. Monitoring pre- and post-oxygenator pressures, checking for clots, and having backup CPB pumps are essential. Maintaining near-normal or mild hypothermia is crucial, inasmuch as hypothermia can increase viscosity. Monitoring hourly urine output and administering adequate heparin to maintain ACT above 480 seconds are emphasized. Although extracorporeal membrane oxygenation membrane lung failure has been reported, there is insufficient evidence to determine the triglyceride levels at which this may occur.[8] Postoperatively, unexplained hypotension, pulmonary edema, and hypoxia should raise suspicion of acute pancreatitis. Falsely low levels of amylase, lipase, and pseudohyponatremia can occur. Elevated markers of hemolysis should be interpreted cautiously, considering that hypertriglyceridemia can lead to spurious elevations in hemoglobin.[9] In crises, early initiation of plasmapheresis may improve tissue perfusion;[10] insulin infusion and heparin infusions can be considered. Maintaining adequate hydration and exclusive breastfeeding is recommended.[11] Initiating MCT oil and omega-3 fatty acids can reduce hypertriglyceridemia. Evidence for the use of fenofibrate and statins in infants is lacking. A study also mentions gene therapy for lipoprotein lipase-deficient patients but highlights its cost as a prohibitive factor.[12] Early dietary counseling, as suggested by Kaitosaari et al,[13] starting as early as 7 months, shows potential benefits in managing hypertriglyceridemia. Liver transplantation is a possible option for familial hypercholesterolemia in older children, but we are not aware of any published reports showing liver transplantation as a possible option for severe hypertriglyceridemia in this age group.

CONCLUSIONS

This case emphasizes the crucial management of severe hypertriglyceridemia in infants undergoing emergency congenital cardiac surgery. The successful outcomes underscore meticulous preoperative planning, vigilant intraoperative monitoring, and timely postoperative interventions. Although specific guidelines for managing hypertriglyceridemia during CPB are lacking, these cases provide insights into potential challenges, emphasizing the need for further research. Documenting such unique cases contributes to collective knowledge, enhancing understanding and management strategies for similar future cases. These cases add valuable insights to the limited literature on hypertriglyceridemia in infants undergoing congenital cardiac surgery, laying the groundwork for further exploration.

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