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CASE REPORT

Severe hypertriglyceridemia in a child with new onset type 1 Diabetes Mellitus - role of therapeutic plasmapheresis

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Abstract

Severe hypertriglyceridemia can complicate diabetic ketoacidosis but is rarely reported in the pediatric population. The recognition of this entity is important for proper management and to prevent associated morbidities. We report a 6-year-old girl with new onset type 1 diabetes mellitus, who presented with diabetic ketoacidosis and hyperlipidemia. In addition to treatment with intravenous insulin, plasmapheresis was performed for management of hypertriglyceridemia. We intend to demonstrate the applicability of this technique in the presence of extremely high serum triglyceridemic levels, as primary prevention of hypertriglyceridemia complications.

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INTRODUCTION

Diabetic ketoacidosis (DKA) is a common presentation of type 1 diabetes mellitus (T1DM) requiring urgent treatment. It consists on hyperglycemia, acidosis, and ketonemia[1].

As insulin is required for lipoprotein lipase (LPL) activity that hydrolyzes and degrades triglycerides carried by chylomicrons and very-low-density lipoproteins (VLDL), a mild increase in serum lipid concentration is commonly seen in DKA. Severe hyperlipidemia is rarely reported in pediatric DKA[2,3].

We report a case of a child with newly diagnosed diabetes presenting with severe hypertriglyceridemia treated with plasmapheresis.

CASE REPORT

A previously healthy 6-year-old girl presented to the emergency department with one-week history of fatigue and lethargy. A 3kg weight loss was reported despite normal intake, polyuria and polydipsia were denied. No abdominal pain or vomiting. No family history of dyslipidemia.

Upon admission: normal body mass index (Percentile 10), blood pressure 93/50 mmHg, pulse rate 105 beats/min, respiratory rate 18/min, and body temperature 36.6 ºC. On physical examination mucous membranes were dry and capillary refill was two seconds. The remainder of the exam was unremarkable.

Bloodwork showed lipemic serum appearance (Figure 1). Serum chemistry showed hyperglycemia (643mg/dL; reference range: 74-109 mg/dL), hypertriglyceridemia (5369 mg/dL; reference range: <150 mg/dL), hypercholesterolemia (total cholesterol 699mg/dL; reference range: <170 mg/dL), creatinine 0.81mg/dL (reference range: 0.32-0.59 mg/dL), BUN 25.6 mg/dL (reference range: 15-36 mg/dL), sodium 126.7mmol/L (reference range: 135-145 mmol/L), amylase 119 U/L (reference range 28-100U/L), hematocrit 39,7% (reference range: 35-45%), glycosylated hemoglobin 12.9% (reference range: 3,8-5,8%), and normal thyroid function. Hepatic enzymes couldn't be measured because of severe hypertriglyceridemia. Blood ketones level was 6.9 mmol/L. Venous blood gas revealed metabolic acidosis with pH 7.227, pCO2 28.6mmHg, $HCO3^-$ 11.6mmol/L, anion gap 17.1 mEq/L.

After receiving appropriate fluid resuscitation, the patient started appropriate fluid replacement and insulin infusion, while maintaining fasting. Lipid profiles 18 hours after admission revealed persistent severe hypertriglyceridemia (4568 mg/dL) and hypercholesterolemia (total cholesterol 562 mg/dL; HDL-cholesterol 12 mg/dL), with normal amylase level (77U/L). The patient remained asymptomatic. An abdominal ultrasound excluded pancreatic abnormalities. Considering severe hypertriglyceridemia and pancreatitis associated risk, a half plasma volume plasmapheresis was performed through a central line (Equipment: Spectra Optia® Apharesis System – Terumo BCT®; anticoagulation with citrate on the rate of 13:1,



Figure 1. Lipemic sérum.

replacement fluid with 5% human albumin). Treatment was well tolerated without adverse effects. The lipemic plasma collection on the effluent bag is shown in Figure 2. Triglyceride level dropped to 1058 mg/dL.

DKA resolved after a 16 hours insulin infusion and was successfully transitioned to subcutaneous insulin. Genetic testing for disorders of lipid metabolism was done and results showed a mutation in APOA5 gene. She was discharged on day 8 with a triglyceride level of 463 mg/dL. After one month and adequate glycemic control, triglyceride levels were 115 mg/dL.

DISCUSSION

This case highlights the occurrence of hypertriglyceridemia in the context of new onset T1DM and the implications of this clinical scenario.

Newly diagnosed patients with T1DM, presenting with DKA have an absolute insulin deficiency that can result in severe hyperlipidemia. A mild increase in serum lipid concentrations is a common feature of insulin deficiency states (30-50% of DKA cases[3,4]) but severe hypertriglyceridemia, defined as a triglyceride level > 1000mg/dL[3], with milky plasma is rare[2-6]. It has been found in 8-12.5% of the adult population with DKA, but data on pediatric population is limited[3,6].



Figure 2. Effluent bag during plasmapheresis.

The mechanism of hypertriglyceridemia in DKA involves insulin deficiency, leading to increased fat mobilization by activating lipolysis and releasing free fatty acids. This accelerates the VLDL formation, which allied to LPL reduced activity decreases removal of VLDL from the plasma resulting in hypertriglyceridemia[1-6].

It is postulated by many authors that genotypic variations affecting LPL or cofactors are the reason why only a few diabetic children present with severe hyperlipidemia[1]. Mutations in APOA5 gene, as shown in our case, have been described to be associated with hypertriglyceridemia[7].

Recognition of this association is important as severe hypertriglyceridemia can complicate DKA by developing pancreatitis[1]. Acute pancreatitis occurs in 2% of children and 11% of adults with DKA[8].

Treatment of hypertriglyceridemia include several days of intravenous insulin, and in severe or refractory cases plasmapheresis is an option[3].

In a literature review of pediatric patients with DKA and hypertriglyceridemia the majority of cases were treated only with intravenous insulin, and time to normalization ranged from 3 to 60 days[1-6]. Only three pediatric cases were treated with plasmapheresis, two with organ failure and one with acute pancreatitis. A 10-year-old girl with DKA and severe hypertriglyceridemia (16.334 mg/dL) complicated with acute pancreatitis and renal insufficiency who failed with conservative treatment but was successfully treated by plasmapheresis[9]. A 14-year-old girl with DKA and severe hypertriglyceridemia with severe metabolic acidosis worsening despite adequate rehydration and insulin therapy. Plasmapheresis was first tried by membrane but failed as lipemic blood clogged the plasma filter. Then, it was successfully done by centrifugation[2]. And a 16-year-old male with type 2 diabetes mellitus who presented with severe hypertriglyceridemia (28 040 mg/dL), acute pancreatitis, and DKA. Despite treatment with insulin infusion and intravenous fluids, his pancreatitis symptoms worsened and lipase level increased, and 2 courses of plasmapheresis were performed with good results[10].

Plasmapheresis, also known as therapeutic plasma exchange (TPE), is an extracorporeal procedure in which plasma is separated from the cellular components of the blood, discarded and exchanged with replacement fluid. It can be performed using two systems: membrane (mTPE), based on molecular size, and centrifugal (cTPE), based on molecular density[11]. A comparison between mTPE devices and Spectra Optia® Apheresis System cTPE found several advantages with the second one, mainly a higher plasma removal efficiency (27-53 vs 80-93%) and a more flexible vascular access need (hemodialysis catheter vs acute central line), with fewer side effects[11].

The frequency and types of complications from therapeutic apheresis depend upon the overall condition of the patient and number of procedures. Although principles of TPE are the same in adults and children, there are technical differences, such as smaller total blood volume and venous access difficulties. Nonetheless, several reviews of reported complications suggest that the incidence of TPE complications in adults and children is similar (2,2-12%) and most of them are mild. The most common complications reported in a study where 1201 procedures were analyzed, the most common complications were pruritus and urticaria, followed by hypertension and hypotension. Other possible complications are anaphylactic reaction, sepsis/bacterial infection, febrile non-hemolytic transfusion reaction, hydroelectrolytic disorders, haemorrhage[12].

Successful use of plasmapheresis in patients with severe hypertriglyceridemia complicated by acute pancreatitis has been reported[13,14]. According to the American Society of Apheresis guidelines, hypertriglyceridemic pancreatitis is a class III indication for TPE, which means that the role of apheresis is not established, and decision making should be individualized[14]. Because of the safety of the technique, plasmapheresis has been used in severe hypertriglyceridemia for prevention of complications with good results and some authors recommend apheresis in patients with serum triglycerides > 1000mg/dL, regardless of symptoms[15]. However, the use of plasmapheresis in primary prevention of hypertriglyceridemia complications is limited due to lack of availability and high costs[11,15].

Our Pediatric Intensive Care Unit realizes over 100 procedures using Spectra Optia®. In our case, to achieve a fast reduction of triglycerides a half-plasma volume cTPE was performed. It was a safe, effective and well tolerated

treatment, with no complications and triglyceride level was reduced by 70.35%.

In conclusion, there are no clear guidelines in the literature on managing pediatric patients with hypertriglyceridemia. This procedure was done in children with signs of organ failure and on the onset of acute pancreatitis. We managed to show that cTPE was an effective and safe treatment in this patient with severe hypertriglyceridemia with increased risk of developing complications, and physicians should consider it as primary prevention to avoid complications when these resources are available.

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