CLINICAL CASE

THERAPEUTIC PLASMAPHERESIS IN PRIMARY PRESENTATION OF DIABETES MELLITUS WITH DIABETIC KETOACIDOSIS, HYPERTRIGLYCERIDEMIA AND ACUTE PANCREATITIS**Tonceanu Andra Maria^{1,2}, R. Palade², RR Grigorescu², T Trotea², Florentina Mușat²**¹Department of Anesthesiology and Intensive Care, Emergency University Hospital, Bucharest²University of Medicine and Pharmacy “Carol Davila” Bucharest, Romania

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Abstract

We present a case of severe hypertriglyceridemia- induced acute pancreatitis associated with diabetic ketoacidosis, managed in intensive care unit. The patient was a 39-year-old woman, with a medical history of Graves-Basedow disease, essential arterial hypertension and morbid obesity (body mass index=31). Firstly, we aggressively corrected hypovolemia and hemodynamic imbalances (administrating fluids and systemic anticoagulant) and then we focused on the infection prevention and control of intra-abdominal pressure, for latter outcome. We decided to start first session of plasma exchange. The patient responded well to the treatment applied. Plasma-exchange was very efficient, reducing TG levels by 60% after the first treatment and achieving a decrease of 77.6% at the third plasmapheresis session. This case was safely and effectively managed with plasmapheresis (three sessions), antibiotics, multimodal analgesia (intravenous and thoracic epidural catheter), early jejunal nutrition and forced mobilization. The patient's evolution was significantly favorable, with a reduction of the peripancreatic necrosis on computer scan, at day 28 and she was discharged with a normal value of TG and without pain or any clinical signs.

Keywords: pancreatitis, plasmapheresis, hypertriglyceridemia**Introduction**

Severe hypertriglyceridemia (HTG), defined as a level of triglycerides (TG) above 1000mg/dl, is the third most common cause of acute pancreatitis, and a potentially life threatening condition. The prognosis depends greatly on our ability to rapidly reduce serum TG concentration [1]–[3]. Plasmapheresis is a procedure where plasma exchange (PE) takes place. During the procedure, the plasma is separated from the blood cells, a large volume of it removed and replaced with a colloid

solution in order to maintain oncotic pressure [4].

Poorly controlled diabetes mellitus and diabetic ketoacidosis can trigger (HTG). Acute pancreatitis in diabetic ketoacidosis usually occurs with severe metabolic acidosis characterized by a low serum pH (<7.1) and high anion gap [1], [5]. Marked elevation of serum TG occurs during episodes of acute pancreatitis. Lack of insulin results in lipolysis in adipose tissue with release of free fatty acids. Increased delivery of free fatty acids to the liver leads to high output of very low density

lipoproteins, which coupled with the inhibition of lipoprotein lipase in peripheral tissues, results in HTG [6-8].

Case presentation

A 39-year-old woman, with a medical history of Graves-Basedow disease, essential arterial hypertension, morbid obesity (body mass index=31), presented to the Emergency Department of our hospital accusing nausea, biliary vomiting and discomfort caused by effort over the last two days, followed by strong abdominal pain located at the right upper quadrant on the day of admission. On physical examination she was conscious, cooperative, afebrile, non icteric, stable hemodynamic, blood pressure was 153/102 mmHg, pulse was 126 bpm and oxygen saturation was 99% on pulse oximetry with oxygen. The abdomen examination was significant for tenderness in the right upper quadrant. Diuresis was normal and laboratory tests revealed metabolic acidosis (pH=7.26), $pCO_2=11$ mmHg, bicarbonate=5 mmol/L, base excess =-22, lactate=5.26, negative BHCG, and urine positive for ketones. On blood tests we also observed high levels of amylase (884 U/L), lipase (9601 U/L) and transaminase (ALT: 85, AST: 113). On the computed tomography evaluation (figure 1), the pancreas appeared enlarged, surrounded by a large amount of fluid and there were no signs of abscess or pseudocyst (Figure 2). Fatty infiltration of the liver without lesions or evidence of cholelithiasis were also described.

Figure 1 - Stranding edema within the peripancreatic fat

Figure 2 - Fat stranding in the pancreatic head consistent with pancreatitis and reactive thickening in the duodenum

At first day on admission in the intensive care unit the serum was lactescent, and the laboratory was not able to detect values of TG and cholesterol. Aggressive hydration, fibrates twice a day, insulin, heparin, and morphine were initiated on the first day of admission

Figure 3 - Plasma exchange

We decide to begin the first session of PE.

After one hour the plasmapheresis filter has clogged (figure 3). We repeated blood test tryglycerides (1293 mg/dl), LDH (413 U/L), CHOL (382 mg/dl), HDLC (20 mg/dl), PCR (261, 14 mg/l), glycemia (427 mg/dl). We begin the second session of PE (figure 4). Intra-abdominal pressure was 35 cmH₂O, and was monitored every 6 hours.

Figure 4 - Second session of plasma exchange

The patient responded well to the treatment applied. Plasma-exchange was very efficient, reducing TG levels by 60% after the first treatment and achieving a decrease of 77.6% at the third plasmapheresis session.

On the third day, the patient became febrile (38,4°C) and blood tests revealed a procalcitonin level of 10 ng/mL and a presepsin level of 1400 pg /ml, so we added to treatment imipenem-cilastatin and levofloxacin.

We have included effective thoracic epidural analgesia (T8-T9), as part of a multimodal analgesia approach, with Naropine and Fentanyl. We chose epidural analgesia because the patient was in real pain, despite intravenous analgesia and to avoid the stress which evokes a complex response pattern, with an increase in catabolic hormones and a reduction in anabolic hormones, altered carbohydrate and protein homeostasis and hypermetabolism with the secretion of cortisol and catecholamines [8], [9].

We integrated the patient into a therapeutic program that includes early mobilization and jejunal nutrition (20 ml per hour, at first, with incremental doses). The thoracic catheter was withdrawn after six days.

The patient's evolution was significantly favorable, with a reduction of the peripancreatic necrosis on computer scan, at day 28 and she was discharged with a normal value of TG and without pain or any clinical signs. The role of multimodal therapy was a success.

Discussion

We can't fully explain the etiology of severe HTG induced acute pancreatitis. The imbalance of lipoproteins metabolism encountered in the setting of diabetes mellitus plays an important role in the etiology of the disease, but in the same time acute pancreatitis can be the trigger for diabetes mellitus [1,2,10]. In our case the patient had dyslipidemia, and also undiagnosed diabetes mellitus. In 1865, Speck et al were the first ones to describe the relation between severe HTG and acute pancreatitis. He suggested that chylomicron-related hyperviscosity induced ischemia, free fatty acid-induced inflammation and a genetic predisposition can explain this type of pathology [8].

Poorly controlled diabetes is the most common cause of HTG, followed by alcoholism and on the third place, by diet and medications [6-7]. The patient was obese but she didn't take any medication.

Plasmapheresis therapy is the removal and replacement of large volumes of plasma in order to filter out pathologic antibodies, cytokines, immune complexes, or other blood components. Centrifugation separates blood and plasma components by stratifying them in different layers according to their size, shape, density, viscosity of the medium and rotor speed, allowing for removal of a particular layer. Filtration, on the other hand, separates plasma from larger components of blood including red blood cells, white blood cells and platelets using filters of varying sizes [3,11].

PE has been used to treat hypertriglyceridemic acute pancreatitis being effective for acute reduction of severe hypertriglyceridemic HTG. This study also suggested that PE may be effective for rapidly reducing TG levels in a patient with severe HTG and acute pancreatitis. Of note, TG levels decrease spontaneously with conservative treatment, and PE has not yet been compared

with conservative treatment in a controlled trial using clinical outcomes as endpoints.

The patient was responsive to the treatment applied, plasma-exchange was very efficient, with the first treatment reducing TG levels by 60% and achieving a reduction of 77.6% at the third plasmapheresis treatment.

The main advantage of plasmapheresis over conservative management consists in a rapid and efficient removal of lipid particles and triglyceridemia-associated pro-inflammatory agents. The earlier therapeutic plasmapheresis is initiated, the more morbidity and mortality decrease [3], [11].

Up to date, there are a few cases of acute severe pancreatitis, with fever and fulminant systemic inflammatory syndrome, which avoid surgery and went home. The key of success was an aggressive multimodal therapy, inclusive plasma-exchange with heparin. We need to proceed very fast. In addition to conservative management, such as intravenous hydration, and pain management, infusions of insulin and heparin have been used to lower TG levels in HTIP and fibrates. Fibrates typically lower TG levels rapidly and effectively and serve as first-line therapy for elevated TG [1,2], but plasmapheresis decreases faster and much aggressively the triglycerides level [11].

We found plasma exchange to be a successful and safe alternative for the treatment of severe HTG. No complications were noted.

Conclusion

We present a case of severe hypertriglyceridemia-induced acute pancreatitis associated with diabetic ketoacidosis in which PE seems to improve the overall mortality and morbidity. We provided an algorithm of treatment which proved to be a safe and effective therapeutic option in the management of potentially life-threatening acute pancreatitis with high TG levels. Further studies are needed

to solidify clinical evidence, and optimize future management guidelines for these patients.

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