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Diabetic Ketoacidosis-induced Hypertriglyceridemic Acute Pancreatitis Treated with Plasmapheresis—Recipe for Biochemical Disaster Management

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ABSTRACT: Diabetic ketoacidosis (DKA)-induced hypertriglyceridemia causing pancreatitis is an interesting phenomenon that has rarely been reported in literature. Plasmapharesis is a well known treatment modality for hypertriglyceridemia-induced pancreatitis. We report a patient with DKA-induced hypertriglyceridemic acute pancreatitis treated successfully with plasmapharesis.

KEYWORDS: DKA, pancreatitis, hypertriglyceridemia, plasmapharesis

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Introduction

Hypertriglyceridemia is the third most common cause of acute pancreatitis, accounting for 1–4% of cases presenting to the hospital.[1] Diabetic ketoacidosis (DKA)-induced hypertriglyceridemia causing pancreatitis is an interesting phenomenon that has rarely been reported in literature.[2] In DKA, insulin deficiency leads to lipolysis and inhibition of lipoprotein lipase in peripheral tissues that leads to elevated triglycerides (TG).[1,2] A toxic role of accumulated free fatty acids in the pancreatic tissues, post-pancreatic lipase mediated hydrolysis of TG has been suggested. TG levels greater than 1,000 U/L have been implicated as a cause of acute pancreatitis. Types I, IV, and V dyslipidemias have also been associated with acute pancreatitis.[3] Types I and V dyslipidemias can cause acute pancreatitis without a predisposing factor, whereas Type IV can do so in the presence of an underlying condition that may increase serum TG levels.[2] Infusions of insulin, heparin, and plasmapheresis have been used to lower TG levels in different subsets of patients.[4] Insulin activates lipoprotein lipase, while heparin leads to the release of endothelial lipoprotein lipases.[4] In combination, these enzymes accelerate chylomicron degradation into glycerol and fatty free acids lowering levels of circulating lipids.

Case

We present the case of a male in his 40's with extensive past medical and surgical history. This included hypertension, dyslipidemia (never worked up in the past, previous reported TG level of 315 mg/dL, managed with 20 mg daily pravastatin), alcohol abuse (≥1 L of hard liquor/day), and recurrent episodes of acute on chronic alcoholic pancreatitis. The patient underwent distal pancreatectomy and splenectomy secondary to splenic subcapsular liquefactive hematomas and a benign cystic lesion in the tail of pancreas, in the setting of

an attack of acute pancreatitis (presumably involving trauma) following an alcohol binge, seven months ago. He developed diabetes mellitus post distal pancreatectomy and was being managed with subcutaneous NPH insulin therapy, 40 units in the morning and 36 units in the evening. HbA1c was 14.4 three months prior to current admission.

He presented to the emergency room with worsening abdominal pain, nausea, and vomiting for 1 day. He reported insulin rationing for a week and therefore had been taking less than the prescribed doses. Physical exam revealed stable vital signs with a BMI of 25.85. Examination of the abdomen revealed diffuse tenderness to palpation, no distension with normal bowel sounds. Initial lab work revealed a milky plasma (Fig. 1), blood glucose of 665 mg/dL, CO_2 of 6 mmol/L, anion gap of 31, a white count of 14,610/mm^3, lipase of 8223 U/L, TG of 4,854 mg/dL, sodium of 126 mg/dL, potassium of 5.3 mg/dL, calcium of 8.3 mg/dL, and albumin of 3.3 g/dL. The patient was found to be in DKA and was admitted to the medical intensive care unit. CT scan (Figs. 2 and 3) revealed severe acute inflammatory changes and edema of the residual pancreas. DKA was treated with intravenous hydration using normal saline, potassium supplementation, and intravenous regular insulin—initial bolus of 0.1 units (u)/kg body weight followed by an infusion at the rate of 0.1 u/kg/hour. When blood glucose was lowered <200 mg/dL, rate of infusion was halved to 0.05 u/kg/hour. Once the anion gap normalized and the patient was able to eat, subcutaneous insulin was overlapped with intravenous infusion for two hours. This was followed by discontinuation of infusion. With DKA being treated, the patient underwent one cycle of plasmapheresis for four hours, following which TG levels decreased from 4,854 to 537 U/L. The patient's symptoms resolved after plasmapheresis and treatment of DKA. He was then transferred to a regular medicine floor. The subsequent stay in the hospital was uneventful and the patient was discharged on the 5th day. TG on discharge was 629 IU/L. Discharge medications included gemfibrozil (600 mg three times daily) for hypertriglyceridemia. The patient was non-compliant with outpatient follow-up once discharged and workup for dyslipidemia could not be completed.

Figure 1. Lipemic plasma.

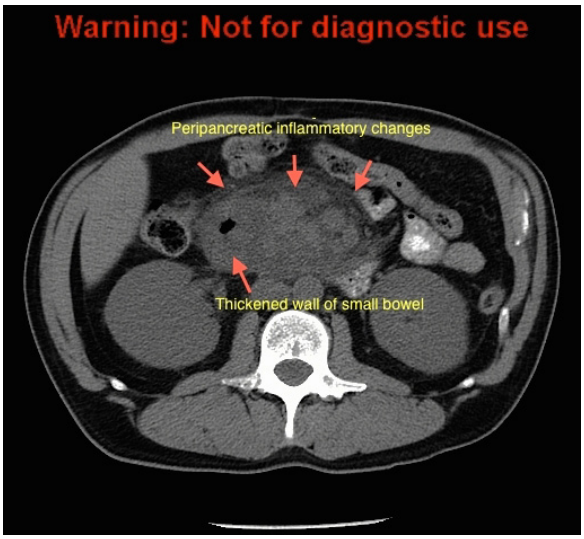

Figure 2. CT abdomen showing peripancreatic inflammatory changes and thickened wall of mall bowel.

Discussion

Plasmapheresis involves removal of a patient's blood, separation of plasma using a first filter, followed by filtration of separated plasma using a second filter. The small pores in the second filter prevent the passage of high-molecular weight molecules (eg, TG). The plasma is then either re-infused into the patient or an isovolumetric substance is used to replace the

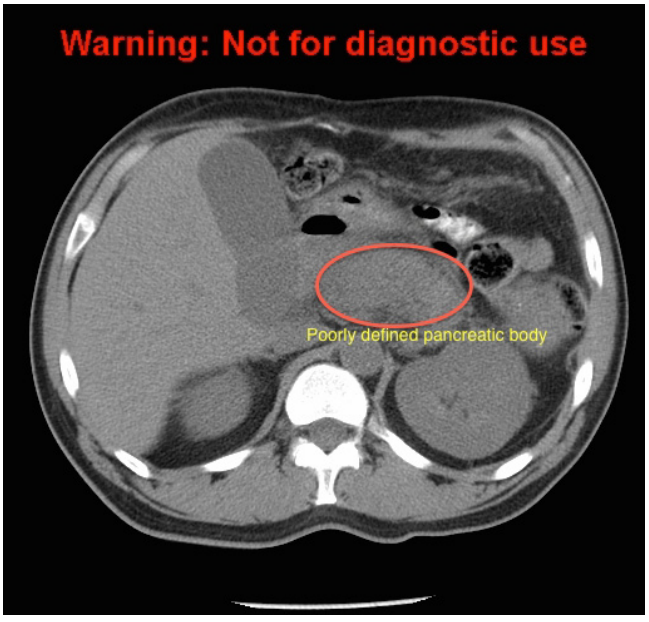

Figure 3. CT abdomen showing poorly defined pancreatic body.

plasma.[5] It is used as an important treatment modality in various neurological, hematological, and rheumatologic diseases.

Successful use of plasmapharesis for patients with hypertriglyceridemic acute pancreatitis has been reported previously in literature.[6,7] Multiple mechanisms have been postulated explaining the utility of plasmapharesis in these patients. These include removal of chylomicrons, proteases, and proinflammatory cytokines and reduction of hyperviscosity.[8] As per the American Society for Apheresis' 2010 guidelines, the recommendation for the use of plasmapharesis in these cases is only Grade 2C, implying weak recommendation with low-quality or very low-quality evidence.[9] This results from the fact that the evidence behind the use of plasmapharesis in these patients is limited to case reports and summaries without any randomized controlled trials. We discuss a few of these reported cases and their outcomes.

Kadikoylu et al reported two cases of hypertriglyceridemia-induced acute recurrent pancreatitis. Both patients were subjected to repeated cycles of plasmapharesis with reduction in amylase and lipase as well as resolution of symptoms.[6] Another study done by Ramirez-Bueno et al involved 11 patients admitted to the intensive care unit with severe hypertriglyceridemic pancreatitis and were treated with plasmapheresis.[5] In all, 8 of these 11 patients needed one cycle of plasma exchange, 2 patients needed two cycles, while 1 patient needed one cycle, to decrease TG levels to less than 1000 mg/dL. Yeh et al enrolled 17 patients with hypertriglyceridemic acute pancreatitis and subjected them to plasmapharesis.[10] Of these, 13 recovered completely with reduction in amylase and TG levels. The remaining patients succumbed to complications from acute pancreatitis, namely, intra-abdominal abscess, septic shock, and multi-organ failure.

In addition to the conventional management of acute pancreatitis in these patients, hypertriglyceridemia needs to be treated effectively to bring down TG below 500 U/L, which has been correlated with marked improvement in symptoms.[11] Normoglycemic patients who are hemodynamically stable and have no contraindications to establishment of central venous access are considered to be good candidates to undergo plasmapheresis.[12] Better outcomes have been noted in patients who are subjected to apheresis within 48 hours of onset of symptoms.[11,12] We treated our patient's DKA with insulin, intravenous hydration, and electrolyte replacement. Once the patient's hyperglycemia resolved, he was subjected to plasmapheresis with excellent results after one cycle.

Author Contributions

Conceived and designed the experiments: AS, AS, SR, TS, PJ. Wrote the first draft of the manuscript: AS, SR, TS, JB, PJ, JA. Contributed to the writing of the manuscript: AS, AS, SR, TS, JB, PJ, KM, MB, JM, JA. Agree with manuscript results and conclusions: AS, SR, TS, JB, AS, PJ, KM, JM, MB, JA. Jointly developed the structure and arguments for the paper: AS, SR, TS, JB, AS, PJ, KM, JM, MB, JA. Made critical revisions and approved final version: AS, SR, TS, JB, AS, PJ, KM, JM, MB, JA. All authors reviewed and approved of the final manuscript.

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