SAGE Open Medical Case Reports
Volume 10: 1–4

DOI: 10.1177/2050313X221135597
journals.sagepub.com/home/sco
SAGE

Rapid resolution of hypertriglyceridemia-induced pancreatitis via plasmapheresis: A unique case report

Victoria Wang[1], Anna Jinnah[2], James R Pellegrini Jr[3] and Brandon Pelletier[4]

Abstract

Hypertriglyceridemia is a well-established cause of acute pancreatitis. Initial treatment for hypertriglyceridemia-induced pancreatitis has consisted of supportive measures; however, triglyceride levels can remain high, causing prolonged organ failure and sepsis. Plasmapheresis has been proposed as a treatment option to effectively reduce triglyceride levels. We present a patient case of hypertriglyceridemia-induced pancreatitis that was treated with standard acute pancreatitis interventions along with plasmapheresis, after which triglyceride levels reduced significantly. Further research is necessary to determine the clinical benefits of plasmapheresis in treating this type of pancreatitis.

Keywords

Hypertriglyceridemia, acute pancreatitis, plasmapheresis

Date received: 21 July 2022; accepted: 7 October 2022

Introduction

Hypertriglyceridemia (HTG) is the third most common cause of acute pancreatitis in the United States after gallstones and chronic alcohol abuse, accounting for up to 10% of cases.[1] A triglyceride (TG) level over 1000 mg/dL is usually required to diagnose HTG-induced pancreatitis (HTGP); however, the level above which pancreatitis occurs is unknown and varies with individuals.[2,3] HTGP patients tend to be male, younger, and with a history of diabetes.[1,4,5] These patients also appear to have a more severe disease course than those with pancreatitis induced by other factors, often requiring intensive care unit (ICU) admission and meeting sepsis criteria.[3,4]

The pathophysiology of HTGP is not well understood. It is believed that TGs are broken down into toxic free fatty acids by pancreatic lipases, causing pancreatic cell injury and ischemia.[2,6,7] Free fatty acids also lead to the release of pro-inflammatory factors such as tumor necrosis factor-alpha, interleukin-6, and interleukin-10.[1] HTGP may also have a genetic component, as cystic fibrosis transmembrane conductance regulator and apolipoprotein E gene mutations are seen more frequently in affected patients.[1,2] The severity of pancreatitis depends on the level of the inflammatory response by the pancreas and the lipotoxicity from TG breakdown.[6,8]

Initial treatment for HTGP consists of supportive measures such as fluid resuscitation, bowel rest, and analgesics, in addition to intravenous insulin and heparin to lower TG levels.[2] Even with such treatments, TG levels can remain high, leading to prolonged organ failure as well as longer stays in the ICU and increased consumption of resources. Plasmapheresis has been proposed as a treatment option that most rapidly reduces TG levels and resolves pancreatitis symptoms.[3,5] We present a case of HTGP in a young man promptly resolved via plasmapheresis.

[1]New York Institute of Technology, College of Osteopathic Medicine, Old Westbury, NY, USA
[2]American University of the Caribbean School of Medicine, Cupecoy, Sint Maarten
[3]Department of Internal Medicine, Nassau University Medical Center, East Meadow, NY, USA
[4]Department of Internal Medicine, Onslow Memorial Hospital, Jacksonville, NC, USA

Corresponding Author:
Victoria Wang, New York Institute of Technology, College of Osteopathic Medicine, 101 Northern Boulevard, Old Westbury, NY 11568-8000, USA.
Email: vwang02@nyit.edu

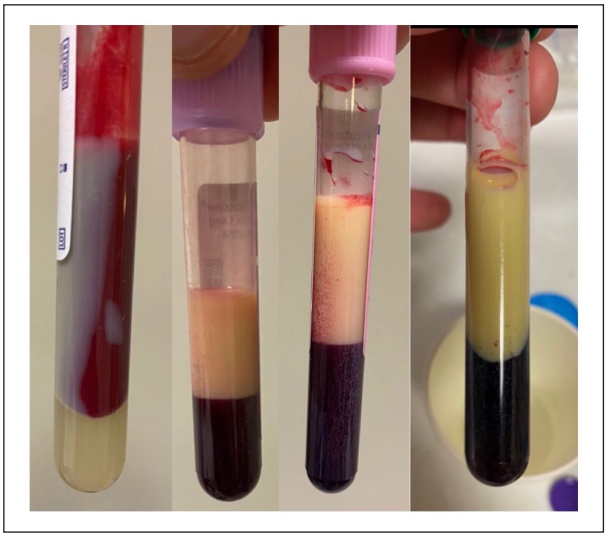

Figure 1. Initial blood sample (far right) and subsequent dilutions (from right to left).

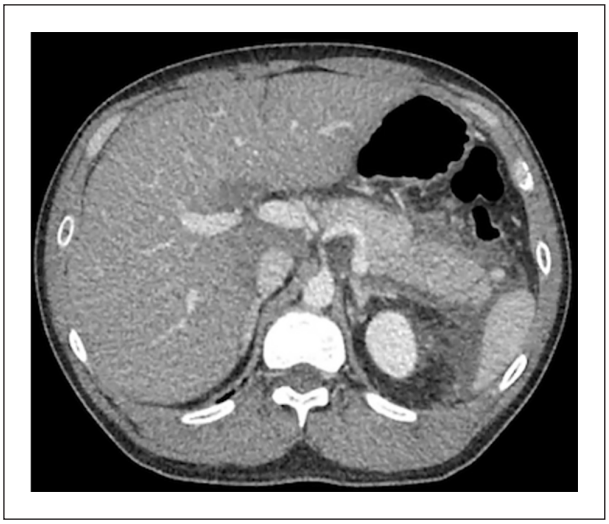

Figure 2. Computed tomography scan of the abdomen and pelvis with contrast, axial view.

Case presentation

A 34-year-old man with a medical history significant for alcohol dependence presented to the hospital with a 1-day history of left-sided, cramping abdominal pain radiating to the back. He denied prior episodes or any inciting incidents. He also denied any known history of diabetes mellitus, medication use, pancreatitis, or a family history of genetic dyslipidemias.

On physical examination, it was noted that the patient was not obese (body mass index (BMI) 24.4) and in no acute distress. Vital signs were notable only for tachycardia at 112/min. There was moderate tenderness to palpation in the right upper quadrant, left upper quadrant, and left lower quadrant. The laboratory analysis was initially delayed as the patient's blood sample was too lipemic to be analyzed using traditional techniques (Figure 1). After 32 rounds of manual dilutions of the blood sample with isotonic saline, laboratory workup was significant for leukocytes 12 k/μL (normal 4.5–11.0 k/μL), neutrophils 81.8% (normal 40%–60%), potassium 3.2 mEq/L (normal 3.7–5.2 mEq/L), random glucose 136 mg/dL (normal 70–100 mg/dL), calcium 6.8 mg/dL (normal 8.5–10.2 mg/dL), alanine aminotransferase 73 U/L (normal 4–36 U/L), aspartate aminotransferase 80 U/L (normal 8–33 U/L), alkaline phosphatase 135 IU/L (normal 44–147 IU/L), TGs 9708 mg/dL (normal $<$ 150 mg/dL), low-density lipoprotein 373 mg/dL (normal 50–100 mg/dL), and lipase 245 U/L (normal $<$ 160 U/L).

Computed tomography of the abdomen and pelvis with contrast revealed acute interstitial pancreatitis with peripancreatic fluid surrounding the pancreatic tail within the anterior pararenal space, in addition to fatty infiltration of the terminal ileum submucosa that raised concern for inflammatory bowel disease (Figure 2).

The patient was admitted to the medical ICU for management of HTGP. He was kept on nil per os and started on an insulin drip with a dextrose 10% in water drip titrated to maintain euglycemia, high-volume intravenous fluids, electrolyte replenishment, and analgesia. The patient's serum TG level was initially measured to be 4025 mg/dL. Given the patient's severe clinical condition, plasmapheresis was initiated to treat the HTG, which was the underlying cause of his pancreatitis, with a volume replacement of 1250 cm^3 of fresh frozen plasma and 1250 cm^3 of 5% albumin. After one cycle, the TG level was found to be 603 mg/dL. The insulin drip and other treatments were continued during and after plasmapheresis. After 1 day, the TG level was measured to be 304 mg/dL. The patient was then transferred to the medical floors for further management.

Discussion

When HTGP is suspected, initial conservative management includes aggressive intravenous hydration, bowel rest, and analgesia. Insulin and heparin have been used as HTGP-specific pharmacologic treatments. Insulin activates lipoprotein lipase (LPL), thereby accelerating the clearance of TGs.[2] Insulin also reduces the activity of hormone-sensitive lipase, decreasing the release of free fatty acids from adipocytes and the synthesis of TGs.[9] It has also been postulated to improve immunoparalysis by upregulating the expression of human leukocyte antigen on monocytes and decreasing cell apoptosis.[2] Insulin carries the risk of hypoglycemia, which can be avoided with concomitant dextrose administration and frequent blood glucose checks. Heparin also has an effect on LPL by stimulating its release from epithelial cells, further lowering TG levels.[2] However, continuous heparin infusion has been demonstrated to deplete LPL, eventually resulting

in rebound HTG.[2] Plasmapheresis with albumin replacement significantly reduces TG levels by rapidly removing TGs and chylomicrons from the plasma, thus preventing further inflammation and damage to the pancreas. Plasmapheresis may also remove pro-inflammatory markers and cytokines, further decreasing inflammation.[1,2]

Long-term HTG management is aimed at reducing the risk of pancreatitis and preventing atherosclerotic cardiovascular disease.[9] For TG levels over 500 mg/dL, fibrate therapy should be initiated with omega 3 fatty acids as adjunctive therapy.[2] Patients with known atherosclerosis or who are at increased risk should also be started on statin therapy.[9] Lifestyle interventions, such as weight loss, diet modifications, aerobic exercise, and alcohol cessation are critical in managing HTG.[9] Patients with concurrent diabetes should also aim for tight glycemic control while those with other risk factors that can increase atherosclerosis, such as hypertension and tobacco use, should also be addressed.[10]

During our patient's hospital stay, initial symptomatic treatment and an insulin drip over 2 days reduced his TG levels by 58.5%. The addition of one session of plasmapheresis to these therapies further reduced his TGs by 85%, indicating that the combination of supportive and interventional therapies contributed to his swift recovery. A systematic review found that TG levels reported in 83 cases of HTGP had a similarly dramatic mean reduction of 85.4% after one or two sessions of plasmapheresis.[5] Most of these patients required ICU admission with a median length of stay of 15 days (range, 3–150).[5] Contrary to this study, our patient required a stay of only 2 days in the medical ICU. Another case study reported a similarly rapid reduction in TG levels after plasmapheresis for HTGP; the patient was discharged in a stable condition less than 96 h after initial admission.[11]

Studies on the effects of plasmapheresis in HTGP generally report improvement in symptoms and laboratory tests. Limited data is available regarding its impact on pancreatitis severity, such as organ failure and local complications.[5] There are also no specific recommendations for starting points or end points for plasmapheresis due to the lack of randomized controlled studies on the treatment. In addition, no studies have clearly demonstrated morbidity or mortality benefits. However, one randomized controlled study, the Bi-TPAI trial, is under development to compare intensive insulin therapy to plasmapheresis in HTGP cases within 24 h after diagnosis.[12] The primary endpoint is the length of time necessary for TG levels to drop to 500 mg/dL; the secondary endpoints are ICU and hospital length of stay; 28-day mortality; the severity of HTGP according to the revised Atlanta criteria, the Acute Physiology and Chronic Health Evaluation II score, the Ranson score, and CT grading; incidence of hypoglycemia, HTGP complications according to the revised Atlanta criteria; and cost-effectiveness.[12] Implementation of studies such as this may provide clinical evidence as to the integration of plasmapheresis in the standard care of HTGP.

Conclusion

We present a case of HTGP treated with plasmapheresis in addition to standard acute pancreatitis therapies. Our patient experienced a shortened hospital stay compared to prior studies along with rapid alleviation of his symptoms and reduction of lab abnormalities (approximately 85%), thus indicating that using plasmapheresis as a primary treatment for HTGP may be cost-effective and resource-saving. Further studies that define the clinical benefits of plasmapheresis will be important in bettering the clinical management of HTGP.

Authors' note

This article has not simultaneously been submitted to any other journal for review and/or publication.

Acknowledgements

The authors wish to extend their sincere thanks to the patient presented in this case report.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iD

Victoria Wang https://orcid.org/0000-0001-7026-6304

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