Journal of Community Hospital Internal Medicine Perspectives

Volume 12 | Issue 1 Article 16

2022

Tetrad of DKA, Hypertriglyceridemia induced Pancreatitis and Splenic vein thrombosis

Beenish Faheem
St. Joseph's University Medical Center, Paterson, NJ, USA, beenishfaheem@students.aucmed.edu

Balraj Singh
St. Joseph's University Medical Center, Paterson, NJ, USA

Hamdallah Ashkar
St. Joseph's University Medical Center, Paterson, NJ, USA

Parminder Kaur
St. Joseph's University Medical Center, Paterson, NJ, USA

Sachin Gupta
Tower Health Center, West Reading, PA, USA

See next page for additional authors

Tetrad of DKA, Hypertriglyceridemia induced Pancreatitis and Splenic vein thrombosis

Authors

Beenish Faheem, Balraj Singh, Hamdallah Ashkar, Parminder Kaur, Sachin Gupta, and Michael Maroules

Tetrad of DKA, Hypertriglyceridemia Induced Pancreatitis and Splenic Vein Thrombosis

Beenish Faheem*, Balraj Singh, Hamdallah Ashkar, Sachin Gupta, Paminder Kaur, Michael Maroules

Abstract

Patients with diabetes mellitus have diabetic dyslipidemia that occurs due to disturbances in glucose metabolism and can lead to hypertriglyceridemia (HPTG). Severe HPTG is associated with significantly increased risk of developing acute pancreatitis (AP). Acute pancreatitis (AP) is characterized as an inflammatory condition where inactive digestive enzymes become activated causing pancreatic tissue destruction. Hypertriglyceridemia and the inflammatory state that ensues therein also gives rise to a hypercoagulable state in patients with AP. Splenic vein thrombosis (SVT) is a rare complication of both AP and chronic pancreatitis (CP). We report a Case of 55-year-old Filipino male with past medical history of hypertension and uncontrolled type 2 diabetes mellitus (T2D), who presented with abdominal pain and was found to have diabetic ketoacidosis (DKA), and severe HPTG which led to acute pancreatitis, further complicated by SVT requiring anticoagulation. Our case highlights the importance of strict glycemic control among diabetic patients, the prompt management of AP in the setting of HPTG, and treatment of SVT.

Keywords: Multiple myeloma, Vitamin B12, Vitamin B12 deficiency, CNS involvement, Leptomeningeal myelomatosis, Leptomeningeal carcinamatosis

1. Introduction

The most common forms of diabetes are type 1 diabetes (T1D) and type 2 diabetes (T2D).[1] In T1D, there is a complete deficiency of insulin due to the pancreatic beta cell destruction, while T2D is characterized by insulin resistance leading to hyperglycemia. As of 2020, 34 million Americans have diabetes, and approximately 90−95% of them have T2D.[2] Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes and although it is more frequently associated with T1D, it can also occur, though not as commonly, among patients with T2D.[3] According to CDC surveillance, the overall, DKA hospitalization rates took a turn toward a steady increase around 2009 to 2914 at an annual average rate of 6.3%.[3] Patient with DM can have diabetic dyslipidemia due to disturbances in glucose metabolism, where patients can have elevated serum triglyceride (TG) levels, low high-density lipoprotein cholesterol (HDL-C) and high levels of low-density lipoprotein cholesterol (LDL-C).[4] Hypertriglyceridemia effects 15−20% of the adults nationally and is associated with T2D, metabolic syndrome and visceral obesity. Elevated TG levels further cause damage with release of free fatty acids (FFA) which cause inflammation and ultimately lead to an increase in insulin resistance and impairment in the beta cell function of the pancreas.[4] The HPTG associated with diabetes is classified into mild to moderate (TG 150−499 pg/dL), and severe HPTG (TG > 500 pg/dL).[4] Prompt management of HPTG is necessary to prevent the feared complication of developing acute pancreatitis (AP) and then its downstream problems. We report a Case of where the patient with known history of T2D presented with DKA due to medication noncompliance, who was found to have severe HPTG that induced AP ultimately leading to the development of splenic vein thrombosis.

Received 15 July 2021; revised 11 October 2021; accepted 19 October 2021.
Available online 31 January 2022

* Corresponding author at:

E-mail address: beenishfaheem@students.aucmed.edu. (B. Faheem).

https://doi.org/10.55729/2000-9666.1015

2. Case presentation

We report a Case of a 55-year-old Filipino male with past medical history of hypertension (HTN) and type 2 diabetes mellitus (DM) who presented with epigastric pain radiating towards the back, associated with nausea, and vomiting of two days in duration. He had history of alcohol abuse but quit over 10 years ago. Home medications included insulin, metformin, amlodipine and lisinopril. Patient denied any use of herbal supplements, or any other new medications. Physical examination demonstrated a patient in moderate distress, afebrile with temperature 36.8 °C, an elevated blood pressure (BP) of 151/96 mmHg, tachycardia with a heart rate (HR) of 103 beats/min, and tachypnea with a respiratory rate (RR) of 24 breaths/min. His abdomen was non-distended, with epigastric tenderness without guarding. A right upper quadrant ultrasound showed normal gallbladder wall thickness, with no gallstones or sludge, and no pericholecystic fluid. A computed tomography (CT) scan of the abdomen and pelvis with contrast revealed an acute pancreatitis (Fig. 1), without evidence of pancreatic necrosis, but with hepatomegaly and steatosis.

The laboratory parameters were as follows: WBC: 20.7 × 10^9/L, Hb: 17.4 g/dL, Hct: 52.0%, PLT: of 556 K/mcL, glucose: 259 mg/dL, urea: 9 mg/dL, creatinine 0.79 mg/dL, AST: 52 U/L, ALT: 16 U/L, amylase: 58 U/L, lipase: 2270 U/L, triglyceride (TG): 3355 mg/dL, albumin: 4.1 g/dL, calcium: 8.1 mg/dL, HbA1c: 15.7%. The blood gas analyses showed the following: pH: 7.20 mm/Hg, pCO2: 24 mm/Hg, pO2: 79 mm/Hg, HCO3: 9.4 mmol/L and lactate: 1.8 mmol/L. Patient was treated for diabetic ketoacidosis (DKA) with IV Insulin for 2 days, given fluids, and electrolyte replacement. Patient was also diagnosed with acute pancreatitis due to hypertriglyceridemia in the setting of DKA and uncontrolled type 2 diabetes mellitus.

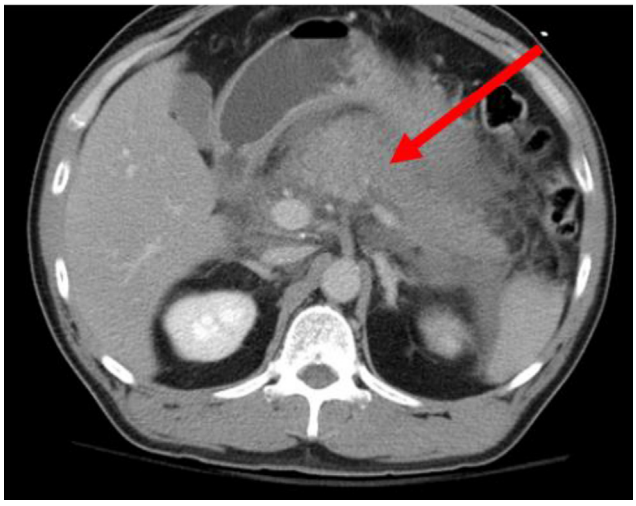

Fig. 1. Acute Pancreatitis. Pancreas is diffusely edematous with prominent. peripancreatic stranding. stranding and fluid which extends into the surrounding mesentery and retroperitoneum with some distal extension along the pericolic gutters. No definite evidence of pancreatic necrosis. No focal fluid collection.

His hypertriglyceridemia was managed with intravenous (IV) regular insulin and heparin drip. The TG levels began trending down. On Day 2 TG: 1773 mg/dL, Day 3: TG: 628 mg/dL, Day 4: 196 mg/dL, Day 5: 245 mg/dL and Day 6: 213 mg/dL. Patient was started on Atorvastatin 40 mg at bedtime daily.

On day 4 patient's white blood cell count increased to WBC: 18.0 × 10^9/L with tachycardia HR 110. A repeat CT scan of the abdomen and pelvis revealed worsening pancreatitis with small areas of low attenuation within the pancreatic parenchyma suspicious for necrosis. A prominent fluid collection was noted anteriorly between the pancreas and the stomach which measured approximately 4.6 × 13.2 × 7.2 cm. Another large fluid collection also developed along the left paracolic gutter measuring 6.2 × 5.0 × 19 cm. In addition, this imaging not only confirmed an early formation of pseudocyst (Fig. 2), but also demonstrated a new occlusion and thrombosis of the splenic vein.

The patient was subsequently started on Lovenox 60 mg twice daily for the splenic vein thrombosis during the remainder of his hospital stay. Patient was discharged on a six-month course of Xeralto 20 mg daily.

3. Discussion

Hypertriglyceridemia (HPTG) can be of primary or secondary types.[5] Current classification of HPTG is based on fasting TG levels and can be divided into moderate (150–1000 mg/dL) and severe (>1000 mg/dL) forms.[6] The primary type of HPTG is genetic or induced by environmental factors.[5] The secondary type of HPTG is a common type of lipid abnormality seen among patients with metabolic syndrome, visceral obesity, type 2 diabetes (T2D), cholelithiasis, alcohol, pregnancy, and medications such as Tamoxifen.[5] Upwards of 50% of patients with T2D have simultaneous HPTG.[6] Among the T2D patients it is the insulin resistance that leads to HPTG with increased peripheral lipolysis and thereby increased free fatty acid (FFA) delivery to the liver.[5]

Acute pancreatitis (AP) is an inflammatory condition of the pancreas presenting with abdominal pain and elevated pancreatic enzymes.[7] Gallstones and alcohol use is associated with approximately two-

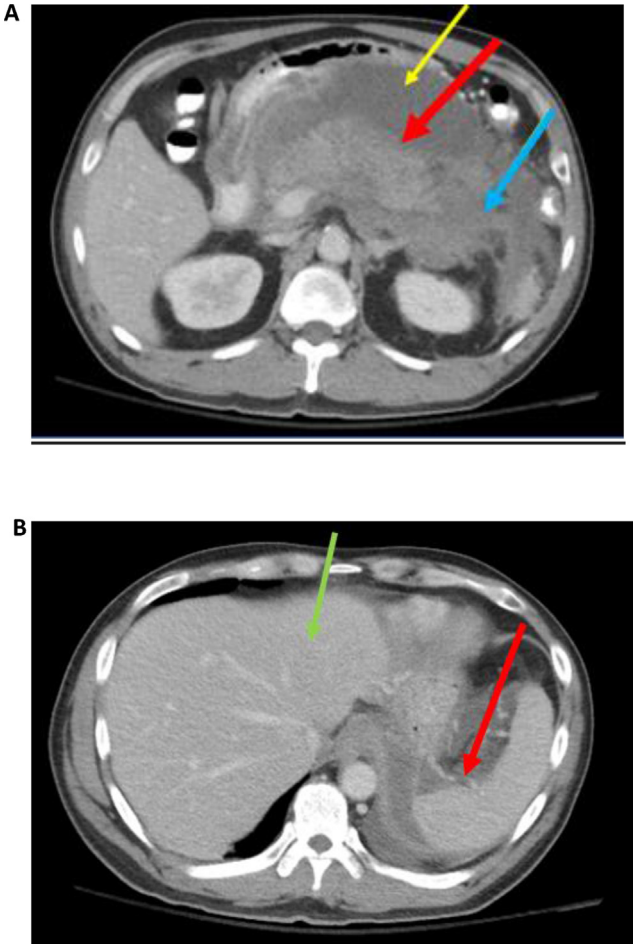

Fig. 2. Severe pancreatitis with (new) occlusion of the splenic vein and new suspected areas of pancreatic necrosis. Prominent increase in peripancreatic fluid and fluid extending along the left paracolic gutter suspicious for early pseudocyst formation. A: Severe pancreatitis (red arrow) with interval increase in peripancreatic fluid collection (yellow arrow), with suspected area of pancreatic necrosis (blue arrow). The fluid collection is seen anteriorly between the pancreas and the stomach which measures approximately 4.6 × 13.2 × 7.2 cm. B: Splenic vein thrombosis.

thirds of cases of pancreatitis. Hypertriglyceridemia (HPTG) is a rare but known cause of AP.[8] HPTG has become the third most common cause of acute pancreatitis (AP). The risk of developing AP increases progressively with increasing serum levels of TG $\geq$ 500 mg/dL. Moderate HPTG is associated with slightly increased risk of developing AP.[6] The risk of developing AP is between 5 and 20% in patients with severe HPTG.[9] The pathophysiology of HPTG-induced AP (HPTG-AP) is still unclear, but it is generally accepted that in the setting of excess serum triglycerides (TG), the pancreatic lipase hydrolyzes the TG leading to a large accumulation of FFA and glycerin within the pancreas.[5] These FFA are mostly unsaturated fatty acids (UFA) which trigger an inflammatory reaction, the release of intracellular calcium, ultimately causing pancreatic acinar necrosis. With elevated serum FFA levels, FFA molecules aggregate into micelles which leads to pancreatic ischemia. The ischemia further triggers acidosis which activates trypsinogen to become active trypsin causing pancreatic auto-digestion, hence AP. In addition, these FFA also directly damage the pancreatic vascular endothelial cells leading to vascular leakage and activation of coagulation cascade.[5] There are various complications of AP that include pseudocyst formation, chronic pancreatitis (CP), pancreatic necrosis, and complications associated with hypercoagulability such as splenic vein thrombosis (SVT).[10] Hypercoagulability in AP can present as mild intravenous thrombosis or disseminated intravascular coagulation (DIC). Diabetes Mellitus (DM) have underlying microvascular complications which may also be associated with increased risk of developing thrombosis.[1] SVT is a rare complication that can be seen in both AP and CP.[11] Splanchnic vein thrombosis consists of 4 types: mesenteric vein, splenic vein, portal vein, and hepatic vein thrombosis.[12]

SVT is defined as "primary" or "secondary," depending on the presence or absence of risk factors. Pancreatitis is the most common cause of splenic vein thrombosis.[11–13] Other causes of SVT include pancreatic cancer, lymphoma, and iatrogenic including post-surgery such as splenectomy, gastrectomy, and splenorenal shunt.[10,11,14] Splenic vein thrombosis in pancreatitis results from inflammation caused due to the anatomic location of the splenic vein along posterior aspect of the pancreas. The etiology is multifactorial – damage by venous compression from enlarged lymph nodes, fibrosis, pseudocysts, or edema.[10] Pancreatitis-induced SVT is reported to have an overall incidence of 14.1%, while its frequency due to HPTG has been recorded as 3.6%.[15,16] Patients may be asymptomatic or symptomatic. Symptomatic patients have upper gastrointestinal bleeding due to esophageal or gastric varices or hypertensive gastropathy. Patients develop a localized form of portal hypertension with SVT where collateral blood flow is formed through splenoportal or gastroepiploic venous system ultimately leading to gastric, esophageal, or colonic varices.[16] These varices may serve as a potential source for gastrointestinal (GI) bleeding, a further complication of SVT. On physical examination, patients may have evidence of ascites and splenomegaly.

Clinicians advise anticoagulation in some patients with acute splenic vein thrombosis, but evidence-based guidelines are lacking. The goal of anticoagulation in this setting is to prevent recurrent

thrombosis, prevent thrombus extension, and promote recanalization. However, while patients are often at risk for recurrent thrombosis, they are also at risk for variceal bleeding. As a result, the decision to start anticoagulation must be made on a Case-by-case basis.

Ninth edition of the American College of Chest Physicians Practice Guidelines recommended treatment with anticoagulants for patients with symptomatic splanchnic vein thrombosis (Grade 1B) but advised against anticoagulation with asymptomatic thrombosis (Grade 2C).[17,18] However, in a study by Tufano. et al. 35, 521 patients with symptomatic splanchnic vein thrombosis had a ratio between VTE recurrence and major bleeding of 5–10, while in 309 patients with incidental splanchnic vein thrombosis, this ratio was 15–16.[19] The authors of this study proposed that patients with incidental thrombosis should be treated with anticoagulants after a careful analysis of risk factors for hemorrhagic complications.[12,19] Splenectomy is the first line treatment in variceal bleeding with splenic artery embolization and percutaneous recanalization available as options for non-surgical candidates.[13]

4. Conclusion

It is important patients with underlying diabetes maintain strict glycemic control to prevent downstream cascade of complications such as diabetic ketoacidosis and hypertriglyceridemia (HPTG). Moderate to severe HPTG can lead to increased risk of developing acute pancreatitis (AP). Both acute and chronic pancreatitis can rarely develop splenic vein thrombosis in the setting of HPTG. Patients with splenic vein thrombosis, if symptomatic, should be treated with anticoagulation. This Case highlights the importance of considering HPTG is the etiology of AP and splenic vein thrombosis as a complication in patients who are diabetic or obese with metabolic syndrome.

Funding

None.

Conflict of interest

All authors declare that there are no conflicts of interest.

References

1. Jialal I, Amess W, Kaur M. Management of hypertriglyceridemia in the diabetic patient. *Curr Diabetes Rep*. 2010; 10(4):316–320. https://doi.org/10.1007/s11892-010-0124-4.
2. US department of health and human services centres for disease control and prevention. *Nat Diab Statist Rep*; 2020. https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.
3. Benoit SR, Zhang Y, Geiss LS, Gregg EW, Albright A. Trends in diabetic ketoacidosis hospitalizations and in-hospital mortality — United States, 2000–2014. *MMWR Morb Mortal Wkly Rep*. 2018;67:362–365. https://doi.org/10.15585/mmwr.mm6712a3external icon.
4. Parhofer KG. Interaction between glucose and lipid metabolism: more than diabetic dyslipidemia. *Diabetes Metab J*. 2015;39(5):353–362. https://doi.org/10.4093/dmj.2015.39.5.353.
5. Guo YY, Li HX, Zhang Y, He WH. Hypertriglyceridemia-induced acute pancreatitis: progress on disease mechanisms and treatment modalities. *Discov Med*. 2019 Feb;27(147): 101–109. PMID: 30939294.
6. Parhofer KG, Laufs U. The diagnosis and treatment of hypertriglyceridemia. *Dtsch Arztebl Int*. 2019 Dec 6;116(49): 825–832. https://doi.org/10.3238/arztebl.2019.0825. PMID: 31888796; PMCID: PMC6962767.
7. Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. *Gastroenterology*. 2019;156:254.
8. Kota SK, Kota SK, Jammula S, Krishna SV, Modi KD. Hypertriglyceridemia-induced recurrent acute pancreatitis: a Case-based review. *Indian J Endocrinol Metab*. 2012;16(1): 141–143. https://doi.org/10.4103/2230-8210.91211.
9. Wang Sheng-Huei, et al. Relationship between plasma triglyceride level and severity of hypertriglyceridemic pancreatitis. *PLoS One*. 11 Oct 2016;11(10), e0163984. https://doi.org/10.1371/journal.pone.0163984.
10. Moosa AR, Gadd MA. Isolated splenic vein thrombosis. *World J Surg*. 1985;9:348, 39.
11. Evans GRD, Yellin AE, Weaver FA, et al. Sinistral (left-sided) portal hypertension. *Am Surg*. 1990;56:758–763.
12. Tafur AJ, Kalsi H, Wysokinski WE, et al. The association of active can- cer with venous thromboembolism location: a population-based study. *Mayo Clin Proc*. 2011;86:25–30.
13. Bernades P, Baits A, Levy P, et al. Splenic portal venous obstruction in chronic pancreatitis. *Dig Sci*. 1992;37:340–346.
14. Madsen MS, Petersen TH, Sommer H. Segmental portal hypertension. *Ann Surg*. 1996;204:72–77.
15. Gündüz Ercan, et al. Acute pancreatitis and splenic vein thrombosis due to hypertriglyceridemia. *Case Rep Gastrointest Med*. 2015;2015:729510. https://doi.org/10.1155/2015/729510.
16. Butler James R, et al. Natural history of pancreatitis-induced splenic vein thrombosis: a systematic review and meta-analysis of its incidence and rate of gastrointestinal bleeding. *HPB: Off J Int Hepato Panc Biliary Assoc*. 2011;13(12):839–845. https://doi.org/10.1111/j.1477-2574.2011.00375.x.
17. Lloret Linares C, Pelletier AL, Czernichow S, et al. Acute pancreatitis in a cohort of 129 patients referred for severe hypertriglyceridemia. *Pancreas*. 2008;37:13.
18. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012; 141(suppl 2):419–494.
19. Tufano A, Ageno W, Di Micco P, et al. Outcomes during anticoagulation in patients with symptomatic vs. incidental splanchnic vein thrombosis. *Thromb Res*. 2018 Apr 1;164:69–74.