IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 7 Ser.18 (July. 2020), PP 38-41
www.iosrjournals.org

Hypertriglyceridemia another Cause of Acute Pancreatitis: A Case Report

DR. PYARA MASIHA TOPNO (MD. MEDICINE)
DR. THAKURMANI (MD. MEDICINE)
Central Hospital, Dhanbad, Jharkhand
Country: India

Abstract
Hypertriglyceridemia (HTG) is a rare but well known cause of acute pancreatitis (AP), after alcohol and gall stone disease. It is alleged to account for up to 10% of all pancreatitis episodes. Studies suggest that in patients with triglyceride (TG) levels>1000 mg/dL (>11.3 mmol/L), hypertriglyceridemia-induced acute pancreatitis (HTGP-AP) occurs in approximately 15-20% of all subjects referred to Lipid Clinics. This can be a life-threatening complication if the degree of HTG is severe enough. It might be primary in origin or secondary to alcohol abuse, diabetes mellitus, pregnancy, or drugs. A serum triglyceride (TG) level of more than 1,000 to 2,000 mg/dL in patients with type I, IV, or V hyperlipidemia (Fredrickson's classification) is the identifiable risk factor. A thorough family history of lipid abnormalities should be obtained, and an attempt to identify secondary causes should be made. HTG-induced AP typically presents as an episode of AP or recurrent AP. Until now, there is no clear evidence which patients with severe HTG will develop pancreatitis and which will not. Underlying pathophysiological concepts include hydrolysis of TG by pancreatic lipase and excessive formation of free fatty acids with inflammatory changes and capillary injury. Additionally hyperviscosity and ischemia may play a decisive role . The clinical course of HTG-induced AP is not different from other causes. . Clinical management of HTG pancreatitis is similar to that of other causes. The mainstay of treatment includes dietary restriction of fatty meal, life style change and lipid-lowering medications (mainly fibric acid derivatives). Insulin infusion in diabetic patients with HTG can rapidly reduce triglyceride (TG) levels. Although there are limited experiences with plasmapheresis, lipid apheresis, heparinization and insulin application, these can support the treatment of HTG- induced AP. Use of apheresis is still experimental and better designed studies are needed to clarify its role in the management of HTG pancreatitis. Control of TG levels to 500 mg/dL or less can effectively prevent recurrences of pancreatitis.

Date of Submission: 17-07-2020 Date of Acceptance: 01-08-2020

I. Introduction

Acute Pancreatitis (AP) is a serious gastrointestinal disorder with various possible etiologies, gall stones and alcohol being the most common. Metabolic, structural, and iatrogenic causes account for 20 – 25% of the cases. Hyperlipidemia in the form of hypertriglyceridemia or chylomicronemia, although less frequent, is one of the well-accepted underlying causes of acute pancreatitis in 7% of the cases — the most common after gall stones and alcohol. Typically hypertriglyceridemia-induced pancreatitis occurs in a patient with a pre-existing lipid abnormality, along with the presence of a secondary precipitating factor (e.g., poorly controlled diabetes, alcohol or medication). The diagnosis of AP requires 2 of the following 3 features: (1) abdominal pain characteristic of AP, (2) serum amylase and/or lipase ⩾3 times the upper limit of normal, and (3) characteristic findings of AP on imaging, particularly computed tomography (CT) scan. The clinical severity of AP is stratified into 3 categories according to the revised Atlanta classification 2012: mild (no organ failure), moderately severe (transient organ failure <48 hours), and severe (persistent organ failure >48 hours).

HTG amounts for approximately 3% of all the causes for AP, main causes being gallstones and alcohol. AP is a well-recognized complication of elevated TG levels. Although the exact mechanism is unknown, there is the view that an elevated cholesterol level alone may not lead to pancreatitis. When serum TGs are elevated above 800 mg/dL, there is invariably chylomicronemia, which may impair circulation in the capillary beds, exposing the chylomicrons to pancreatic lipase, thus damaging the pancreatic acini and microvasculature . The treatment of AP consists of fluid resuscitation, pain management, and nutritional support. Clinical management of HTG pancreatitis is similar to that of other causes. The mainstay of treatment includes dietary restriction of fatty meal, life style change and lipid-lowering medications (mainly fibric acid derivatives). Insulin or apheresis may be given to help lower HTG. We hereby report the case of a 48-year-old Male with a history of dyslipidemia presenting with recurrent episodes of acute pancreatitis.

II. Case Study

A 48-years-old male patient presented in the emergency department (Central hospital Dhanbad) with pain abdomen radiating to the back since two days. The patient had four episodes of bilious vomiting and had fever at the time he came to the hospital. He had similar history in the past . Patient had history of type 2 diabetes, hypertension, and combined dyslipidemia .He was not receiving hypolipidemic agents for last three months against physician's advice . On examination, patient was conscious and febrile . His pulse rate was 100beats/min, and respiratory rate was 18 breaths/min. His blood pressure was 160/90 mm of Hg. He was maintaining saturation in room air. On examination, there was tenderness in the upper abdomen and umbilicus. No free fluid per abdomen clinically. Bowel sounds were sluggish.

On investigating, erect X-ray abdomen was normal. Serum amylase was 380 mg/dL, lipase 902 mg/dL. Total counts were 20,540 cells/cumm with neutrophilia. LFT, Renal function tests , Lactate dehydrogenase and serum calcium were normal. Other investigations were as follows,total cholesterol 750 mg/dl, LDL 250 mg/dl, serum VLDL 430 mg/dl and serum triglyceride of 1055 mg/dL. Liver function tests (LFTs) and serum calcium levels were normal . Fasting blood sugar was 180mg/dl and post prandial blood sugar was 290 mg/dl. Ultrasonography of abdomen showed hepatomegaly with grade 2 fatty infiltration, pancreas appeared diffusely bulky with evidence of peripancreatic inflammatory changes and also showedmild free fluid in paracolic gutter. Ultrasound showed no common bile duct calculi and gallbladder was normal.

Treatment was started with insulin, telmisartan, atrorvastatin, fenofibrate, omega -3-fatty acid , antioxidants and, aggressive intravenous fluid therapy with Opioids for pain control . Infusion of insulin was initiated at a rate of 1 to 2 U/kg/day with 5% dextrose in 100-mL infusion to prevent hypoglycemia. His blood glucose level was ranging between 180 mg/dL and 210 mg/dL (random = 140-200 mg/dL). He never developed hypoglycemia during the duration of insulin infusion. The patient improved significantly with insulin infusion alone along with supportive measures. . The patient was nil per orally (nothing by mouth) initially, and from day 4 of hospitalization, he began tolerating oral feeds in addition to fenofibrate, which was initiated at a dose of 90 mg/day.. His last TG level recorded was 325 mg/dL during the hospital stay, and the patient was discharged after recovery from AP on long-term fenofibrate therapy. The patient was followed-up after 3 months from the time of discharge with the TG level of 200 mg/dL without any further complications. The patient was counseled to continue fenofibrate indefinitely in order to prevent further attacks of AP.

III. Discussion

Acute pancreatitis is defined as inflammation of the pancreas that develops suddenly and can be life-threatening. The incidence of AP in the United States is 40 per 100 000 persons. AP is the leading cause of admissions to the hospital for gastrointestinal-related disorders in the United States as well as many other countries.

HTG, although rare, is the third leading cause of AP after gallstones and alcohol use, and it can cause up to 7% AP cases. Gallstones and alcohol abuse are the two most common causes of acute pancreatitis (AP). Hypertriglyceridemia is an uncommon but a well-established etiology of acute pancreatitis, with a reported incidence of 2-4% [1–3]. National cholesterol Education Program ATP III categorizes triglyceride (TGs) level as normal (<150), borderline high (150-199), high (200-499), and very high (>500 mg/dL) (1 mmol = 88.5736 mg/dL) . Typically, TG levels >800 mg/dL have been associated with AP; however, the level above which AP may occur is unknown and varies with individuals.

The etiology of HTG can be broadly divided into 2 categories: primary and secondary. While primary one causes more severe HTG, it is the interplay of both primary and secondary factors that leads to severe HTG. Severe HTG is commonly seen with familial chylomicronemia syndrome (FCS), primary hypertriglyceridemia, and mixed hypertriglyceridemia also known as Fredrickson Type I, IV, and V, respectively, in pregenomic era. FCS (I) and mixed hypertriglyceridemia (V) lead to more severe HTG and often present early, whereas primary hypertriglyceridemia (IV) presents in adulthood usually precipitated by secondary factor. Common genetic defects leading to severe HTG include lipoprotein lipase deficiency, LPL gene mutation, and Apolipoprotein C II deficiency in addition to mutations in GPIHBP1 (glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1), LMF1, and other genes involved in lipoprotein generation and metabolism . A severe HTG is likely to have monogenic pattern where mild to moderate HTG is likely to have polygenic inheritance . HTG can be primary in <5% of the cases due to genetic causes and more often secondary to other causes such as Diabetes , Obesity pregnancy excess carbohydrate intake hyperthyroidismn alcohol hepatitis sepsis renal failure and Drug such as estrogen glucocorticoids Beta blockers Bile acid binding resins thiazide tamoxifen cyclosporine protease inhibitors and isotretenin .

There are a number of proposed mechanisms by which hypertriglyceridemia can cause pancreatitis. It may be secondary to rapid accumulation of chylomicrons in the pancreatic vasculature . Chylomicrons are the largest lipid-transporting lipoprotein and can form a thrombus plug and obstruct the pancreatic circulation during rapid buildup causing ischemia and acidosis to the organ . The acidic environment may cause premature

activation of trypsinogen leading to autodigestion. Another hypothesis is that it may be secondary to the release of free fatty acids from triglycerides by pancreatic lipase . These pro-inflammatory free fatty acids can induce free radical formation and damage to the pancreas or may in fact cause direct injury through chemical irritation together with lisolecithin . Free fatty acids were found to cause edema and hemorrhage of canine pancreatic glands by Saharia *et al* . Hyperlipidemia induced pancreatitis in pregnancy is believed to be secondary to acute adipose infiltration and fat embolism of pancreatic vessels as a result of fat dissociation by human placental lactogen from the syncytiotophoblasts and release of a substantial aggregate of free fatty acids .

TREATMENT

Initial treatment of hypertriglyceride-induced pancreatitis is no different from treating other causes of pancreatitis (bowel rest, aggressive intravenous hydration, pain control and anti-emetics). A recent study shows that goal-directed hemodynamic management guided by functional hemodynamic parameters such as stroke volume variation, compared to CVP-guided therapy, led to a significantly improved survival, tissue oxygenation, and microcirculatory perfusion, as well as less histopathologic damage in porcine model of severe acute pancreatitis .

Management strategies

Triglycerides should be decreased and maintained at <500mg/dL to prevent progression to pancreatic necrosis and organ failure .As of now, there are no definite guidelines for treating hypertriglyceride-induced pancreatitis but previous case reports and series have shown success with intravenous insulin and/or heparin , and plasmapheresis . Insulin may be considered the first choice with or without heparin in patients with concomitant hyperglycemia, but appears to be slower in action compared with apheresis, which decreases serum triglycerides and decrease symptoms in a very short period of time .

Intravenous insulin ± heparin

Intravenous insulin and heparin administration should be considered in patients with concomitant hyperglycemia . Insulin activate lipoprotein lipase which degrade chylomicrons into glycerol and free fatty acids resulting in rapid reduction of triglyceride levels . Success has been reported using infusion of 5% dextrose with regular insulin (control serum glucose to <200mg/dL) together with 5000 units of intravenous heparin twice daily in decreasing serum triglyceride levels to <500 mg/dL and improve symptoms of pancreatitis within 4 days . Subcutaneous regular insulin dosed at 0.1 unit/kg decreases triglyceride levels within 4 hours but the effect is not sustainable long term . Intravenous insulin is more efficacious than subcutaneous insulin for treating hypertriglyceride-induced pancreatitis.

While insulin has been shown to be effective when used as monotherapy , intravenous heparin does not. Heparin stimulates the release of endothelial lipoprotein lipase and causing an initial rise of the circulating enzyme but is immediately followed by its degradation in the liver resulting in its further depletion and recurrence of hypertriglyceridemia . That is why heparin is recommended only as an adjunct treatment to insulin. The other hand insulin use in non-diabetics has no clear evidence. A single bolus of low molecular weight heparin (Dalteparin) was found to deplete lipoprotein lipase similarly to unfractionated heparin .

Patients with HTG-AP are more likely to develop more profound systemic inflammatory response syndrome and end organ damage than in other types of pancreatitis making therapeutic plasma exchange most beneficial to reduce serum triglyceride levels, as it was proposed that its efficacy is superior especially when there is evidence of shock or end-organ failure due to systemic inflammatory response syndrome .

Fibrates are the mainstay of therapy, they reduce plasma triglyceride levels by up to 50% and raise the high-density lipoprotein (HDL) cholesterol by 20%. They modulate peroxisome proliferator activated receptors-α (PPAR-α) in the liver, with decreased hepatic secretion of VLDL and increased lipolysis of the plasma triglyceride . They also reduce small dense LDL particles and increase HDL .

Statins reduce the cholesterol by inhibiting hydroxylmethylglutaryl CoA reductase, thereby reducing coronary heart disease end points in type 2 diabetes .

Omega-3-fatty acids (eicosapentanoic and docosahexanoic acid) reduce plasma triglycerides by 20% when used in combination with other triglyceride-lowering therapies.

Antioxidant therapies (Selenium, β carotene, vitamin C, α-tocopherol) have been used in the reduction of recurrent pancreatitis episodes that have remained markedly hypertriglyceridemic after medical therapy, by virtue of their protection from free radical-induced acinar damage. Other options include niacin, bile acid binding resins, and glitazar drugs.

IV. Conclusion

Hypertriglyceridemia is a common clinical problem that can be exacerbated by numerous medications and medical conditions. Markedly elevated triglyceride levels can lead to pancreatitis, a serious and potentially fatal complication. General and specific therapy is available to reduce triglyceride levels during the acute phase of pancreatitis, which may improve the outcome. Nutrition, pharmacologic therapy and avoiding agents that can elevate triglycerides may be essential in preventing further attacks.

Bibiliography

[1]. Fortson MR, Freedman SN, Webster PD 3rd. Clinical assessment of hyperlipidemic pancreatitis. Am J Gastroenterol 1995;90:2134-9.

[2]. Lithell H, Vessby B, Walldius G, Carlson LA. Hypertriglyceridemia - Acute pancreatitis - Ischemic heart disease. A case study in a pair of monozygotic twins. Acta Med Scand 1987;221:311-6. 11. Hegele RA. Monogenic dyslipidemias: Window on

[3]. L. Linares, A. L. Pelletier, S. Czernichow et al., "Acute pancreatitis in a cohort of 129 patients referred for severe hypertriglyceridemia," *Pancreas*, vol. 37, no. 1, pp. 13–22, 2008.

[4]. S. Sandhu, A. Al-Sarraf, C. Taraboanta, J. Frohlich, and G. A. Francis, "Incidence of pancreatitis, secondary causes, and treatment of patients referred to a specialty lipid clinic with severe hypertriglyceridemia: a retrospective cohort study," *Lipids in Health and Disease*, vol. 10, article 157, 2011. K. Bessembinders, J. Wielders, and A. van de Wiel, "Severe hypertriglyceridemia influenced by alcohol (SHIBA)," *Alcohol and Alcoholism*, vol. 46, no. 2, Article ID agq088, pp. 113–116, 2011.

[5]. Kimura W, Mossner J. Role of hypertriglyceridemia in the pathogenesis of experimental acute pancretitis in rats. Int J Pancreatol. 1996;20:177–84]

[6]. Yadav D, Pitchumoni CS. Issues in hyperlipidemic pancreatitis. J Clin Gastroenterol. 2003;36:54–62.

[7]. Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Alméras N, et al. Hypertriglyceridemic waist: A marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small dense LDL) in men? Circulation. 2000;102:179–84.

[8]. Hegele RA. Monogenic dyslipidemias: Window on determinants of plasma lipoprotein metabolism. Am J Hum Genet. 2001;69:1161–77 . Vonlaufen A, Wilson JS, Apte MV (2008) Molecular mechanisms of pancreatitis: current opinion. *J GastroenterolHepatol*23:1339-1348. 8.Saharia P, Margolis S, Zuidema GD, Cameron JL (1977) Acute pancreatitis with hyperlipemia: studies with an isolated perfused canine pancreas. *Surgery*82: 60-67

[9]. Qihui C, Xiping Z, Xianfeng D (2012) Clinical study on acute pancreatitis in pregnancy in 26 cases. *Gastroenterol Res Pract* 2012: 271925.

[10]. Nair S, Yadav D, Pitchumoni CS (2000) Association of diabetic ketoacidosis and acute pancreatitis: observations in 100 consecutive episodes of DKA. *Am J Gastroenterol* 95: 2795-2800. Näsström B, Olivecrona G, Olivecrona T (2001) Lipoprotein lipase during continuous heparin infusion: tissue stores become partially depleted. *J Lab Clin Med* 138: 206-213.

[11]. Zhang K, Cox K, Sellers Z (2017) Plasmapheresis for Hypertriglyceridemia-Induced Acute Pancreatitis in a Child: A Case Report and Brief Review of the Literature. *Pancreas* pp: 58-59.

[12]. Barter PJ, Rye KA. Cardioprotective properties of fibrates: Which fibrate, which patients, what mechanism? Circulation. 2006;113:1553–5.

[13]. Rubins HB, Robins SJ, Collins D, Nelson DB, Elam MB, Schaefer EJ, et al. Diabetes, plasma insulin and cardiovascular disease: Subgroup analysis from the Department of Veterans Affairs high density lipoprotein intervention trial (VA-HIT) Arch Intern Med. 2002;162:2597–604.

[14]. Frick MH, Elo O, Haapa K, Heinonen OP, Heinsalmi P, Helo P, et al. Helsinki Heart Study: Primary-prevention trial with gemfibrozil in middle aged men with dyslipidemia.Safety of treatment, changes in risk factors and incidence of coronary heart disease. N Engl J Med. 1987;317:1237–45.

[15]. Gami AS, Montori VM, Erwin PJ, Khan MA, Smith SA Evidence in Diabetes Enquiry System (EVIDENS) Research Group. Systematic review of lipid lowering for primary prevention of coronary heart disease in diabetes. BMJ. 2003;326:528–9.

[16]. Hooper L, Thompson RL, Harrison RA, Summerbell CD, Ness AR, Moore HJ, et al. Risks and benefits of omega 3 fats for mortality, cardiovascular disease and cancer: Systematic review. BMJ. 2006;332:752–60.

[17]. Topol EJ. Intensive statin therapy-A sea change in cardiovascular prevention. N Engl J Med. 2004;350:1562–4.

DR. PYARA MASIHA TOPNO, et. al. "Hypertriglyceridemia another Cause of Acute Pancreatitis: A Case Report." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(7), 2020, pp. 38-41.