

Hypertriglyceridemia-induced recurrent acute pancreatitis: A case-based review

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ABSTRACT

Hypertriglyceridemia is a rare, but well-known cause of acute pancreatitis. A serum triglyceride level of more than 1000 to 2000 mg / dl is the identifiable risk factor. It typically presents as an episode of acute pancreatitis or recurrent acute pancreatitis. The clinical course and routine management of Hypertriglyceridemia-induced pancreatitis is similar to other causes. A thorough family history is important, as is the identification of secondary causes of hypertriglyceridemia. The mainstay of therapy includes dietary restriction of fatty meal and fibric acid derivatives. We hereby report the case of a 37-year-old lady with a family history of dyslipidemia presenting with recurrent episodes of acute pancreatitis. We also review the literature for pathogenesis and management of hyperlipidemia.

Key words: Acute pancreatitis, fibric acid derivatives, hypertriglyceridemia, hyperlipidemia

INTRODUCTION

Acute pancreatitis is a common condition with various possible etiologies, gall stones and alcohol being the most common.^[1] Metabolic, structural, and iatrogenic causes account for 20 – 25% of the cases.^[2] 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.^[3] 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 triglyceride levels of more than 1000 to 2000 mg / dl in patients with type I, III, IV, and V hyperlipoproteinemia (Friedrickson's classification) is the identifiable risk factor.^[4] Genetic factors

determine over 60% of the variability in serum lipids.^[5] The secondary causes of hypertriglyceridemia have to be ruled out. Most patients can be effectively treated with the existing drug therapy. Heparin and insulin have a role to play in the treatment.^[6] Other novel modalities include plasma exchange and lipid aphaeresis.^[7] Here we report a lady presenting with recurrent pancreatitis, with features of hyperlipidemia, and review the literature for pathogenesis and management of hyperlipidemia.

CASE REPORT

A 37-year-old female presented with a chief complaint of epigastric pain for three days. The pain was continuous, radiating to the back, and associated with two episodes of bilious vomiting. She was not receiving hypolipidemic agents for last three months against physician's advice. Four years back she presented with similar complaints and was diagnosed as having acute pancreatitis with type 2 diabetes, hypertension, and combined dyslipidemia. Treatment was started with insulin, telmisartan, atorvastatin, fenofibrate, and a low-fat diet. In between, after stopping treatment on her own, she ended up with two episodes of acute pancreatitis. Laboratory parameters during the previous three presentations are depicted in Table 1. Two of her elder brothers died at the age of 40 to 45 years, because

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Table 1: Laboratory parameters of the patient during the previous three presentations with acute pancreatitis

	Laboratory Parameters		
	22 / 01 / 2007	09 / 04 / 09	26 / 03 / 2010
Triglyceride (mg / dl)	980	2074	1350
Cholesterol (mg / dl)	374	456	408
LDL Cholesterol (mg / dl)	220	258	238
VLDL cholesterol (mg / dl)	104	128	97
Fasting blood sugar (mg / dl)	194	304	270
Post lunch blood sugar (mg / dl)	317	450	380

of coronary artery disease and combined dyslipidemias. One younger sister was also a known case of combined dyslipidemia, on treatment.

On examination, her pulse rate was 120 / minute, blood pressure 150 / 100 mm Hg, respiratory rate 26 / minute, and temperature 101.4⁰F. She was somnolent and dehydrated. There was a markedly tender and rigid epigastrium, with diminished bowel sounds and hepatosplenomegaly. She had arcussenilis and lipemiaretinalis, but no eruptive xanthoma. Initial laboratory findings were a total leukocyte count of 16000 / cmm with 86% neutrophils, platelets 220000 / cmm, and c-reactive protein 17.2 gm / dl. Serum electrolytes, calcium, liver, and renal function tests, and lactate dehydrogenase and coagulation tests were normal. Serum was lipemic. Other investigations were as follows, total cholesterol 741 mg / dl, Low-density lipoprotein (LDL) cholesterol 249 mg / 74 mg / dl, very-low-density lipoprotein (VLDL) cholesterol 416 mg / dl, and triglycerides 2080 mg / dl. Fasting blood sugar (FBS) was 174 mg / dl and post-lunch blood sugar (PLBS) was 286 mg / dl. Ultrasonography of the abdomen showed a grade 1 fatty liver, hepatosplenomegaly with a bulky body, and the tail of the pancreas. Enlarged and edematous pancreas with smooth, ill-defined margins, a non-visualized pancreatic duct, and peripancreatic fat stranding were seen in a computed tomogram of the abdomen [Figure 1]. The patient was conservatively managed with intravenous fluids and narcotics for pain control. On the basis of high triglycerides, cholesterol, and VLDL cholesterol, a diagnosis of type IIb hyperlipoproteinemia (Familial Combined Hyperlipidemia / FCHL) was established. Treatment with fenofibrate 160 mg, atorvastatin 20 mg, and omega-3 fatty acids 2 g, twice daily, with antioxidants was started. After stabilization endoscopic retrograde cholangiopancreatography found no anatomic abnormality. The patient was discharged with insulin, antihypertensive, and hypolipidemic agents.

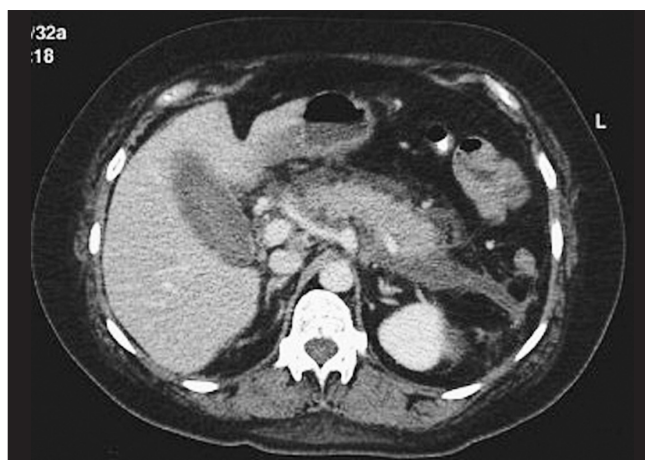


Figure 1: CT abdomen showing enlarged and edematous pancreas with smooth, ill-defined margins, non-visualized pancreatic duct, and peripancreatic fat stranding

DISCUSSION

The association between acute pancreatitis and hyperlipidemia is well known, both as a precipitant and as an epiphenomenon.^[8] The coexistent medical conditions such as diabetes should prompt further workup.^[9] Hypertriglyceridemia can be primary in less than 5% of the cases, due to genetic causes and more often secondary to other causes like diabetes, obesity, pregnancy, excess carbohydrate intake, hypothyroidism, alcohol, hepatitis, sepsis, renal failure, and drugs like estrogen, glucocorticoids, β blocker, bile acid binding resins, thiazide, tamoxifen cyclosporine protease inhibitors, and isotretinoin.^[10]

In our patient, the presence of a family history of dyslipidemia, with laboratory values of high cholesterol, LDL cholesterol, VLDL cholesterol, and triglycerides, led us to the diagnosis of type IIb hyperlipoproteinemia.

Chylomicrons are triglyceride-rich lipoprotein particles. They are present in the circulation when triglycerides are > 10 mmol / l (900 mg / dl). These are large enough to occlude the pancreatic capillaries, leading to ischemia and subsequent acinar structural alteration, as also a release of pancreatic lipase. Enhanced lipolysis leads to an increased concentration of free fatty acids, which results in the release of inflammatory mediators and free radicals culminating in inflammation, edema, and necrosis.^[11] Our patient had a total of four episodes of pancreatitis (each time triglycerides were > 900 mg / dl) after stopping the hypolipidemic agent each time.

Chylomicrons are the product of dietary fat absorption. Therefore, abstinence from eating after pancreatitis may allow rapid metabolism of the triglyceride-rich chylomicrons.^[12] Other non-pharmacological measures

include weight reduction, reduced calories, fat, and refined carbohydrate intake. Our patient was advised to restrict fat to 10 – 15% of total energy intake (about 15 – 20 gm / day) with reduction in saturated fats and unsaturated and trans fats.^[12]

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%.^[13] 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.^[14] They also reduce small dense LDL particles and increase HDL.^[15] Statins reduce the cholesterol by inhibiting hydroxymethylglutaryl CoA reductase, thereby reducing coronary heart disease end points in type 2 diabetes.^[16] Omega-3-fatty acids (eicosapentanoic and docosahexanoic acid) reduce plasma triglycerides by 20% when used in combination with other triglyceride-lowering therapies.^[17] 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.^[18] Our patient had been prescribed a combination of fenofibrate, atorvastatin, omega-3 fatty acids, and antioxidants. Other options include niacin, bile acid binding resins, and glitazar drugs. Novel modalities include the use of medium chain triglycerides (they do not require chylomicron formation for absorption), plasmapheresis,^[13] insulin and heparin,^[19] and lipoprotein lipase gene therapy.^[20]

CONCLUSION

Hypertriglyceridemia is a common clinical problem, and if markedly elevated, can lead to pancreatitis. General and specific therapies are available to reduce triglycerides during the acute phases of pancreatitis. Nutrition, pharmacological therapy, and avoiding aggravating factors are essential for preventing further attacks.

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