CASE REPORT

Hypertriglyceridaemia induced pancreatitis management: A case report

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Abstract

Acute pancreatitis results in high morbidity and mortality. Gallstones and alcoholism are considered leading causes of acute pancreatitis. However, increasing prevalence of obesity, diabetes and lifestyle choices has resulted in Hypertriglyceridaemia induced pancreatitis (HTAP) becoming more common. HTAP is said to be more severe than other causes. The treatment options available vary including intravenous (IV) insulin, heparin, plasma exchange, fibrates, niacin, omega three fatty acids and dietary restrictions. This is a case report of a patient presenting with HTAP and the dilemma treating physicians faced in trying to balance the need for urgent treatment with invasiveness of procedure and paucity of evidence.

Keywords: Hypertriglyceridaemia induced Acute pancreatitis (HTAP), Lipoprotein lipase (LPL), Triglycerides (TG), Deep vein thrombosis (DVT), Systemic inflammatory response syndrome (SIRS), Hypertriglyceridaemia (HTG), Infusions, Intravenous (IV).

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Introduction

Hypertriglyceridaemia (HTG) is the third major cause of acute pancreatitis accounting for about 1 to 35% of acute cases and more than 50% of pancreatitis cases in pregnant females. The risk of developing pancreatitis is 20% in people with a triglyceride (TG) level of more than 2000mg/dl.[1] HTG can be primary or secondary to multiple causes like uncontrolled diabetes, certain medications, excessive dietary fats, refined sugars, nephrotic syndrome, pregnancy, hypothyroidism and alcohol intake. According to some authors, secondary causes are insufficient to cause acute pancreatitis on their own, and an underlying primary disorder should be sought.[2,3]

Primary Hypertriglyceridaemia is either due to genetic mutations in the Lipoprotein lipase gene or mutations in several of its co factors.[4]

For the purpose of definition, triglycerides should be considered as a cause of acute pancreatitis if the TG level is more than 500mg/dl and no other cause can be found.[4] It is suggested that triglycerides are metabolized by pancreatic lipases, both inside and outside the pancreas, leading to free fatty acid formation. Excessive fatty acid formation exceeds the binding capacity of albumin, forming microaggregates which block pancreatic capillaries and give rise to ischaemia, resulting in acute pancreatitis.[1] Also, fatty acids and chylomicrons increase plasma viscosity contributing to ischaemia and triggering pancreatitis.[3] This case report presents a patient with hypertriglyceridaemia induced acute pancreatitis (HTAP).

Case Report

A 51year old diabetic, hypertensive female presented to North West General Hospital Peshawar in July 2022 with a 3-day history of epigastric pain, nausea, vomiting and fever. She was using insulin, dapagliflozin for diabetes and atenolol for hypertension. Her HbA1c was 9.6% (normal below 5.7%) and estimated BMI was 30 kg/m2 (normal 18-22.9 kg/m^2).[5] Her mother had diabetes, but the rest of her history was unremarkable. On examination, she was haemodynamically stable but had tachycardia, tachypnoea, and was maintaining saturation on 3L oxygen via nasal cannula. Her abdomen was distended, with tenderness over epigastrium and absent bowel sounds.

Before presenting to our hospital, she was admitted to a local hospital where an ultrasound showed acute pancreatitis. Her serum amylase and lipase were 646 and 408 U/L with normal lab ranges of (0-98) and (0-51) U/L respectively. She fulfilled the revised Atlanta criteria (6) for the diagnosis of acute pancreatitis, which requires any two of the following 1-epigastric pain 2-raised pancreatic enzymes three times greater than normal lab values and 3-radiological findings consistent with acute pancreatitis to be present. Her renal functions were normal and liver function tests were not suggestive of gallstones as a likely cause.

Her ultrasound did not reveal any dilated intra or extra hepatic biliary channels. CT abdomen also had similar findings, with a severity score of 8/10, a small necrotic area in the head of pancreas and fluid collection in abdomen (figure A). On further investigation, her serum lipid profile showed grossly elevated triglyceride level in blood of more than 5000 mg/dl (Normal less then 150 mg/dl). Family history of dyslipidaemias and premature cardiovascular events was negative. She denied ever been told by doctors

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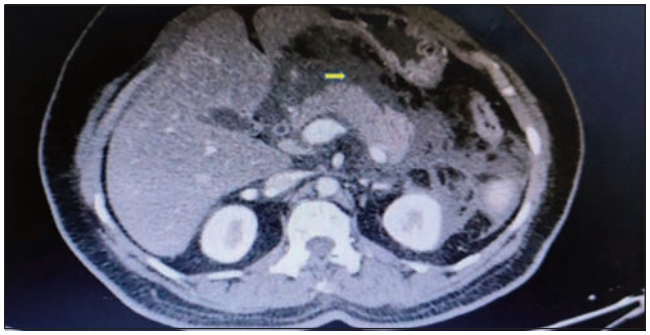

Figure-A: CT scan of patient showing pancreatic oedema, peri-pancreatic fluid collection.

Figure-B: Lipaemic serum removed during plasma exchange.

about her high blood lipids levels. Her labs showed hypocalcaemia with ionized calcium levels of 2.8 mg/dl (normal 4.5-5.4 mg/dl) and hypomagnesaemia serum magnesium level 1.48 (normal 1.58-2.55 mg/dl). Her ECG showed QT interval prolongation.

She was immediately administered IV fluids, pain relief, and Venous thromboembolism prophylaxis. For hypertriglyceridaemia, she was started on IV insulin infusion and dextrose. IV calcium and magnesium replacements were given. After 24 hours, serum triglycerides were reduced to 2500 mg/dl, but were still higher than the acceptable level of 1000 mg /dl. Serum calcium was still low and patient was tachycardiac and tachypnoeic, though haemodynamically she remained stable.

Her blood glucose level on arrival was 232 mg/dL. She was started on regular insulin at a rate of 6 units per hour and dextrose 5% infusion at 100 ml per hour. Her insulin was tapered gradually to 1 unit per hour as her blood glucose started declining. The insulin infusion was finally stopped, when her blood glucose reduced to 88mg/dL. Patient's persistent symptoms of systemic inflammatory response and continuously lowered serum calcium levels prompted the need for a more aggressive strategy, in order to prevent the progression of acute pancreatitis to a fulminant course. The patient and her family were counselled and a single session of plasma exchange was performed (figure B). This resulted in a reduction of triglyceride levels to less than 1000 mg/dl, after which, the patient showed symptomatic improvement in her tachycardia and tachypnoea. She was started on oral gemfibrozil and was advised to avoid fat intake. Her serum calcium normalized and remained stable in next four days, after which she was discharged home. A two week follow up via phone showed that she was healthy with no active problems.

Discussion

Management of triglyceride induced pancreatitis is based on severity. Most of the patients can be managed with insulin infusion. Insulin enhances the activity of lipoprotein lipase which metabolizes and reduces triglycerides. The dose of insulin required is 0.1 to 0.3 units per kg, which may lower serum glucose rapidly and therefore needs to be given with adequate glucose replacement. Studies suggest that the insulin dose should be adjusted according to change in serum triglyceride levels rather than serum glucose levels for optimal triglyceride lowering response to take place. This can be difficult to achieve, as was in the case of our patient.[1,2]

Other therapies like heparin have little value due to only transient improvement in serum Lipoprotein Lipase levels.[7] According to some authors,[8-10] triglycerides do not directly cause injury to pancreatic tissue but the free fatty acids derived from metabolism of triglycerides are actually responsible for pancreatic injury. But since free fatty acids are not routinely measured, triglycerides level is the option in assessing pancreatitis caused by hypertriglyceridaemia.[8]

Plasma exchange is used for HTAP in situations where there are worsening inflammatory signs like tachycardia, tachypnoea and persistent hypocalcaemia.[2] According to some studies, plasma exchange does not have additional triglyceride lowering effect any quickly than IV insulin and so does not affect mortality.[9,11] These studies are mostly limited by their retrospective nature and small sample size. In this patient, a single session of plasma exchange was able to reduce triglyceride levels to below 1000 mg/dl.

First use of apheresis for the treatment of hypertriglyceridaemia was reported in 1978. It is said to have a temporary effect and other measures should be instituted to control and maintain triglyceride levels in normal ranges. Some studies suggest that plasma exchange needs to be performed every few weeks where issue is noncompliance and non-responsiveness to routinely used therapies.[7,9] Additionally, apheresis also removes the proteases responsible for systemic inflammation. However, whether this confers any additional benefit is unknown.[9] Most studies consider plasma exchange to be expensive and associated with adverse effects of catheter placement like bleeding,

infection, thromboembolism, volume load or depletion, coagulation abnormalities and electrolyte disturbances. But this should be weighed against the potential complications of severe acute pancreatitis.[4,8]

It is also observed that patients who are diabetic, obese, and have a very high baseline serum triglyceride levels have slower response to IV insulin, thereby necessitating plasma exchanges in these patients.[1]

Also, persistent symptomatic hypocalcaemia and signs of SIRS, like tachycardia and tachypnoea, are red flags to consider aggressive management strategies. The rapidly progressive nature of acute pancreatitis and its propensity to become fulminant should be taken in to account while suggesting management options.

The level of triglycerides has direct correlation with the incidence rate of acute pancreatitis; a single episode predisposes the patients to further attacks of pancreatitis at lower triglyceride levels. As a result of increasing prevalence of obesity and diabetes, hypertriglyceridaemia as a cause of pancreatitis will supersede other causes like gallstones and alcoholism.[12] Patients with diabetes may have coexisting Diabetic Keto Acidosis (DKA) with pancreatitis and may create confusion in diagnosis, especially if the history of prior diabetes is unknown. The preferred treatment in coexisting DKA and HTAP is insulin therapy if it can lower triglyceride levels in an appropriate time frame.[4] The decision to do plasma exchange, and its timings are highly individualized.

Although therapeutic plasma exchange should not be used as a first line treatment option in HTAP, it should be considered early in patients with suboptimal response to the first line therapy or rapidly progressive and persistent symptoms. Ionized serum calcium, tachycardia, tachypnoea should be used as a guide to timely therapy initiation. The severity of hypertriglyceridaemic pancreatitis is said to be greater than that caused by alcohol or gallstones.[4] Also, all patients having HTAP should undergo genetic testing. In this patient beta blockers may also have contributed to the development of hypertriglyceridaemia. Human genetic research has resulted in a plethora of treatments available for hypertriglyceridaemia. Notable options are lipoprotein lipase gene therapy (Glybera), microsomal triglycerides transfer protein inhibitor (lomitapide), diacylglycerol acyl transferase inhibitors (predigastat) and omega three fatty acids (epanova, vascepa) etc.[13] A clinician should be familiar with the availability and side effect profile of these novel agents.

Conclusion

Hypertriglyceridaemic pancreatitis may increase in incidence due to rising prevalence of diabetes and life style choices. Since pancreatitis has a high potential for deterioration, plasma exchange can be considered as a therapeutic option in patients not responding to medical therapy, provided a certain set of criteria are met.

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