Pancreatitis Secondary to Hypertriglyceridemia: A Case Report

Hipertrigliseridemiye Sekonder Pankreatit: Olgu Sunumu

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ABSTRACT

Acute pancreatitis is a very common inflammatory condition of the pancreas. Most cases of acute pancreatitis are caused by either biliary stones or alcohol. However, another common but often under looked cause of pancreatitis is hyperlipidemia, specifically, hypertriglyceridemia. We aimed to present the case of a 45 year old gentleman with a history of familial hyperlipidemia who presented with severe acute pancreatitis. On the presentation of the patient, the lab was unable to process his blood sample due to the severity of his hyperlipidemia. After treatment was initiated with intravenous insulin lab, investigations showed severe hypertriglyceridemia. He denied smoking and drinking alcohol. His medications include atorvastatin, fenofibrate, omega-3, and insulin however he was poorly compliant with his medications. He has no known allergies and denies any previous surgical procedures. His family history was significant for hypertriglyceridemia and diabetes in his father and uncle. The patient responded very well to therapy with insulin infusion and his triglyceride levels started to trend down over the course of admission. His clinical status improved as well and he was discharged asymptomatic and doing well five days after admission. We will discuss this case followed by the different treatment modalities for hypertriglyceridemia induced acute pancreatitis.

Keywords: *Pancreatitis, hypertriglyceridemia, insulin, plasmapheresis*

ÖZ

Akut pankreatit, pankreasın çok yaygın enflamatuar bir durumudur. Akut pankreatit vakalarının çoğu safra taşları ya da alkolden kaynaklanır. Bununla birlikte, pankreatitin yaygın, ancak sıklıkla gözden kaçan başka bir nedeni hiperlipidemi, özellikle hipertrigliseridemidir. Şiddetli akut pankreatit ile başvuran ve ailesel hiperlipidemi öyküsü olan 45 yaşında erkek olgu sunmayı amaçladık. Hastanın başvurusu esnasında, hiperlipidemisinin ciddiyeti nedeniyle laboratuvar tarafından kan örneği çalışılamadı. İntravenöz insülin ile tedaviye başlandıktan sonra laboratuvar incelemeleri sonucunda şiddetli hipertrigliseridemi saptandı. Hastanın sigara ve alkol kullanma öyküsü yoktu. İlaçları arasında atorvastatin, fenofibrat, omega-3 ve insülin bulunuyordu. Bilinen bir alerjisi yok ve daha önceki herhangi bir cerrahi işlem yapılmamıştı. Aile öyküsü, babası ile amcasında hipertrigliseridemi ve diyabet olması açısından önemliydi. Hasta, insülin infüzyonu ile tedaviye çok iyi yanıt verdi ve trigliserid düzeyleri, hastaneye yatış sırasında düşmeye başladı. Klinik durumu düzeldi ve semptomları geriledi. Yatışından beş gün sonra iyileşti. Bu vakayı takiben hipertrigliseridemiye bağlı akut pankreatitin farklı tedavi yöntemlerini tartışacağız.

Anahtar Kelimeler: *Pankreatit, hipertrigliseridemi, insülin, plazmaferez*

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INTRODUCTION

Acute pancreatitis is an acute inflammatory damage of the pancreas causing various degrees of involvement both of adjacent and distant organ systems (1). It originates within the pancreatic acinar cells leading to necrosis, systemic inflammatory response syndrome (SIRS), and eventually multi-organ failure (2). The incidence of acute pancreatitis ranges from five to thirty cases per 100.000 worldwide (3). The two most common etiologies are biliary stones (40-70%) and alcohol (25-35%) (4). Other causes include metabolic, structural, and iatrogenic etiologies (5). Reports showed that hyperlipidemia is the most common cause of acute pancreatitis that is not due to gallstones or alcohol, causing up to 4-5% of all cases of acute pancreatitis (6). Furthermore, it has been reported that acute pancreatitis occurs in up to 12-38% of patients with hyperlipidemia (1).

For the diagnosis of hypertriglyceridemic pancreatitis (HTG-AP) to be made, serum triglyceride levels have to be above 15 mmol/L (6). For a patient to have such levels of triglycerides, most will have a form of primary or genetic defect in lipid metabolism (7). The possible mechanism for HTG-AP involves hydrolysis of triglycerides by pancreatic lipase and release of free fatty acids leading to the development of damage on the acinar cells and microvascular membranes (5,6). However, the detailed mechanism of HTG-AP remains poorly understood (8). Clinical manifestations of HTG-AP are similar to those of acute pancreatitis due to other causes (1). It is critical to perform an early evaluation and rapid treatment for HTG-AP cases due to the high mortality rate and systemic complications (9).

We present the case of a middle aged patient with type II diabetes mellitus known to have familial hypertriglyceridemia who presented with acute pancreatitis.

CASE REPORT

A 45-year-old gentleman with a background of type II diabetes mellitus and familial hypertriglyceridemia presented in the Emergency Department complaining of left sided stabbing abdominal pain radiating to the back that started 3 hours prior to his presentation. His symptoms were associated with nausea but no vomiting. No diarrhea, fever, shortness of breath, dysuria or other significant symptoms. He mentioned having a similar episode about six years ago where he was diagnosed with acute pancreatitis and treated medically.

He denied smoking, drinking alcohol, or illicit drug use. His medications include atorvastatin, fenofibrate, omega-3, and insulin however he was poorly compliant with his medications. He has no known allergies and denies any previous surgical procedures. His family history was significant for hypertriglyceridemia and diabetes in his father and uncle.
On physical examination he was vitally stable, alert and oriented. He had evident xanthelasma. He seemed uncomfortable due to pain. On abdominal examination, he had severe epigastric tenderness. Otherwise, the abdomen was soft with no evidence of rebound tenderness or Rovsing's sign. No organomegaly was detected and bowel sounds were normal.

The blood sample sent for investigation could not be processed by the laboratory as the sample was hyper-lipemic. Plain computed tomography (CT) of the abdomen (Figure 1) revealed peri-pancreatic fat stranding near the tail and distal body with no other remarkable findings. An ultrasound scan of the abdomen was done to rule out biliary causes of pancreatitis and it was found to be normal.

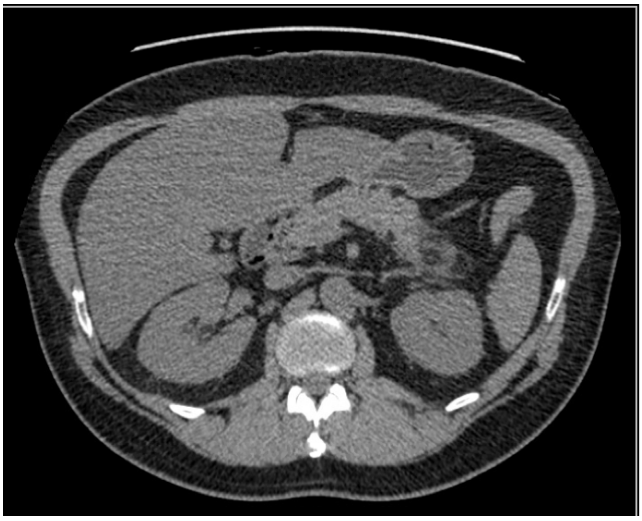

Figure 1: Plain computed tomography of the abdomen

At this point the patient was admitted for evaluation and management of acute pancreatitis, most likely secondary to hypertriglyceridemia in view of his hyper-lipemic blood sample. He was started on insulin infusion at a slow rate to maintain blood glucose levels between 8-12 mmol/L alongside intravenous hydration with dextrose replacement if glucose levels drop below 10 mmol/L. His blood glucose levels were being monitored hourly and the triglyceride levels were being repeated every 12 hours to assess the progress of his condition. The decision was made to discontinue fenofibrate at the time being as the medication itself predisposes to acute pancreatitis however his other medications were continued. Apheresis/plasma exchange were considered initially but the decision was made to reserve

them in case of any deterioration in his condition or development of multi-organ dysfunction.

His laboratory investigations done the following day (Table 1) showed evidence of severe hypertriglyceridemia in addition to hypercholesterolemia, hyperglycemia, and hypernatremia. His lipase level was significantly elevated as well. CT abdomen with contrast with a pancreatic protocol showed mild to moderate peri-pancreatic inflammatory changes with no fluid collections (Figure 2).

Table 1. Initial blood investigations

Parameter	Value	Normal Range
Sodium (mmol/L)	127	136-145
Potassium (mmol/L)	3.55	3.4-5.1
Creatinine (micromol/L)	40	62-106
Urea (mmol/L)	1.8	2.8-8.1
Amylase (IU/L)	41	28-11
Lipase (IU/L)	242	13-60
Total Protein (g/dL)	64	6.6-8.7
Albumin (g/dL)	33	3.5-5.2
Total Bilirubin (micromol/L)	6.6	<21
Direct Bilirubin (miromol/L)	4.7	<5
Alkaline Phosphatase (IU/L)	76	40-129
aspartate aminotransferase (IU/L)	27	<40
Alanine aminotransferase (IU/L)	21	<41
Total Cholesterol (mmol/L)	15.3	3.9-5.2
High Density Lipoprotein (mmol/L)	0.41	1.1-1.6
Low Density Lipoprotein (mmol/L)	Unreportable	
Triglycerides (mmol/L)	40.5	0.5-1.7
Cholesterol/HDL Ratio	37.39	<4.5
Glycated hemoglobin/hemoglobin A1c	9.7	4.6-6.2
Thyroid Stimulating Hormone (milli IU/L)	2.53	0.27-4.2
Glucose (mmol/L)	13	3.9-6.1
Hemoglobin (g/L)	15.8	131-172
Platelets (x109/L)	260	140-400
White Cell Count (x109/L)	14.4	4-11
C Reactive Protein (mg/dL)	88	<5

The patient responded very well to therapy with insulin infusion and his triglyceride levels started to trend down over the course of admission (Figure 3). His clinical status improved as well and he was discharged asymptomatic and doing well five days after admission. He was discharged on omega 3, metformin, atorvastatin, insulin, and niacin. It was decided to not continue fenofibrate due to its pancreatitis inducing properties. He was seen for follow up in the endocrinology clinic and he was doing well with no further complications.

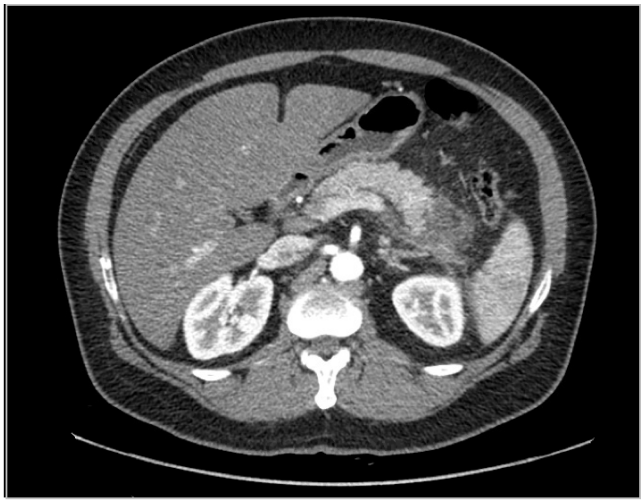

Figure 2: CT Abdomen with IV Contrast

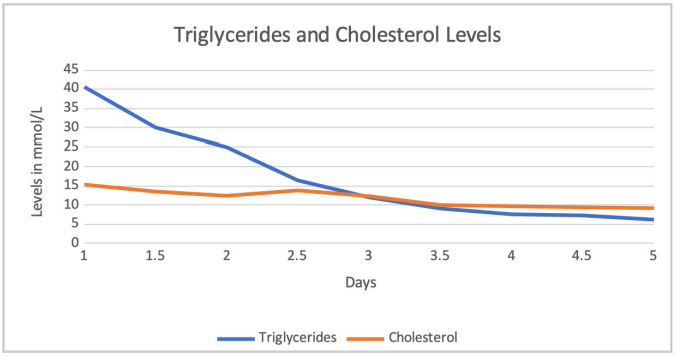

Figure 3. Triglyceride and Cholesterol levels during the course of admission

DISCUSSION

It is clearly evident that hyperlipidemia is an important clinical problem that should always be considered in the differential diagnosis of acute biliary pancreatitis. Hyperlipidemia has been linked to pancreatitis both as a casual or precipitating factor, and as an associated phenomenon (1,5). It is very unusual for HTG-AP to occur with triglyceride levels below 15-20 mmol/L (6). However, mild elevations in triglyceride levels are very common during the early phase of acute pancreatitis secondary to any etiology (7). Hypertriglyceridemia has been reported to be the causative factor in at least 5-7% of cases of acute pancreatitis, and failure to consider and investigate it as a cause may lead to delay in management (10).

Though the clinical presentation of HTG-AP is usually similar to pancreatitis due to other causes, studies showed that when caused by hypertriglyceridemia, patients tend to have a higher risk of developing edematous necrotizing pancreatitis (11). Furthermore, a recent study showed that patients with HTG-AP are usually younger and have higher chances of developing SIRS followed by cardiopulmonary and renal insufficiency (12). Moreover, another retrospective analysis showed that patients with HTG-AP have higher chances of being males, consume high fat diets, have higher body mass index, and have a higher prevalence of multiple organ dysfunction (13).

Though the detailed mechanisms involved in HTG-AP are not very clear, several ideas have been postulated (8). Chylomicrons, which are triglyceride rich lipoprotein particles, usually become present in the circulation with serum triglyceride levels above 10 mmol/L, and these particles are believed to be responsible for pancreatic inflammation. They can affect circulatory flow in capillary beds, resulting in ischemia which may disturb the acinar structure and expose these chylomicrons to pancreatic lipase (14). This leads to hydrolysis of triglycerides and release of free fatty acids which damage the acinar cells and microvascular membranes, resulting in release of inflammatory mediators which cause necrosis, edema, and inflammation (5,6).

Since HTG-AP may be more severe, it is important to establish the diagnosis and initiate management rapidly. Though no standardized treatment protocol is established for HTG-AP, several treatment options are available including oral lipid-lowering agents, intravenous insulin with or without heparin, and plasmapheresis (15). The main goal of therapy in HTG-AP is to rapidly lower serum triglyceride levels and contain the systemic inflammatory response (16). Both heparin and insulin stimulate the activity of lipoprotein lipase leading to acceleration of chylomicron degeneration. This not only leads to improvement in microcirculation, but it prevents neutrophil activation (17). Furthermore, the safety and effectiveness of insulin therapy in these patients has been demonstrated in multiple studies (18).

Plasmapheresis can be very effective in direct removal of chylomicrons. Another treatment option that has proven its effectiveness is short time veno-venous hemofiltration which lowers tumor necrosis factor-α levels and increases IL-10 levels in the circulation (17). A prospective randomized controlled trial found high volume hemofiltration to be superior to insulin combined with heparin, however this therapy is very expensive and poses at least a 100-fold cost increase over insulin therapy (19).

After resolution of the acute illness, therapy should concentrate on preventing recurrence by control of triglyceride levels. It is important to control secondary medical conditions including diabetes mellitus and hypothyroidism. Hypertriglyceridemia not controlled with a low fat diet should be managed with lipid lowering agents. The drugs of first choice are fibric acid derivatives such as fenofibrate and gemfibrozil as they are well tolerated and are highly effective. Another effective and less expensive option is niacin which could be taken alone or in combination with a fibrate, however its use may be limited due to side effects including flushing and hepatic transaminitis. For refractory cases, omega-3 fatty-acid products may be used as adjunctive therapy (20).

CONCLUSION

Hypertriglyceridemia is an important cause of acute pancreatitis that should be pursued in the differential diagnosis of acute non-biliary pancreatitis. Acute management is very important in order to reduce complications and mortality. Several treatment modalities are present; the combination of heparin and insulin was found to be effective in acute management, however long term outcomes need more research. Plasmapheresis is a very effective treatment modality however it is very expensive and its effect is transient. Lifestyle modification and lipid lowering therapy are very important for prevention of recurrence of HTG-AP.

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