Acute pancreatitis secondary to hypertriglyceridemia: report of two cases

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ABSTRACT

Acute pancreatitis is a reversible inflammatory process. Hypertriglyceridemia as a cause of acute pancreatitis reaches frequencies of 1.3-11% according to the literature when triglyceride levels reach values over 1,000 mg/dl; nevertheless hypertriglyceridemia is observed in 12-39% of acute pancreatitis cases as an associated factor.

The objective of medical treatment is to increase lipoprotein-lipase activity, and to increase chylomicron breakdown thus diminishing serum triglycerides to levels smaller than 500 or even 200 mg/dl (when possible) using a variety of strategies including insulin administration.

In the present article, we report two cases of severe pancreatitis induced by hypertriglyceridemia that were managed with insulin infusion; both responded adequately, as measured by a significant reduction of triglyceride levels at 48 hours post-treatment.

Key words: Pancreatitis. Hypertriglyceridemia. Hyperlipidemia.

INTRODUCTION

Acute pancreatitis is a reversible clinical condition that may affect only the pancreas or have a multisystemic impact. Clinical stages range from mild to severe. The final stage presents with a high mortality rate –between 10.0 and 30.0% according to the presence of sterile necrosis or infection (1).

The etiology of acute pancreatitis is diverse. However, main causes include cholelithiasis and alcohol consumption (2). Hypertriglyceridemia is a less common factor related to acute pancreatitis. Its prevalence is between 1.3 and 11.0% when serum levels reach over 1,000 mg/dL. Nevertheless, hypertriglyceridemia is associated with acute pancreatitis in 12.0 to 39.0% of all cases. Reported cases show other less common causes of pancreatitis including metabolic, vascular, mechanical, infectious, and idiopathic factors.

Patients with type-I, -IV or -V hyperlipidemia, according to Fredrickson’s classification, have a higher risk for acute pancreatitis when serum triglyceride levels are not controlled (3).
The present article reports two clinical cases of severe acute pancreatitis related to hypertriglyceridemia. These cases were treated with insulin therapy and a good clinical outcome was observed. In addition, the article reviews some available therapeutic options for this diagnosis.

**CASE 1 REPORT**

A 32-year-old female patient was in an intensive care unit for twelve days due to non-irradiated epigastralgia for one day. This pain did not improve with ranitidine treatment. An emergency clinical evaluation found hyperamylasemia and hypertriglyceridemia (5,080 mg/dL). Liver and biliary ultrasounds found no abnormality. Intensive care unit treatment was necessary due to grade-III dehydration, systemic inflammatory response syndrome (SIRS), and severe pain. This woman had history of obesity and dyslipemia controlled with lovastatin 20 mg/day. She irregularly took gemfibrozil and homeopathic substances (espiruline and apple vinegar). She had used oral contraceptives for twelve years.

Important clinical-physical findings were somnolence, tachycardia, and tachypnea. The abdomen was soft, with pain in the epigastric area without peritoneal irritation. Physical examination revealed no other significant sign. Blood pressure was 114/70; heart rate, 105 per minute; breathing rate, 28 per minute; oxygen saturation, 90%; and body mass index, 32.5. A diagnosis of acute pancreatitis associated with hypertriglyceridemia was done. She reached a basal APACHE score of 11 points, and after 24 hours of 5 points. An abdominal contrast CT scan revealed a Balthazar E acute pancreatitis with less than 30% necrosis (Fig. 1).

A multidisciplinary management was proposed. Gastrointestinal follow-up and nutritional support were programmed. Insulin was administered. A significant decrease in serum triglycerides was obtained after 48 hours (from 5,080 to 369 mg/dL). After seven days, leukocytosis, tachycardia, and C-reactive protein (CRP) above 16 mg/dL were observed. Then, meropenem was prescribed. After two days with this treatment clinical improvement was significant (no pain, fewer leukocytes and neutrophils), and the patient was moved to a lower-level care unit.

**CASE 2 REPORT**

A 38-year-old woman was admitted to the emergency room. She suffered from epigastric and mesogastric abdominal pain. Pain had set on 12 hours before with irradiation to the back, bile emesis, dyspnea, general discomfort, and no fever. Three weeks before she had looked for medical help, and reported respiratory symptoms after fat-rich foods. She had a history of recent hypothyroidism without treatment, mammoplasty, lipectomy, and cesarean section.

Baseline evaluations found an anxious, painful, somnolent patient. Vital signs included: BP 109/60; cardiac rate, 109 per minute; respiratory rate, 20 per min; body temperature, 37.8 °C; oxygen saturation, 94%. Relevant clinical findings included pallor, dry oral mucosa, and limited thoracic movement because of pain with basal hypoventilation. The abdomen was distended and soft, peristalsis was present, and deep-palpation tenderness was found at the epigastric and mesogastric regions, without peritoneal irritation.

Serum analyses reported 18.9 g of hemoglobin; 44.3%, hematocrit; 14,000 leukocytes (70% neutrophils; 22% lymphocytes; and 7% monocytes); 252,000 platelets; sodium 124 mEq/L; potassium 3.37 mEq/L; chloride 100 mEq/L; calcium 0.86 mmol/L; magnesium 1.9 mg/dL; creatinine 0.58; BUN 7.4; human chorionic gonadotropin; 130 mg/dL; and amylase 537. Serum was lipemic in appearance and coagulation tests were normal.

Abdominal ultrasounds revealed increased periporal echogenicity, an enlarged pancreas, and diffuse echogenicity. Peripancreatic liquid was found without biliary lithiasis. Acute pancreatitis was diagnosed and clinical evaluation was continued to clarify a potential etiology. Pain treatment and hydration did not improve the clinical condition. For hypotension, somnolence, and low urination treatment in a critical care unit was started. Dopamine and norepinephrin were necessary to control blood pressure, and morphine to control pain. Other laboratory tests included C-reactive protein 6.5 mg/dL; total cholesterol, 1,029 mg/dL; triglycerides, 7,508 mg/dL; and lipase, 6,660 U/L. Arterial blood gases reported pH: 7.33; PO₂, 77%; PCO₂, 26; HCO₃; 13; and BD; -10.

Hypertriglyceridemia was considered the etiological factor of acute pancreatitis, and insulin infusion (2 U per hour) was started. The baseline APACHE index was 19 points, which suggested severe acute pancreatitis. After a
24-hour treatment, the clinical condition’s outcome was detrimental, with APACHE index reaching 38 points.

After 12 hours of insulin infusion, serum triglycerides were 2,224 mg/dL, and total cholesterol was 674 mg/dL. After five days of treatment these levels were back in their normal range (Fig. 2).

The patient had respiratory failure that needed endotracheal intubation and mechanical ventilation. After 48 hours intraabdominal hypertension was observed (32 mmHg), with acute renal failure and respiratory distress syndrome. Emergency laparostomy showed pancreatic edema with necrosis areas. A peritoneal lavage was performed with no complications.

Given the multisystemic involvement intravenous meropenem (1 g every 8 hours and immunomodulating therapy (human immunoglobulin 5%, Pentaglobin®, 16.8 ML C/1 hour) were given.

Peritoneal lavage was required on six occasions. A vacuum-assisted closure system was applied. Enteral nutritional support and blood derivative transfusion were necessary.

At eight days after admission clinical and hemodynamic improvement was clear. On day 10 she was extubated successfully. On day 15 another peritoneal lavage was performed, and a peritoneal fluid sample was sent to the laboratory. In this sample oxacillin-resistant S. epi-
**Pathophysiology**

Several mechanisms have been described to explain acute pancreatitis in patients with hyperlipidemia. The first one is direct damage to pancreatic tissue by fatty acids. Fatty acids are non-toxic because albumin transports them; but in the presence of hypertriglyceridemia a high level of free fatty acids is observed. Endothelial lipase degrades them and increases pancreatic lyssolecithin activity (9).

A second explanation is related to chylomicrons. These lipids may damage distal pancreatic blood circulation, thus inducing ischemia (described in patients with type I hyperlipidemia). This change alters acinar function and exposes pancreatic tissue to triglycerides, thus activating pancreatic lipase. This activity induces inflammation and sustained pancreatic enzyme activity. Additionally, a high concentration of free fatty acids reduces pH. Decreased pH may activate trypsinogen.

A third explanation is genetically decreased lipoprotein lipase activity. This problem is generally a recessive autosomal condition. Muscle and fat tissue synthesize this enzyme. After synthesis it is transported to the capillary endothelium in order to reduce chylomicrons. Chylomicrons have high levels of triglycerides. Moreover, this enzyme hydrolyzes lipoproteins with high levels of triglycerides to fatty acids and glycerol. These substances are carried to the liver, muscle, myocardium, and fat cells. Lipoprotein lipase deficiency induces impaired plasmatic chylomicron breakdown (10).

Other alterations may involve lipoprotein metabolism. Hypothyroidism deteriorates lipoprotein metabolism and LDL receptors. This action predisposes to elevated serum lipoprotein, and increases the risk for pancreatitis if thyroid function worsens or higher levels of thyroid hormones are needed.

**Management**

The treatment of hypertriglyceridemia is indicated in induced pancreatitis by this etiology as well as in pancreatitis due to other causes, like those of biliary origin. No standard treatment has been described for this disease. Little information is available, the majority as case reports; as this is an infrequent pathology, management guidelines are scarce (11). Additional studies are needed to standardize available recommendations.

Bearing in mind the above-mentioned limitations, treatment is conservative and seeks to decrease triglyceride levels and prevent complications such as multorgan dysfunction or sepsis. Treatment objectives include increasing lipoprotein activity and chylomicron breakdown, and decreasing plasma triglyceride levels below 500 or 200 mg/dL if possible with several strategies.

Fasting has an important role for acute pancreatitis secondary to hypertriglyceridemia. Fasting increases chylomicron and triglyceride metabolism, whose main source is fat-rich food. Treatment reduces serum levels within three days, as in the present cases. Some reports describe accelerated reductions within 24 hours. However, high levels may be found after 15 days when baseline levels were very high, according to etiology.

Therapeutical options include insulin, heparin, plasmapheresis, and apoprotein c2. Insulin and heparin are most used and described because of widespread availability (Table I). Insulin and heparin induce endothelial...
lipoprotein lipase. Moreover, heparin transfers this enzyme from the endothelium to the serum; and insulin encourages chylomicron metabolism. Plasmapheresis may be a useful option for acute and chronic cases if pharmacotherapy and nutritional interventions were not adequate and a risk for recurrence is present. In acute cases plasmapheresis decreases plasma TG, proinflammatory cytokine, protease and blood viscosity levels. Low viscosity improves tissue blood circulation.

Ideal doses for these drugs, and which one is the best option according to severity, are unknown. Some cases present with good outcomes with supportive management alone. These interventions decrease TGs. Other interventions such as Chinese traditional medicine show good results.

Other measures such as early administration of fibric acid derivatives should be considered. Treating secondary causes prevents recurrence with periodical controls and multimodal treatment. Evaluate associated risk factors like diabetes, hypothyroidism, alcohol abuse, and other measures.

Treating hypertriglyceridemia is always necessary regardless of etiology. High levels of triglycerides associated with acute pancreatitis, for example biliary lithiasis, impairs prognosis. There is no standard management and few cases have been reported. Acute pancreatitis secondary to hypertriglyceridemia is infrequent, and thus no management guidelines are available (12). More research is needed regarding standard evaluation and treatment.

Keeping in mind the above limitations, the treatment of acute pancreatitis secondary to hypertriglyceridemia is supportive. It attempts to reduce triglycerides and to prevent other complications such as infections and multisystemic failure (13). The objective of medical management is to increase lipoprotein lipase activity and chylomicron metabolism (14), and to decrease serum triglycerides below 500 or even 200 mg/dL if possible.

CONCLUSIONS

Acute pancreatitis associated with hypertriglyceridemia is a recently described medical condition. Early diagnosis is needed for the best treatment. Currently, evidence is not enough for indicating a therapeutic clinical guideline, and ideal management must be determined.

Is plasmapheresis indicated for acute cases? May insulin facilitate a true induction of lipoprotein lipase, or its results may be explained by serum glycemic control?

Serum triglycerides must be measured in patients with acute pancreatitis. Hypertriglyceridemia is related to other clinical conditions that may worsen the prognosis.

REFERENCES