Severe Acute Pancreatitis As A First Symptom Of Primary Hyperparathyroidism: A Rare Case Report
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Citation

Abstract
A case of severe acute pancreatitis with normal values of serum calcium in a 59 year old woman is presented. The patient was operated for chololithiasis and choledocholithiasis because of misleading ultrasonography. No stones were found during the duct exploration. Parathyroid adenoma was suspected when serum calcium values were elevated postoperatively and a new acute pancreatitis attack followed, despite of the presence of a Kehr catheter in the duct. After the excision of the adenoma, the function of pancreas and serum calcium returned to normal. The case suggests a close relationship between hyperparathyroidism and acute pancreatitis and lead to the suspicion of a parathyroid adenoma in cases of severe acute pancreatitis with normal serum calcium levels.

INTRODUCTION
Hyperparathyroidism (HPT) is rarely implicated as a cause of acute pancreatitis episodes to a frequency of less than 1% [12,3]. When these two conditions coexist, the course of pancreatitis may be complicated. Some studies suggest that parathyroidectomy may ameliorate the course of pancreatitis [4,5], but others have not confirmed this observation [1]. Pseudocyst formation may also confuse the appliance of appropriate therapy, and some authors suggest a conservative approach for the uncomplicated ones along with the adenoma parathyroidectomy [4]. Serum calcium level is believed to be associated to the severity of acute pancreatitis attack. Normalization of serum calcium levels may ameliorate the course of pancreatitis and prevent the recurrence of the disease [12]. Preoperative biochemical and ultrasonographic evaluation of a patient during an acute episode of pancreatitis may be misleading, because serum calcium may be lower than normal (Ranson's criteria) and common duct dilatation may be caused by the pressure of pancreatic head balge.

This article introduces a case of a 59 years old woman with two acute episodes of pancreatitis leading to two pseudocyst formations. The patient had normal or low serum calcium values, with ultrasonographic suggestion of cholecystolithiasis and bile duct dilatation. Parathyroid adenoma was suspected after postoperative serum calcium elevation and a new postoperative episode of a mild acute pancreatitis attack.

CASE REPORT
A 59 years old woman was admitted with acute epigastric pain, vomiting and mild fever. Her medical history was free and she had no alcohol abuse. Laboratory data revealed serum amylase level 812 U/L, (n.v:30-110U/L) and serum calcium level 7,26mg/dl (n.v:9-10,5mg/dl). Percutaneous ultrasonography (US) and dynamic computed tomography (CT) that followed showed diffused inflammation of pancreatic tissue with formation of two pseudocysts and cholecystocholedoholithiasis.

Although primarily, the patient responded well to conservative treatment (fluid resuscitation, nasogastric suction, analgesia, antibiotic and somatostatin analogue therapy) a new episode of mild acute pancreatitis, took place. Afterwards patient underwent open cholecystectomy, common bile duct exploration with placement of a T-tube (Kehr). No stones were found in bile cyst or in the bile duct, except some mud in the cyst. The post-operative course was uneventful. Cholangiography via the Kehr catheter was normal. On 10th postoperative day after Kehr catheter was closed, patient developed acute epigastric pain, with
elevation of serum amylase level (770 U/L) and also increased serum calcium level (12.9 mg/dL). The Kehr catheter was opened again. A new CT scan showed no evidence of the pancreatic pseudocyst and no edema or peri-pancreatic fluid. Ultrasonography of the neck (Fig 2) showed a mass near the left lower lobe of the thyroid gland suspected for parathyroid adenoma that confirmed by scintigraphy (99mTc-Myoview Sesta-mibi). Serum parathormone level then was measured and was found twice the normal value.

A typical left parathyroidectomy was conducted along with biopsy of the right lower parathyroid gland. Histopathologic examination showed typical parathyroid adenoma. The Kehr catheter was then closed and extracted after two days. Postoperative course was uneventful and patient is 2 years after in good health.

**DISCUSSION**

The first report of pancreatic lithiasis associated with primary hyperparathyroidism (HPT) was published in 1947 [9]. However, pancreatitis began to be considered as a manifestation of primary HPT in 1957 [4]. The incidence of co-existence of both pathological conditions is between 2.9% and 7% [4], although a transient hyperamylasemia with abdominal symptoms after parathyroidectomy may be encountered up to 9.3% [4].

Pancreatitis is associated to primary HPT predominantly in middle-aged men. Patients with asymptomatic hyperparathyroidism and/or slight hypercalcaemia develop pancreatitis less common than those with moderate or severe hypercalcaemia. In about 16% the cause of HPT is parathyroid carcinoma with calcific pancreatitis and 70% of the patients who suffer from acute relapsing or chronic pancreatitis have calcifications [9,10]. The two conditions are more common in men (53-60%) even though primary HPT is twice more common in women than men, with most common symptoms pain and vomiting, as it was in our case [4]. Renal symptoms are the commonest complication of primary HPT such as nephrolithiasis (50%), as it was in our patient. Bone disease associated to HPT and pancreatitis is up to 26% [4].

The cause of pancreatitis may be persisted hypercalcaemia which may result to an increase to the calcium content of the pancreatic juice and may lead to an accelerated intra-pancreatic conversion of trypsinogen to trypsin, which can insult the ducts and parenchyma of pancreas. Other conditions of hypercalcaemia than HPT, have also been implicated for pancreatitis, such as parental nutrition, calcium infusion, myeloma, severe hyperparathyroidism, metastatic brain cancer, renal transplantation [11]. Some authors point out that the symptoms of primary HPT are so variable, such as, nephrolithiasis, polyuria, depression, nausea, peptic ulcer pancreatitis, that is difficult to be diagnosed. A rare symptom reported is hoarseness [12]. This was also noticed in our patient who suffered also among other symptoms from depression, anxiety and hoarseness.

Some authors suggest performing parathyroidectomy in renal recipients with persistent hypercalcaemia more than 3 mmol/L even though other predisposing to pancreatitis factors as prednisone, gallstones and immunosuppressive medication, may also coexist to these patients [11,12].

The relationship between pancreatitis and hyperparathyroidism was thought to be the transformation of inactive to active trypsinogen by hypercalcaemia [11], narrowing of pancreatic duct and vessels from calcification, with resulting pancreatic tissue necroses [1]. This may have resulted to pseudocyst formation in the case of our patient.

Some authors report cases of acute pancreatitis after parathyroidectomy for PHPT [11,12] but others find no such relationship [11,13]. Even though some authors suggest that patients with PHPT and markedly increased values of serum calcium and PTH must be firstly treated for hyperparathyroid crisis with intra venous fluids and furosemide for the danger of pancreatitis and be operated later, until they have stabilised [13], it is reported that patients with pancreatitis and PHPT have higher values of PTH and serum calcium than those having no pancreatic involvement [13]. Our patient had normal or lower serum calcium values during the acute phase of pancreatitis and elevated when pancreatitis subsided.

Pancreatitis associated with HPT may be often rather severe and can be complicated by calcification or pseudocyst formation [15], even though less than 10% of patients with HPT develop inflammatory disease of the pancreas, including both acute and chronic pancreatitis [13]. In our case two pseudocysts were formed after the first acute episode of pancreatitis. The pseudocysts were uncomplicated and resolved after six months and one year postoperatively.

Pancreatic pseudocysts treatment is controversial since 25% to 50% of fluid collections after acute pancreatitis attack will be absorbed within 6 to 8 weeks spontaneously [13]. Indications of not resolution of the cyst are the size of more
than 6 cm, multiple cysts, chronic pancreatitis and progressive cyst enlargement [6, 15]. Complications as rupture, hemorrhage, and infection of the cysts may also occur. It seems that parathyroidectomy and correction of hypercalcaemia can reverse the side effects of pancreatitis when there is no permanent damage to the gland, such as chronic calcific pancreatitis with persistent abdominal pain, which require surgical intervention [6, 15]. However, in cases that pseudocyst size is causing gastric outlet obstruction, parathyroidectomy must be accompanied by a pseudocyst drainage procedure [6, 15].

From the present case it is concluded that in cases of acute pancreatitis with negative findings from the bile ducts, even if serum calcium levels are below normal values, it seems worthwhile to investigate the patient for PHPT, even more if symptoms from uropoetic, myosceletic and nervous systems are reported. Although primary HPT is an uncommon cause of pancreatitis, its early recognition and treatment assists to avoid unnecessary bile duct and pancreatic surgical intervention.

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