OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Case Report | **Endocrinology and Metabolic Diseases**

Acute Pancreatitis: Think of Primary Hyperparathyroidism

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DOI: 10.36348/sjmps.2023.v09i05.009 | **Received:** 07.04.2023 | **Accepted:** 10.05.2023 | **Published:** 26.05.2023

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Abstract

Primary hyperparathyroidism is a relatively common endocrine disorder that can lead to hypercalcemia and, consequently, cause long-term renal and skeletal complications. Usually, the diagnosis of this disorder is made at an asymptomatic stage. We report three cases of primary hyperparathyroidism revealed by acute pancreatitis, which is an unusual initial manifestation. The three patients, aged 55, 61, and 78 years, experienced acute epigastric pain accompanied by vomiting. Laboratory tests showed hyperlipasemia, and the abdominal CT scan revealed acute necrotizing pancreatitis. After an investigation into the underlying causes, the diagnosis of primary hyperparathyroidism was confirmed, and imaging identified the presence of parathyroid adenoma in all three patients. Parathyroidectomy was performed and the anatomopathological examination confirmed the diagnosis of parathyroid adenoma.

Keywords: Primary hyperparathyroidism, hypercalcemia, acute pancreatitis, parathyroid adenoma, hyperlipasemia, abdominal CT scan.

INTRODUCTION

Primary hyperparathyroidism (HPT1) is an endocrine disorder which definition is biological: "it is the inappropriate secretion of parathyroid hormone (PTH) by one or more abnormal parathyroid glands, resulting in hypercalcemia". Its incidence has increased steadily over the past two decades due to the routine measurement of serum calcium levels, with a current rate of 20.8 per 100,000 individuals.

While HPT1 was classically associated with osteoporosis and kidney stones, these symptoms are becoming less common, and currently, 80% of cases are diagnosed at an asymptomatic stage [1]. Thus, HPT1 is rarely linked to the occurrence of acute or chronic pancreatitis, nevertheless there is some controversy regarding the frequency of this association, which has been reported in 3.6% of cases [2].

Although hypercalcemia is the main cause of HPT1, other mechanisms may be involved. Acute pancreatitis is exceptionally the revealing mode of primary hyperparathyroidism. We report an original series of three observations.

CASE PRESENTATION

Observation n°1:

A 55-year-old female patient without significant medical history was admitted to the *emergency department (ED)* with *acute* epigastric pain and *incoercible vomiting*. Clinical examination revealed epigastric tenderness and a negative Murphy's sign. Laboratory results showed a serum lipase of 3224 U/l (41 times the upper limit of normal). Abdominal computed tomography (CT) scan revealed acute stage E alithiasis Balthazar pancreatitis, the pancreas was heterogeneous with areas of hypodense necrosis and peripancreatic necrotic collections (figure n°1).

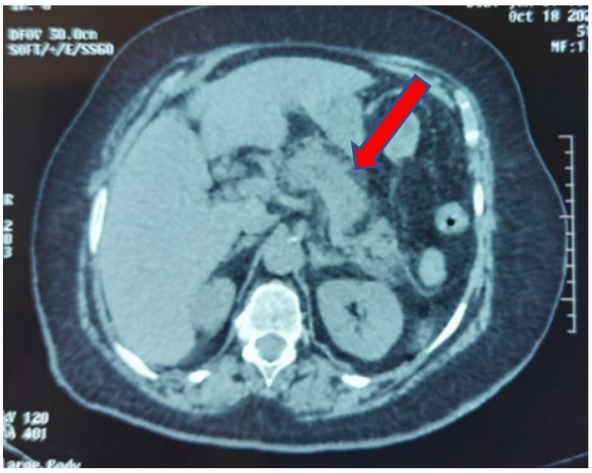

Figure 1: Cross-sectional scan showing a heterogeneous pancreas with hypodense areas of peripancreatic necrotic collections in the first patient

Observation n°2:

A 78-year-old female patient with no medical history presented with epigastralgia, vomiting and alteration of the general state. Hyperlipasemia was found, and abdominal CT scan *showed moderately severe acute pancreatitis* with 30-50% of pancreatic necrosis rated as Balthazar Stage C with no evidence of obstacle or gallstones.

Observation n°3:

A 61-year-old female patient without any medical history was admitted to the ED for management of acute stage D alithiasis Balthazar pancreatitis revealed by epigastralgia associated with vomiting. Clinical examination revealed epigastric tenderness without muscular defense.

The three patients were managed with food restriction, infusion of hydroelectrolytic solutions and analgesics.

Etiological investigations (table 1) documented acute pancreatitis secondary to primary hyperparathyroidism in all three patients. This was confirmed by the presence of hypercalcemia, hypophosphatemia, and elevated levels of PTH, after ruling out other common causes of acute pancreatitis such as gallstones, excessive alcohol consumption, and high triglyceride levels. Parathyroid adenoma was found in the three patients (table 1).

After medical preparation with rehydration, forced diuresis and intravenous infusion of biphosphonates, the parathyroidectomy was performed and anatomopathological examination confirmed parathyroid adenoma in the three patients.

The evolution was marked by the normalization of the phosphocalcic balance in two patients, and the occurrence of a hungry bone syndrome in one patient requiring calcium and *vitamin D supplementation* with a good clinico-biological outcome.

Table n°1: Etiological investigations documented acute pancreatitis secondary to primary hyperparathyroidism in all three patients

Investigations	**Case 1**	**Case 2**	**Case 3**
Calcemia (mg/L)	180	163	177
Phosphatemia (mg/L)	20	18	19
PTH	1141	1233	392
Calciuria (mg/24H)	504	475	460
Cervical ultrasound	Right posteroinferior parathyroid nodule measuring 49mm	Right parathyroid nodule measuring 19 mm	Right parathyroid nodule
MIBI scintigraphy	Right posteroinferior parathyroid nodule		
CT scan or MRI	Right parathyroid nodule		Right paratracheal parathyroid nodule measuring 17*15*21 mm
Anatomopathological study	Parathyroid adenoma	Parathyroid adenoma	Parathyroid adenoma
Evolution	good	good	Hungry bone syndrome

DISCUSSION

These three cases illustrate an exceptional initial manifestation of HPT1 that is acute necrotizing pancreatitis. It is a serious condition that can have a high mortality rate in its severe form. Alcohol and gallstones dominate its etiologies while other metabolic causes (hyperlipidemia, hypercalcemia) are rare [3].

In 1940, Smith and Cook [4] were the first to describe acute pancreatitis due to hyperparathyroidism. This condition is observed in 1.5-7% of cases, and it is believed to be caused by hypercalcemia since patients with HPT1 who develop pancreatitis have higher levels of calcium compared to those without pancreatic involvement [5]. A recent study by Misgar *et al.*, reported acute pancreatitis in 9% of patients and demonstrated a causal relationship between hypercalcemia and the occurrence of acute pancreatitis [6]. This link can be explained by three possible pathophysiological mechanisms. The first mechanism suggests that hypercalcemia causes de novo activation of inactive trypsinogen to active trypsin, leading to autodigestion of the gland and subsequent pancreatitis. The second mechanism proposes that hypercalcemia promotes precipitation of ionized calcium in pancreatic juice, causing lithiasis formation which is responsible for pancreatitis. The third mechanism suggests that hypercalcemia leads to intravascular coagulation, resulting in necrotic and hemorrhagic lesions that lead to the development of pancreatitis [7]. In addition to calcium, genetic factors such as mutations in the SPINK 1 (serine protease inhibitor Kazal type 1) and CFTR (cystic fibrosis transmembrane conductance regulator) genes may also predispose patients with HPT1 to recurrent acute pancreatitis [6].

The management of acute pancreatitis resulting from HPT1 involves urgent symptomatic treatment consisting of three key components: rehydration, adequate analgesia, and appropriate nutritional intake [8]. In the other hand, the etiological treatment is based on performing a parathyroidectomy preceded by appropriate medical preparation to correct hypercalcemia. Our three patients had severe hypercalcemia treated by abundant rehydration with injectable bisphosphonates. Following normalization of their calcium levels, they underwent parathyroidectomy.

The classical surgical treatment of HPT1 corresponds to a complete surgical exploration of the cervical and upper mediastinal region through a Kocher cervicotomy. This approach permits an accurate assessment of parathyroid lesions and their subsequent removal.

This classic treatment is necessary in case of associated thyroid involvement or multi-glandular lesion, as well as in those with suspected multiple endocrine neoplasia, parathyroid carcinoma, or recurrent disease [9].

Minimally invasive surgery is increasingly recommended and consists of an elective unilateral approach, which reduces morbidity, operating time, length of hospital stay, and scarring. Its indications are reserved for sporadic HPT1 without associated diffuse thyroid nodular pathology. This procedure is suitable when a single parathyroid adenoma is detected through high-resolution ultrasound and MIBI scintigraphy [10].

After parathyroidectomy, the risk of recurrence of acute pancreatitis in the long term is not clear due to the lack of studies with long-term follow-up. Nevertheless, in a study conducted by Misgar *et al.*, the recurrence rate was very low (0.4%) with a median follow-up of 16 months [6]. Thus, the data in the literature emphasize the importance of parathyroid surgery in these patients. It has been suggested that parathyroid surgery should precede any pancreatic surgery because of its beneficial effect on the course of the latter [6].

CONCLUSION

Our three observations illustrate an exceptional unusual manifestation of primary hyperparathyroidism and highlight the importance of conducting a phosphocalcic assessment in any acute pancreatitis in order to establish an early and adapted management allowing improving the associated morbimortality.

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