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Acute Pancreatitis Caused by Hypercalcemia as an Initial Manifestation of Primary Hyperparathyroidism (PHPT): A Rare Case Report

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Abstract **Case Report**

Acute pancreatitis (AP) is a frequent gastrointestinal emergency with gallstones and chronic alcohol consumption being the most common causes. Other etiologies can also be identified such as hypercalcemia, which remains a rare yet deadly cause of acute pancreatitis. In this case, hypercalcemia is usually the result of hyperparathyroidism. The latter's causative diseases must be investigated carefully. Herein, we report the case of AP related to hypercalcemia from a parathyroid adenoma. By reporting this case and reviewing the literature, we aim to raise the practitioners' attention to this association as it is crucial for timely diagnosis and appropriate management of these cases.

Keywords: Hypercalcemia, Acute pancreatitis (AP), gastrointestinal emergency, diagnosis.

INTRODUCTION

Acute pancreatitis has a great variety of etiologies. It is accepted that alcohol consumption and biliary lithiasis are responsible for almost 80-90% of all cases [1]. Other rarer causes include neoplastic obstruction of the bile tract or the sphincter of Oddi, metabolic disorders such as hypertriglyceridemia or Hypercalcemia, trauma, infection, and autoimmune diseases [2]. Up to 10% of cases are described as idiopathic pancreatitis because no main cause of the disease could be established. Hypercalcemia as a cause of pancreatitis is very rarely reported, and it is usually the result of hyperparathyroidism. We report the case of an elderly female patient with Hypercalcemia-induced acute pancreatitis as the first manifestation of a benign parathyroid adenoma.

CASE REPORT

A 73-year-old woman presented at the emergency department with sudden and severe epigastric pain and vomiting. Her medical history mentioned a history of hypertension and atrial fibrillation with antivitamin K treatment. She denied any history of smoking or alcohol consumption. She had no history of similar episodes and did not report any medication that could cause acute pancreatitis.

The pain started 10 days earlier and had worsened over the past 2 days. It was located in the upper abdomen and radiating to the back (pancreatic type pain) associated with nausea and vomiting, evolving in a context of apyrexia and conservation of general condition.

Clinical examination revealed a distended abdomen with painful percussion and palpation of the epigastrium. No fever was noted and the patient's vital signs were stable. Blood analysis showed signs of inflammation with an elevated C-reactive protein (CRP) of 316 mg/l (< 5 mg/L) and leukocytosis of 13600 (4.3-10 × 10E9/L). The pancreatic enzyme (serum lipase) was elevated at 2543 U/L (13-300 U/L). The renal function, liver tests, and triglyceride levels were all normal. In contrast to what was expected in a case of severe pancreatitis, serum calcium was increased at 132 mg/L (85-105 mg/L), and the albumin-modified serum calcium concentration was 37 g/dl, while phosphorus level was normal.

The patient was diagnosed with acute pancreatitis, and a computed tomography (CT) scan confirmed the diagnosis and placed it at a Balthazar Grade E, with tomographic signs of 30 to 50% glandular necrosis, which corresponds to a score of 8 in the CT severity index (CTSI) (figure 1). No cholelithiasis or biliary tract dilatation was noted in ultrasound, which excluded gallstone pancreatitis.

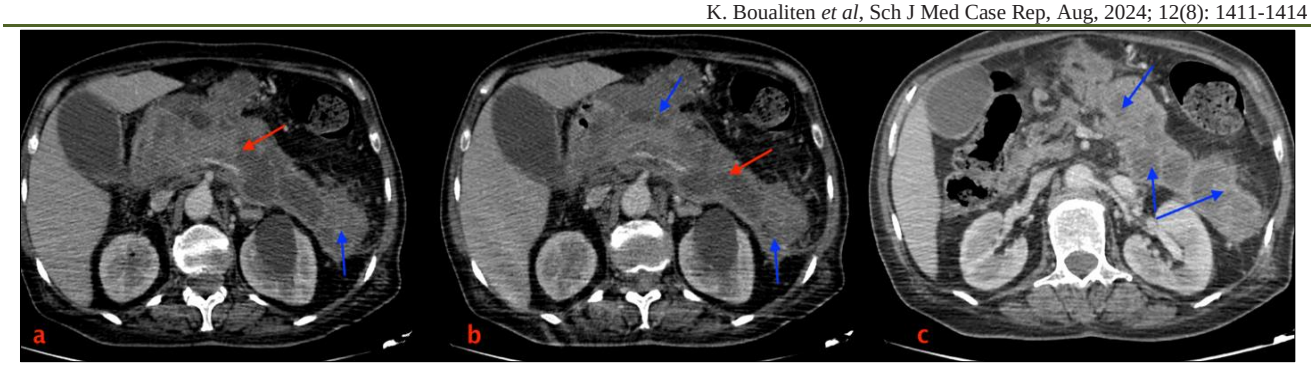

Figure 1: Axial CT scan of the abdomen showing signs of acute pancreatitis with glandular necrosis (red arrows) and multiple ill-defined peripancreatic fluid collections extending to the left para renal space and the omental bursa (blue arrows)

The patient was treated conservatively with intravenous fluids and analgesia. After the exclusion of alcohol-induced and auto-immune pancreatitis (with a negative serum IgG4 level), elevated serum calcium levels remained another potential etiology of acute pancreatitis. To investigate this matter, the endocrinology department ordered a parathyroid hormone blood test known as “PTH, intact” which was significantly elevated at 598 pg/ml (12 - 88 pg/ml). This result confirmed the theory of hypercalcemia being caused by hyperparathyroidism. Ultrasound examination and 18F choline-PET with Tc 99 m sestamibi revealed a right inferior parathyroid adenoma (figure 2).

Based on biochemical parameters combined with clinical and imaging manifestations, we concluded with the diagnosis of acute pancreatitis, hypercalcemia, and PHPT.

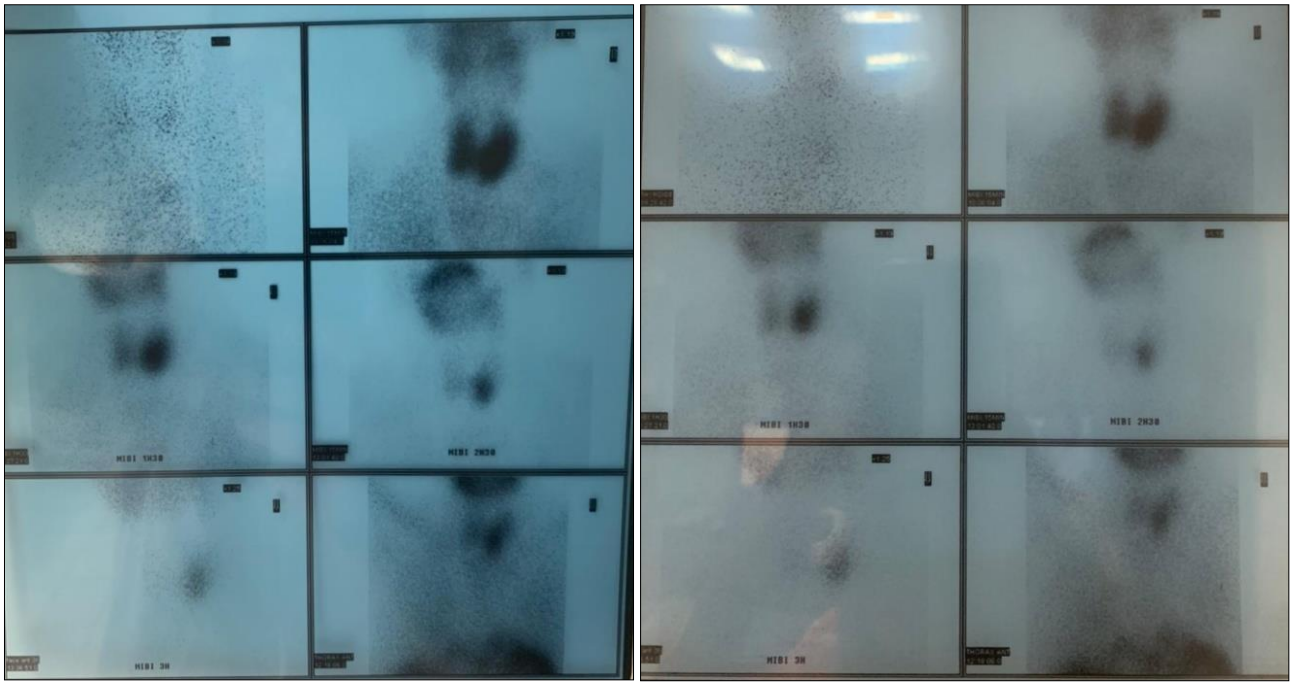

Figure 2: 99m Tc-sestamibi scintigraphy of parathyroid glands: Early & delayed images showed an intense fixation of the left lobe leaving doubt about its pole inferior focus at this level

Due to her heart condition, the patient could not be put on good rehydration or bisphosphonates. The only possible treatment for this patient was calcimimetics which are activators of sensitive calcium receptors. The evolution was marked by a decrease in serum calcium from 131 to 110.

The patient then underwent surgical resection of her adenoma, and a pathology examination confirmed the diagnosis of benign parathyroid adenoma. Serum PTH levels decreased slowly and the patient gradually recovered over the next two weeks. At her six-month follow-up, she was in good clinical condition with normal PTH and calcium levels.

DISCUSSION

Acute pancreatitis has been associated with various predisposing factors. Its diagnosis is retained in

the presence of at least 2 of the 3 following elements: abdominal pain, levels of serum lipase greater than 3 times the normal range, or characteristic imaging aspects such as edema, pancreatic necrosis, or acute necrosis collection in the acute phase or pancreatic atrophy, hypertrophy, calcifications or ductal abnormalities in the chronic form [1].

Gallstones and alcohol are the two most common etiological factors for acute pancreatitis. Additionally, hypertriglyceridemia is linked to 9% of cases of AP. Medication side effects, post-ERCP pancreatitis, infections, and hypercalcemia are only a few of the uncommon causes of AP. Hypercalcemia is defined as an elevated blood calcium level of more than 105 mg/dL. It can occur in several conditions, such as humoral hypercalcemia (caused by the release of chemicals that raise calcium levels); osteolytic hypercalcemia; ectopic hyperparathyroidism; and lymphomas that secrete vitamin D [3]. Hypercalcemia is a well-established cause of acute pancreatitis, with a prevalence of 1.5%-8% and the primary cause of AP due to hypercalcemia is primary hyperparathyroidism (PHPT) [3].

Though the exact physiopathological basis remains uncertain, it is thought that hypercalcemia activates trypsinogen to trypsin, causing the gland to self-digest and promoting the formation of calcium deposits within the pancreatic ducts [4].

Numerous studies discussed the causal relationship between PHPT and pancreatitis. There is no experimental evidence that suggests PHPT is triggered by pancreatitis [5]. As was previously mentioned, the primary defect in PHPT is an inappropriate secretion of PTH and resultant hypercalcemia. PTH levels are therefore taken into account. Thus, PTH levels are a consideration. However, patients who, for example, have elevated PTH levels in the context of renal hyperparathyroidism but do not have hypercalcemia are not at risk for pancreatitis [6].

Beyond the distinctive biochemical features of PHPT such as high serum calcium and a low phosphate in the setting of inappropriately high or normal PTH, there are few clinical indicators to help identify this condition among patients with acute pancreatitis [7]. Patients who present with long-standing PHPT may have calcium oxalate or calcium phosphate renal stones, renal dysfunction or colic, or even bone defects such as pathologic fractures and osteoporosis. Other clinical presentations such as palpable neck nodules and severe psychological disorders are possible but uncommon [8].

The existence of PHPT does not affect the acute management of pancreatitis episodes, which should prioritize diligent supportive care.

The treatment of AP due to hypercalcemia has 2 objectives: treating hypercalcemia in the acute phase to prevent life-threatening complications, and then addressing the underlying cause to avoid potential recurrences. The first-line treatments are intravenous normal saline (200-300 mL/h), calcitonin (at a dose of 4 international units/kg), and bisphosphonates (at a dose of 4mg IV over 15-30 minutes) [4].

After the acute pancreatitis phase has resolved and the hypercalcemia has been treated, patients should undergo elective parathyroidectomy to permanently treat the PHPT. New data from a 10-year prospective study showing that parathyroid surgery increases bone mineral density and the development of minimally invasive techniques have shaped guidelines that recommend parathyroidectomy in almost all patients with PHPT who are not contraindicated for surgery [7-9]. Due to the lack of long-term studies, the course of pancreatitis in individuals with PHPT who undergo parathyroidectomy is unclear [10]. The majority of reports only included a two-year follow-up and reported a 42% to 100% resolution in pancreatitis recurrence. Even the pain associated with chronic pancreatitis was alleviated, according to Bhadada *et al*., albeit no quantitative measurements were given [6].

CONCLUSION

Acute pancreatitis caused by hypercalcemia is rare, particularly when this hypercalcemia is related to PHPT. Its clinical features remain nonspecific; thus, the diagnosis can be challenging. We should always exclude pancreatitis caused by chronic alcohol consumption and biliary stones before evoking hypercalcemia-induced pancreatitis. If the latter is suspected, it should draw attention and be subject to complementary explorations in search of endocrine or malignant causes in particular parathyroid tumors.

Informed Consent: Written informed consent was obtained from the patient for publication of this article, including accompanying images.

Conflict of Interest: The authors do not declare any conflict of interest.

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