Acute necrotising pancreatitis as the first and sole presentation of undiagnosed primary hyperparathyroidism

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ABSTRACT

Primary hyperparathyroidism is a recognized, but rare, cause of acute pancreatitis. The pathophysiology of hypercalcemia-induced acute pancreatitis is not well known, but when this combination occurs, pancreatitis is likely to be severe and the degree of hypercalcemia may play an important role in this association. Therefore, the cause of hypercalcemia should be identified early. Surgical resection of the parathyroid adenoma is the ultimate therapy.

We report two cases with severe acute necrotizing pancreatitis associated with hypercalcemia. The cause of hyperparathyroidism was a benign parathyroid adenoma. We highlight the drawbacks in delaying the diagnosis of primary hyperparathyroidism in patients with acute pancreatitis as the sole clinical presentation.

Keywords: *Acute Necrotising Pancreatitis, Primary Hyperparathyroidism, Hypercalcemia.*

Acute pancreatitis is a reversible inflammatory disease of the pancreas that usually follows a mild and self-limited course. Gallstones and alcohol consumption are the leading causes of acute pancreatitis, accounting for 38% and 36% of cases, respectively. [1] Hypercalcemia caused by primary hyperparathyroidism is a rare cause of acute pancreatitis. Patients with primary hyperparathyroidism and hypercalcemia have increased risk of suffering from acute necrotizing pancreatitis episodes. Therefore, hyperparathyroidism as a cause of acute pancreatitis should be identified early. We highlight the drawbacks in delaying the diagnosis of primary hyperparathyroidism in patients with acute pancreatitis as the sole clinical presentation.

CASE HISTORY

We report two cases of acute pancreatitis caused by hypercalcemia due to primary hyperparathyroidism that was not known previously.

CASE 1

A 41 years old hypertensive woman presented to the medical emergency with acute abdominal pain and vomiting. Based on the clinical picture and blood analysis, she was diagnosed to be having the third episode of acute pancreatitis. She had a past history of being admitted two times for pancreatitis episodes in the past 2 years. She also had a past history of being operated for kidney stones in 2007 but she had no records available of the surgery done. She denied any history of alcohol use and there was no family history of pancreatitis. Abdominal ultrasound was carried out and showed mild interstitial pancreatitis. There was no evidence of cholelithiasis or dilated bile ducts. All her preliminary investigations like complete blood count (CBC), renal and liver function tests, erythrocyte sedimentation rate (ESR), urinalysis and lipid profile were normal except serum calcium levels which were repeatedly reported as high (Table 1). On reviewing her medical records, normal serum calcium levels were noted at the time of previous hospital admissions outside. Serum levels of intact parathyroid hormone (iPTH) were determined and showed an increase up to 250 pg/mL (normal range: 15-65 pg/mL). This result confirmed hypercalcemia caused by hyperparathyroidism. Ultrasound of the neck revealed the presence of a hypoechoic lesion inferior to the right lobe of the thyroid gland in the region of the parathyroid gland (Fig. 1). After 6-7 days when the patient had started accepting semisolid diet, she underwent contrast-

Table 1: Blood Investigations at admission and after the Surgical Resection of Parathyroid Adenoma

Investigations	At admission	After surgery
S. Calcium	HIGH	9.0 mg/dl
S. Phosphate	2.0 mg/dl	2.4 mg/dl
S. albumin	3.5 gm/dl	4.6 gm/dl
Corrected S. calcium levels	HIGH	8.4 mg/dl
ALP	113 mg/dl	95 IU/L
iPTH levels	556.5 pg/ml	250 -> 80.0 pg/ml

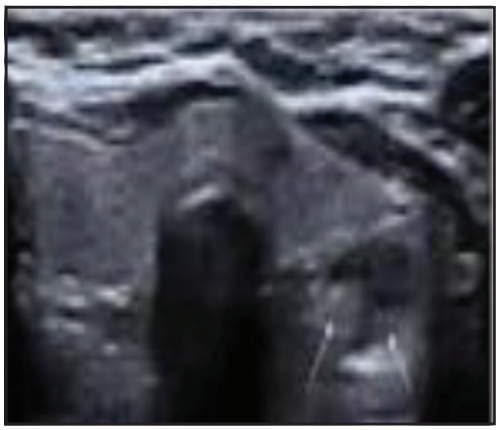

Figure 1

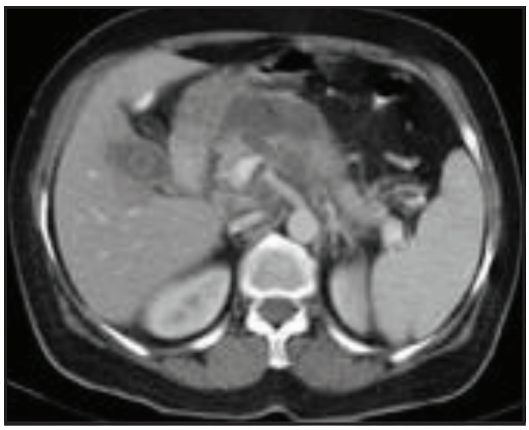

Figure 2

enhanced computerized tomography (CECT) abdomen which was suggestive of acute necrotizing pancreatitis with the acute necrotic collection (modified CTSI score 6/10) (Fig. 2) and left nephrolithiasis (another event related to hypercalcemia). 99mTc-Sestamibi scintigraphy was then carried out which was consistent with a right inferior parathyroid adenoma. The patient was referred for surgical resection of the tumor. Histological examination of the resected tumor confirmed the diagnosis of benign parathyroid adenoma. In the post-operative period, serum levels of iPTH and calcium decreased and the patient required calcium supplements. Following the clinical resolution, the patient was discharged from the hospital. In her follow up period, serum calcium levels had normalized and she had no recurrence of pancreatitis.

CASE 2

A 52 years old, non-alcoholic and non-smoker male patient, presented to the medical emergency with complaints of pain in the abdomen and vomiting. Pancreatic enzymes were elevated - serum amylase was 864 U/L and serum lipase was 522 U/L. All other investigations like CBC, renal and liver function tests, ESR, urinalysis, lipid profile (including triglycerides) and chest x-ray, were normal (Table 2). Based on the clinical picture and blood analysis, he was diagnosed with acute pancreatitis. Ultrasound of the abdomen showed oedematous, hypoechoic bulky pancreas with surrounding fat stranding and absence of gallstones. There was no history of drug intake prior to the onset of abdominal pain. He was treated conservatively, his symptoms improved comparatively and he was accepting oral intake. He was discharged 10 days after admission and was advised to follow up for further etiological workup.

Five days later, he was readmitted to the medical emergency with severe pancreatitis. The patient had developed bilateral pleural effusion as evident by chest X-Ray. There was also mild derangement of the renal functions. We noticed an elevation of serum calcium levels which were normal in the previous admission. On the basis of biochemical parameters, a diagnosis of primary hyperparathyroidism was made. Ultrasound neck was done for further evaluation of primary hyperparathyroidism which revealed the presence of a 1.2×1.6 cm structure with increased internal vascularity seen in the inferior aspect of the right lobe of thyroid – right inferior parathyroid lobe enlargement - suggestive of a parathyroid adenoma.

CECT of the abdomen was done to further elaborate the morphological details of the pancreas which was suggestive of acute necrotizing pancreatitis with the acute necrotic collection, moderate ascites and spleno-portal thrombosis (modified CTSI score 10/10) (Fig. 3). There was the presence of moderate bilateral pleural effusion with consolidation in both lower lobes; also, we observed the presence of left nephrolithiasis. The management of serum calcium was based on rehydration and bisphosphonates. The patient improved with the treatment given and was further referred for surgery but never turned up for the follow-up.

Table 2: Blood Investigations of the patients At admission

Investigations	At admission
S. Calcium	12.4 mg.dl
S. Phosphate	4.1 mg/dl
S. albumin	2.6 gm/dl
Corrected S. calcium levels	12.45 mg/dl
ALP	86 mg/dl
25-hydroxyvitamin D	15.05 ng/ml
iPTH levels	524.0 pg/ml

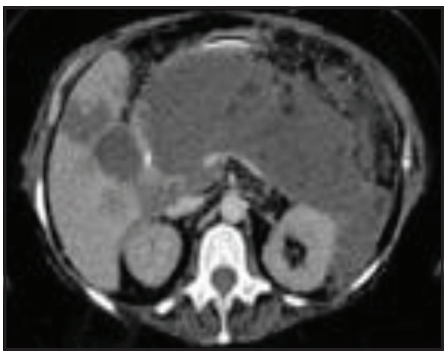

Figure 3

DISCUSSION

Acute pancreatitis caused by primary hyperparathyroidism - induced hypercalcemia is a rare condition. It was first described in 1957, by Cope *et al*. [2] The prevalence of acute pancreatitis in patients with primary hyperparathyroidism, is estimated to be between 1.5% and 7% [3].

No direct causal relationship appeared to be in between the primary hyperparathyroidism and acute pancreatitis, based on epidemiological data. However, it has been shown that hypercalcemia plays a primary role in causing acute pancreatitis in primary hyperparathyroidism. The molecular mechanism underlying hypercalcemia - induced pancreatitis is yet to be elucidated. However, there are two suggested explanations. First, the de novo activation of zymogens by hypercalcemia; the activated zymogens, including trypsin, destroy acinar cells and autodigest the pancreatic tissue resulting in subsequent pancreatitis. Second, hypercalcemia can cause the formation of pancreatic calculi and protein plug by modifying pancreatic secretion resulting in pancreatic duct obstruction and subsequent pancreatitis. The direct toxic action of PTH on the pancreas has also been studied. Genetic linkage has also been found between hyperparathyroidism and pancreatitis. The mutation of serine protease inhibitor Kazal-type I gene (SPINK1) and Cystic Fibrosis Transmembrane Conductance Regulator gene (CFTR) have been found in patients with primary hyperparathyroidism, who develops acute pancreatitis [5].

Acute pancreatitis is usually associated with a decrease in serum calcium levels and low serum calcium levels have prognostic importance [6]. Parathyroid hormone levels should be tested and if the hormone is elevated, imaging of the parathyroid glands should be conducted. It is important to consider the possibility of an ectopic parathyroid adenoma as the cause of acute pancreatitis as earlier described in case reports by Lenz *et al* and Imachi *et al*. [7, 8] In the present two cases, the presence of hypercalcemia in Acute Pancreatitis guided us to detect undiagnosed Hyperparathyroidism and a Parathyroid Adenoma.

CONCLUSION

Through this case report, we have highlighted the drawbacks in delaying the diagnosis of primary hyperparathyroidism in patients with acute pancreatitis as the sole clinical presentation. The role of primary hyperparathyroidism as a causative factor is underestimated when managing patients with acute pancreatitis, and frequently the underlying disease remains undiagnosed for a long time. Proper early diagnosis and management prevent unnecessary morbidity.

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