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Case report

Hypercalcemic Pancreatitis: A Rare Type of Acute Pancreatitis Caused by a Parathyroid Adenoma

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Abstract

Acute pancreatitis is an inflammatory process with multiple etiologies, dominated by biliary lithiasis and alcohol consumption. Primary hyperparathyroidism (PHPT) with subsequent hypercalcemia as a cause of acute pancreatitis is very rare and frequently overlooked and serum calcium level plays a key role in the pathogenesis. Here we present a case of 53 years old female with hypercalcemic acute pancreatitis resulted from primary hyperparathyroidism caused by a left parathyroid adenoma.

Keywords: ***acute pancreatitis, hypercalcemia, primary hyperparathyroidism, parathyroid adenoma,***

Introduction

Acute pancreatitis has multiple etiologies, dominated by biliary lithiasis and alcohol consumption [1]. Among other causes, hypercalcemia associated with acute pancreatitis is rare [2]. Primary hyperparathyroidism (PHPT) with subsequent hypercalcemia caused by parathyroid adenoma causing pancreatitis as the first manifestation is exceptionally rare with debatable and controversial association [3,4]. Although, it is though that elevated parathyroid hormone and high serum calcium levels associated with certain genetic mutations could be responsible for this predisposition in some patients with hyperparathyroidism causing calcium deposit in the pancreatic ducts which then activates the pancreatic enzymes [1,5,6]. Here, we present the case of a hypercalcemic acute pancreatitis as a first presentation of primary hyperparathyroidism caused by a parathyroid adenoma in a middle-aged woman.

Case presentation

A 53-year-old patient, with no relevant pathological history, particularly no history of alcohol intake or biliary system symptoms, presented to the emergency department with sudden onset of severe epigastric pain and vomiting for five days. The Pain was radiating to the back, with no exacerbating or relieving factors. The patient dined fever, diarrhea, cough and expectoration.

Physical examination upon admission found normal temperature, blood pressure, heart rate, and respiratory rate. There was mild upper abdominal tenderness with rebound tenderness.

Laboratory tests revealed elevated lipase of 698 U/L, elevated C-reactive protein (CRP) of 70 mg/L, normal white blood cell count, and 8.2 mg/dl anemia. There was no alteration of liver and renal function tests. Serum Calcium level was elevated (132mg/L) with hypophosphatemia (17mg/L), albumin was within normal range.

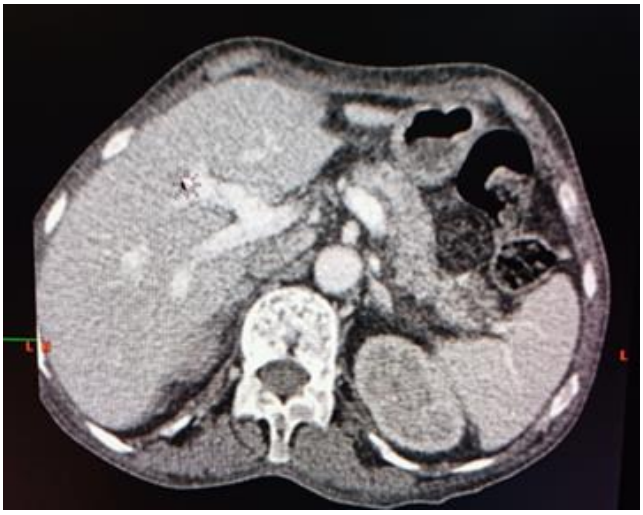
A computed tomography (CT) scan of the abdomen showed a stage C of Balthazar pancreatitis with an infiltration of the peripancreatic fat without necrosis indicating mild pancreatitis, there were no dilatation of bile ducts and the liver and the gallbladder were normal (**Fig. 1**). However, there were multiple lytic lesions involving the axial and the appendicular skeleton with suspicious appearance.

Hypercalcemia induced acute pancreatitis was suspected. Parathyroid hormone (PTH) was very elevated at 1389 pg/ml and 25-hydroxy vitamin D level was low. The diagnosis of hypercalcemia caused by Primary hyperparathyroidism was confirmed.

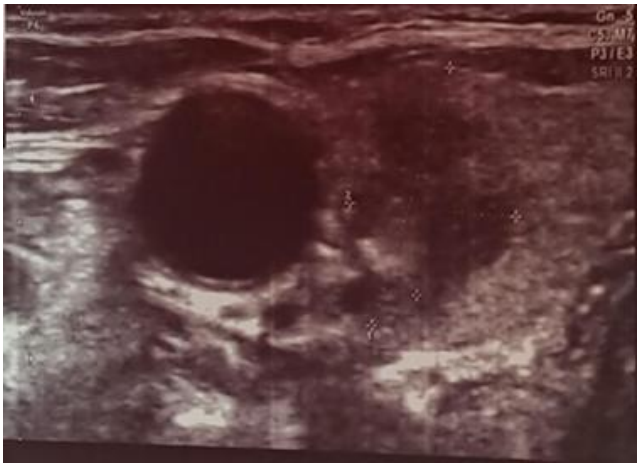
Neck ultrasound showed a nodular thyroid gland with a well-defined oval solid- cystic isoechogenic mass at the inferior left thyroid lobe measuring 25 mm × 14 mm (**Fig. 2**). The neck tomography revealed a multinodular thyroid gland with locally infiltrated heterogenous left parathyroid-dependent lesion suggestive of a parathyroid adenoma (**Fig. 3**). Her thyroid-stimulating hormone (TSH) and free thyroxine levels were normal.

The patient was conservatively managed with intravenous fluids aggressively, and pain medications, concerning the pancreatitis, and Her clinical and biochemical condition were improved. Bisphosphonates was also administered to correct hypercalcemia along with adequate hydration. Vital parameters and urine output were closely monitored, and serum calcium level decreased to 102 mg/L. The patient underwent a total thyroidectomy in which a parathyroid adenoma was identified and was resected carefully. Her PTH level normalized during the surgery droping to 34pg/ml, thus confirming successful adenoma resection. The histopathological examination of the tissue confirmed the diagnosis of left parathyroid adenoma with nodular and diffuse dystrophic goiter without obvious histological signs of malignancy.

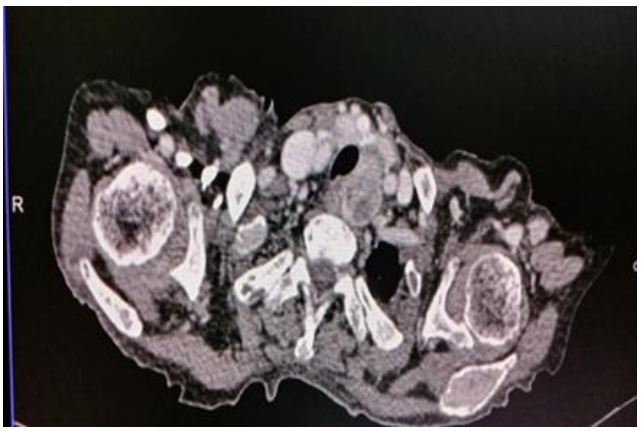
The patient was treated with Levothyroxine (LT4) monotherapy, and calcium level decreased during the immediate postoperative period. The patient did not develop any more hypercalcemia or pancreatitis symptoms at the regular follow-ups, and her TSH and free thyroxine levels stayed within the normal range.



Figures 1: Computed tomography scan of the abdomen showing a stage C of Balthazar pancreatitis with an infiltration of the peripancreatic fat



Figures 2: Neck ultrasound showing a nodular thyroid gland with an oval mass at the inferior left thyroid lobe



Figures 3: Neck tomography showing a multinodular thyroid gland with locally infiltrated left parathyroid adenoma

Discussion

Primary hyperparathyroidism (PHPT) is an endocrine condition characterised by exaggerated secretion of parathyroid hormone (PTH), which results in hypercalcemia, hypercalciuria, and hypophosphatemia [2,6,7]. PHPT is most commonly caused by a solitary parathyroid adenoma (85%-90%) [7,8]. Other less common causes include: Hyperplasia of the four parathyroids, parathyroid carcinoma, and multiple endocrine neoplasia type 1 and 2A [9,10]. Most patients with PHPT are asymptomatic and it is detected upon routine laboratory testing. Clinical manifestations in patient with PHPT secondary to hypercalcemia include recurrent renal calculi, skeletal manifestations, nonspecific gastrointestinal symptoms, cardiovascular and neuromuscular disorders [2,3,11].

Acute pancreatitis is an inflammatory pancreatic process with high morbidity and mortality [9]. Alcohol and biliary tract stones are the most common causes [12]. Hypercalcemia due to primary hyperparathyroidism is a rare cause of acute pancreatitis, with a reported prevalence of 1.5-8%. And since pancreatitis occurs at an advanced stage of parathyroid disease, and PHPT is mostly asymptomatic and diagnosed early; the prevalence of this association in developed countries has decreased [2,5,13,14]. The true association and causal relationship between PHPT and acute pancreatitis has been discussed in literature for decades [15-19], but is still a controversial and debatable issue with Data variations about pancreatitis rates in patients with PHPT, highlighting that the statistically main factor may be hypercalcemia [10,13,20]. Nevertheless, Patients with primary hyperparathyroidism are 10 times more at risk of acute pancreatitis than general population [14].

Although a clear physiopathological base could not be determined, proposed mechanisms of hypercalcemia induced acute pancreatitis include increased intrapancreatic activation of trypsinogen to trypsin causing pancreatic autodigestion, which leads to forming calcium deposits in the pancreatic ducts, followed by pancreatic duct obstruction. Also high cytosolic calcium can generate the activation of nuclear factor Kappa-B (NF-kB) leading to local and systemic inflammation [7,9,21]. In addition, a genetic risk factor has also been found in the setting of hypercalcemia; mutations in SPINK 1 (Kazal-type serine protease inhibitor type1), CFTR (cystic fibrosis transmembrane conductance regulator) and CASR (calcium receptor) genes were suggested as possible mechanisms [4,5].

Hyperparathyroidism is frequently misdiagnosed or overlooked as symptoms are non-specific [2,11]. furthermore, hypercalcemia is a common disorder that is mostly caused by PHPT or malignancy-associated diseases. Usually Serum calcium level is low during acute pancreatitis. Thus, whenever acute pancreatitis is associated with hypercalcemia, complementary explorations should undergo, considering the possibility of hypercalcemia related pancreatitis and try to exclude PHPT [1,11,22]. As a matter of fact, in our case, PHPT could justify the whole clinical presentation: not only hypercalcemia was secondary to PHPT, but also bone lesions were benign and related to PHPT.

Within context of hypercalcemia, the diagnosis of PHPT is based on measuring PTH serum level which is increased [9]. The identification of the parathyroid adenoma as a further work up of PHPT in the preoperative setting is performed by imaging studies such as neck ultrasound, neck tomography or scintigraphy with sestamibi. The later can also detect ectopic locations [5,9].

As far as treatment, the management of acute pancreatitis episodes is not altered by PHPT, which should focus on intensive supportive care [1,10]. Fluid resuscitation with intravenous fluids remains the basis of treatment, with pain management; however, rehydration with lactated Ringer's solution is contraindicated because it contains calcium [9]. After the acute crisis has resolved, patients should undergo elective parathyroidectomy to definitively treat the PHPT [1,10]. Pending the surgery, the management of hypercalcemia is based on rehydration with isotonic saline and bisphosphonates [2,9]. Surgery is the therapy of choice and the resection of the secreting lesion causes a significant reduction in the serum calcium and PT levels. Thus relieving the abdominal symptoms of acute pancreatitis and preventing the recurrence of hypercalcemia [3,11,13].

Conclusion

We report here a case of acute pancreatitis as a first presentation of hypercalcemia due to primary hyperparathyroidism. This case is particularly interesting because the diagnosis is rare and challenging.

It illustrates how acute pancreatitis can predate the diagnosis of underlying parathyroid adenoma. Thus, it is important for clinicians to consider primary hyperparathyroidism when encountering non-biliary, non-alcoholic acute pancreatitis in the setting of hypercalcemia. Additionally, dosing serum calcium levels is essential in acute pancreatitis to prevent the misdiagnosis of secondary causes.

Authors' Contributions

All authors participated in the conception, drafting the work, critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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