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Hypercalcemia in Primary Hyperparathyroidism with Manifestations of Acute Pancreatitis

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ABSTRACT

Background: Primary hyperparathyroidism can result in hypercalcemia and hypophosphatemia which can cause gastrointestinal symptoms, electrolyte disturbances, renal dysfunction, and acute pancreatitis. The association between pancreatitis and primary hyperparathyroidism is rarely discussed. ***Case Illustration:*** We report a 32-year-old man who presented with a history of abdominal pain, nephrolithiasis, and increasing calcium serum. Primary hyperparathyroidism was overlooked until the patient was referred due to pancreatitis. The patient had additional risk factors for pancreatitis such as a history of alcohol consumption and hypertriglyceridemia. The patient had a worsening condition and died because of a septic condition and multiple organ failure. ***Conclusion:*** Hyperparathyroidism can cause acute pancreatitis through hypercalcemia with the mechanisms of trypsinogen activation, pancreatic duct obstruction, and genetics. In patients with acute pancreatitis with hypercalcemia, further hyperparathyroidism evaluation is necessary.

Keywords: primary hyperparathyroidism; pancreatitis; hypercalcemia.

INTRODUCTION

Primary hyperparathyroidism can result in hypercalcemia and hypophosphatemia with various accompanying diseases such as gastrointestinal symptoms, electrolyte disorders, renal dysfunction, and acute pancreatitis, or it can also be asymptomatic.[1,2] Hypercalcemia with acute pancreatitis as the initial symptom is a common feature of primary hyperparathyroidism and its prevalence is estimated between 1,5 - 7%.[3] Primary hyperparathyroidism has been associated with various types of pancreatitis, such as acute, subacute, or chronic calcific pancreatitis.[4,5]

Below we report a case of a 32-year-old man with hypercalcemia in primary hyperparathyroidism with manifestations of pancreatitis. This case report was raised to increase knowledge in identifying manifestations of pancreatitis due to secondary hypercalcemia caused by primary hyperparathyroidism because similar cases are rarely encountered in daily clinical practice.

CASE ILLUSTRATION

A 32-year-old man came with complaints of acute abdominal pain, the pain felt sharp with a stabbing sensation throughout the abdominal area, especially the upper region, since two days before admission. the pain radiates and penetrates the back. Patients also complain of nausea vomiting and fever. The patient had not defecated or farted since the previous day. The patient had a history of alcohol consumption and hypertriglyceridemia Patient also had a history of multiple nephrolithiasis.

On physical examination, the patient was weak with malnutrition (BMI 18.4 kg/m2). The patient is alert, vital signs are within normal limits. On abdominal examination, there were defans muscular with suspicion of peritonitis and hollow organ perforation due to perforated appendicitis the results of the parathyroid hormone examination showed an increase of 132.1 pg/mL (15 – 65 pg/mL). Blood Gas Analysis suggested respiratory acidosis.

The patient then underwent laparotomy, debridement, wound dehiscence, omentectomy, and enterocutaneous fistula. During the operation, pus with a volume of ± 400 ml was obtained in the abdominal cavity and the patient had a drainage tube installed in the right lumbar region, left lumbar region, and hypogastric region. The patient was diagnosed with necrotizing pancreatitis accompanied by intra-abdominal abscess. Furthermore, treatment was continued in the intensive care room, during observation the patient experienced septic shock and his condition worsened, and finally died from multiple organ failure.

DISCUSSION

Primary hyperparathyroidism is a common endocrine disorder characterized by hypercalcemia and elevated or abnormal parathyroid hormone levels.[1] Primary hyperparathyroidism is the result of excessive secretion of parathyroid hormone from one or more parathyroid glands. Primary hyperparathyroidism is caused by a solitary parathyroid adenoma in 80% of cases,

whereas four-gland hyperplasia accounts for 10-15%, multiple adenomas in 5%, and parathyroid cancer in <1% of cases.[5,6] The estimated incidence of primary hyperparathyroidism varies from ~0.4 to 82 cases per 100,000.10 Different from epidemiological data, in this case, the hyperparathyroidism condition occurred in a young man of Asian descent with the cause of the primary hyperparathyroidism not yet determined because radiographic examination had not been possibly carried out due to the patient's condition making it impossible.

In primary hyperparathyroidism, there is a disruption in the normal feedback suppression of serum calcium levels on the synthesis and secretion of parathyroid hormone due to an increase in parathyroid cell mass and/or a decrease in the amount of the CASR protein (which codes for the calcium-sensing receptor) in parathyroid cells.[6,7] Gastrointestinal symptoms such as pancreatitis and gastric ulcers, do not appear to be a feature of modern primary hyperparathyroidism. The relationship between pancreatitis and primary hyperparathyroidism remains controversial. The first report of primary hyperparathyroidism associated with pancreatic lithiasis was published in 1947. [8,9] From data collected between 1950 and 1975 it was found that of 1153 patients with primary hyperparathyroidism, only 17 patients (1.5%) had pancreatitis, and alternative causes for pancreatitis could be described. in some patients.29 The prevalence of acute pancreatitis in primary hyperparathyroidism is estimated to be between 1.5 - 7%. [6,7]

There are three mechanisms of hypercalcemia-induced pancreatitis. First, hypercalcemia can cause de novo activation of trypsinogen into trypsin, resulting in pancreatic autodigestion and causing pancreatitis. Second, hypercalcemia conditions lead to the formation of pancreatic stones, and duct obstruction thereby increasing the risk of acute or chronic pancreatitis. [10,11] Lastly, genetic risk factors can predispose patients with primary hyperparathyroidism to pancreatitis. Mutations in the SPINK1 (Serine Protease Inhibitor Kazal type I) gene and the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene are more often found in primary hyperparathyroidism patients who experience acute pancreatitis. [11,13] In this case, the patient was known to have experienced nephrolithiasis since 2014. Nephrolithiasis in this case was suspected due to hypercalcemia conditions triggered by primary hyperparathyroidism. Hypercalcemia can also cause duct obstruction so in this case acute pancreatitis is suspected to be due to duct obstruction. The patient in this case report is known to have other risk factors that contribute to pancreatitis such as a history of alcohol consumption accompanied by hypertriglyceridemia. Another condition that is suspected to be triggered by increased levels of serum calcium and parathyroid hormone is nephrolithiasis, which the patient had experienced for 6 years before the onset of pancreatitis.

Although pancreatitis due to hyperparathyroidism is rare, if an increase in serum calcium levels is found in acute or chronic pancreatitis, exploration must be carried out to find the cause of endocrine disorders or malignancy in the patient. [9] In this case report, it was found that the patient was overweight before becoming ill with an increase in pancreatic enzymes. Even though the results of imaging cannot be proven, the diagnosis can be made by examining biomarkers of calcium and parathyroid hormone, strengthened by other evidence of complications of hypercalcemia in the form of kidney stones.

The revised Atlanta classification for the diagnosis of acute pancreatitis requires the presence of two or more criteria: abdominal pain suggestive of pancreatitis, serum amylase or lipase levels greater than three times the upper limit of normal, or imaging findings. [14,15] In this case the diagnosis of acute pancreatitis in initial hospital visits is not met. The only supporting criteria are upper abdominal pain such as stabbing pain that penetrates the back, but from examination, the serum amylase or lipase levels did not increase more than three times the upper limit of normal values and no imaging examination was carried out. At the initial hospital visit the patient was suspected of having perforated appendicitis and an exploratory laparotomy was performed. On the second laparotomy at the hospital, it was found that the pancreas had necrosis accompanied by an intra-abdominal abscess, so the diagnosis of necrotizing pancreatitis was confirmed.

Once acute pancreatitis is established and the degree of disease determined, management of acute pancreatitis includes aggressive early intravenous hydration, appropriate nutrition, and pain management.[16] Adequate fluid resuscitation has been shown to reduce mortality in patients with severe sepsis. Although the conditions associated with acute pancreatitis can be handled well, prolonged complications from sepsis cause death in this patient.

CONCLUSION

The condition of acute pancreatitis as a manifestation of primary hyperparathyroidism has a rare prevalence. Hyperparathyroidism can cause acute pancreatitis through hypercalcemia with the mechanisms of trypsinogen activation, pancreatic duct obstruction, and genetics. In patients with acute pancreatitis and hypercalcemia, hyperparathyroidism examination is necessary.

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