Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.0552-17
Intern Med 57: 3075-3078, 2018
http://internmed.jp

【 CASE REPORT 】

Acute Pancreatitis with Disturbed Consciousness Caused by Hyperparathyroidism

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Abstract:
Although hyperparathyroidism has been reported to cause acute pancreatitis, little is known about the mechanism involved. This study describes the case of an 86-year-old woman with acute pancreatitis and consciousness disturbance caused by hyperparathyroidism and hypercalcemia, respectively. The consciousness disturbance caused by severe hypercalcemia probably masked the typical symptoms associated with pancreatitis because she did not report abdominal pain during the clinical course.

Key words: pancreatitis, hyperparathyroidism

(Intern Med 57: 3075-3078, 2018)
(DOI: 10.2169/internalmedicine.0552-17)

Introduction

Acute pancreatitis is an inflammatory disease of the pancreas; acute abdominal pain is the most common symptom. While several causes of acute pancreatitis have been described, including hyperparathyroidism, there have only been a few reports of patients with acute pancreatitis caused by hyperparathyroidism who did not experience abdominal pain. This report describes the case of a patient with acute pancreatitis and consciousness disturbance caused by hyperparathyroidism and hypercalcemia, respectively.

Case Report

An 86-year-old woman was referred to our hospital due to consciousness disturbance. She had a history of acute pancreatitis of unknown etiology. A physical examination at admission revealed the following findings: body temperature, 36.8℃; blood pressure, 129/78 mmHg; heart rate, 119/min; and respiratory rate was 25 breaths/min. A blood test revealed leukocytosis (24,280/μL), a normal platelet count (151,000/mm^3), increased serum concentrations of C-reactive protein (CRP, 25.4 mg/dL) and amylase (273 IU/L), a normal serum level of aspartate aminotransferase (AST, 27 IU/L) and the modest elevation of alanine aminotransferase (ALT, 77 IU/L) and triglycerides (83 mg/dL). Her serum calcium level was markedly elevated (17.5 mg/dL) relative to her serum albumin level, while her serum phosphorus level was decreased (2.2 mg/dL). Her serum concentrations of blood urea nitrogen (43 mg/dL) and creatinine (1.81 mg/dL) were also elevated. Her serum lactate dehydrogenase level was normal (159 IU/L). A blood gas analysis showed hypoxemia (pO_2, 60.2 mmHg) and low base excess (BE, -3.7 mEq). A brain computed tomography (CT) scan showed no major abnormalities. She had not been treated with Vitamin D. These findings suggested that her consciousness disturbance was caused by hypercalcemia. Intravenous fluid resuscitation combined with the administration of calcitonin (40 units/day) was initiated.

Although the patient had not reported abdominal pain, abdominal CT was performed to identify any inflammatory foci and to determine the etiology of hyperamylasemia. Unexpectedly, abdominal CT revealed the diffuse enlargement of the pancreatic parenchyma with surrounding fluid collection (Fig. 1), a finding fully consistent with acute pancreatitis (1). She had no history of alcohol consumption, and choledocholithiasis was not detected by abdominal CT or ultrasonography. She was diagnosed with acute pancreatitis secondary to hypercalcemia, since hypercalcemia is known to trigger acute pancreatitis (1, 2). Based on the Japanese criteria, the prognostic factor score in this case was 5

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Received: November 19, 2017; Accepted: March 29, 2018; Advance Publication by J-STAGE: June 6, 2018
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points (3) (BE, <-3 mEq; blood urea nitrogen, >40 mg/dL; CRP, >15 mg/dL; systemic inflammatory response syndrome (SIRS); and age, >70 years). Contrast-enhanced CT was not performed because of renal dysfunction. Plain CT showed that the panniculitis extended to the anterior pararenal space; thus, the CT grade was considered to be 1 or 2. Consequently, she was diagnosed with severe acute pancreatitis (3). These findings suggested that consciousness disturbance caused by severe hypercalcemia masked the typical pancreatitis-related symptoms, including the acute onset of persistent and severe epigastralgia.

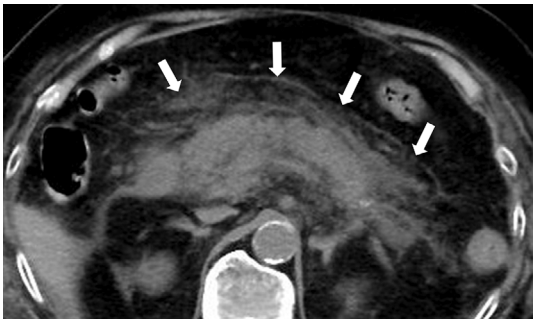

Figure 1. **Abdominal computed tomography showed the diffuse enlargement of the pancreatic parenchyma with surrounding fluid collection (arrows).**

Intravenous fluid resuscitation in combination with the administration of calcitonin and antibiotics (carbapenem) reduced her inflammatory responses, improved her consciousness level and kidney function, and reduced her serum ALT level. At 12 days after her admission, the patient's serum amylase concentration was normal and did not increase again during the remainder of her clinical course (Fig. 2). At 14 days after her admission, her corrected calcium concentration was normal, and calcitonin injection was replaced by zoledronic acid injection as maintenance therapy. At this time, her serum concentration of intact parathyroid hormone (PTH) was extremely high (470 pg/mL; normal range <50 pg/mL), while her PTH-related protein level was normal. The fractional urinary excretion of calcium was high (13%), suggesting primary hyperparathyroidism rather than familial hypocalciuric hypercalcemia, caused by mutations in the parathyroid calcium-sensing receptor gene (4). Parathyroid imaging using ^{99m}Tc-methoxyisobutylisonitrile revealed a marked uptake by the left lobe of her parathyroid gland in the delayed phase (Fig. 3), a finding consistent with primary hyperparathyroidism (4). No apparent neck tumor was detected by ultrasonography or CT. She had no family history of neuroendocrine tumor or hypercalcemia. A further exami-

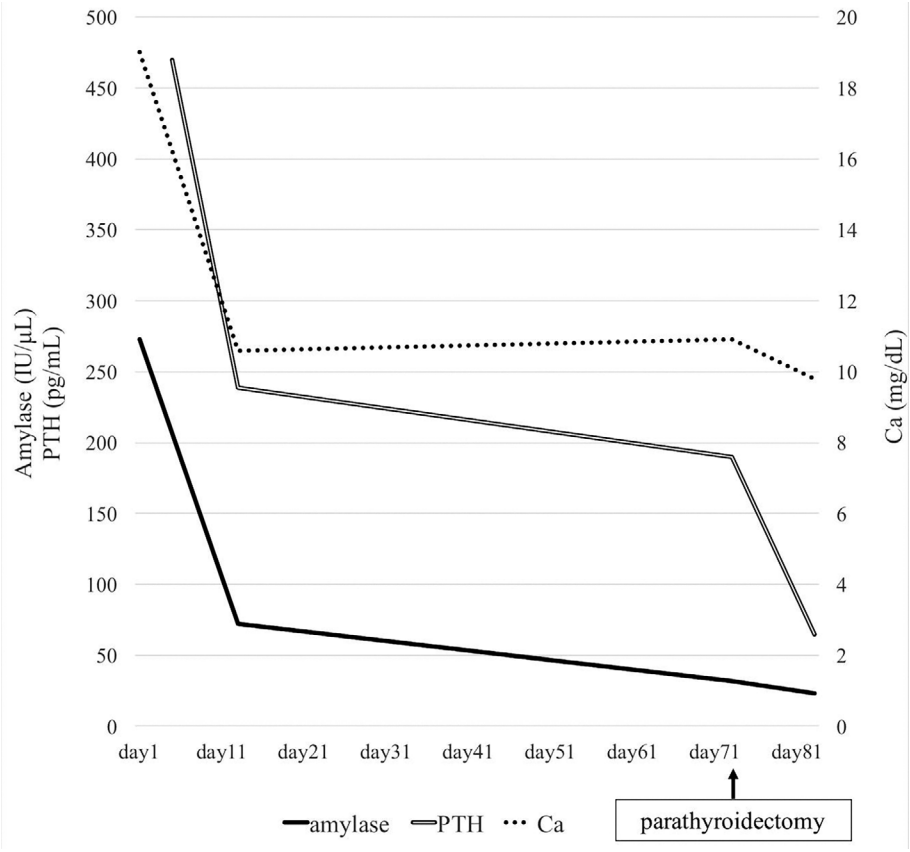

Figure 2. **The serum concentrations of amylase (solid line), calcium (dotted line), and intact parathyroid hormone (double line) during the disease course of this patient. The patient's serum amylase and calcium concentrations improved 12 days after admission, whereas the intact parathyroid hormone concentration was markedly reduced after surgery, which was performed 74 days after admission.**

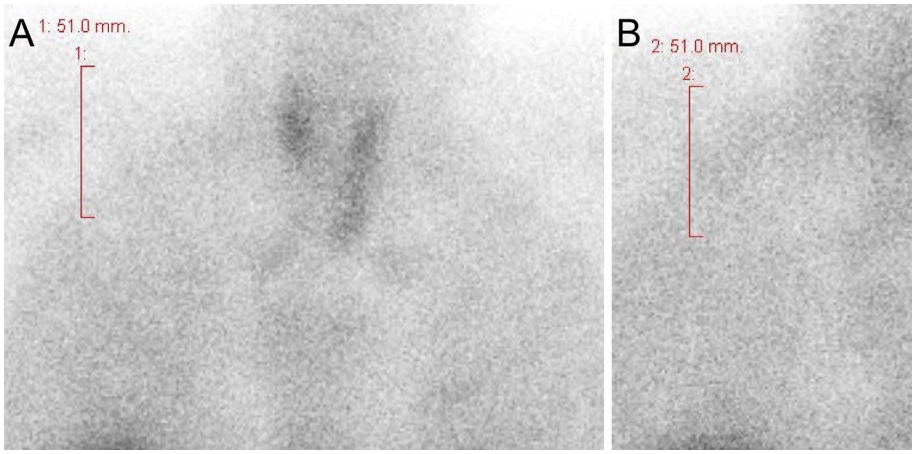

Figure 3. Parathyroid imaging by ^{99m}Tc-methoxyisobutylisonitrile. (A) Early parathyroid imaging 10 minutes after the injection of ^{99m}Tc-methoxyisobutylisonitrile. (B) Delayed imaging at 2 hours after injection showed the marked uptake of radioactivity by the left parathyroid lobe (arrows).

nation showed no evidence of a skin lesions or neuroendocrine tumor. Based on these results, she was finally diagnosed with acute pancreatitis caused by hypercalcemia due to hyperparathyroidism. At 74 days after admission, she underwent left lower parathyroidectomy under general anesthesia. The left lobe of her parathyroid gland was enlarged. Her serum concentration of intact PTH, which was 190 pg/mL before resection, decreased markedly to 64 pg/mL and 40 pg/mL at 5 and 15 minutes after resection, respectively. She was diagnosed with parathyroid hyperplasia. Her serum calcium and intact PTH concentrations normalized after parathyroidectomy (Fig. 2).

Discussion

There have been several reports of acute pancreatitis caused by hyperparathyroidism (6-11, 14, 15). The frequency of pancreatitis associated with hyperparathyroidism in patients of 20-70 years of age has been reported to range from 1.5% to 15.3% (5, 6). Hyperparathyroidism is often only discovered after two or three episodes of recurrent pancreatitis (7, 8). Similarly, in this case, the patient had a history of pancreatitis; however, she had not been diagnosed with hyperparathyroidism prior to the present admission. The evaluation of parathyroid hormone levels is important for the diagnosis of hyperparathyroidism when pancreatitis is associated with an increase in the serum calcium level. In this case, parathyroid hyperplasia caused acute pancreatitis. On the other hand, parathyroid adenoma and carcinoma have also been reported to cause acute pancreatitis (6, 9-11).

Although the relationship between hyperparathyroidism and acute pancreatitis remains unclear (2), several observations suggested that acute pancreatitis in this patient was caused by hyperparathyroidism. First, the major etiologies of acute pancreatitis include alcohol consumption, the intake of high-fat foods, the administration of pancreatitis-causing drugs, and choledocholithiasis, none of which were present in this patient. Second, she had no family history of pancreatitis. Third, her serum amylase and calcium concentrations normalized after parathyroidectomy, with no recurrence of pancreatitis during the 12-month follow-up period. Thus, these findings strongly suggested that the pathogenesis of acute pancreatitis in this patient resulted from hypercalcemia caused by hyperparathyroidism.

It remains unclear how hypercalcemia secondary to hyperparathyroidism predisposes a patient to acute pancreatitis. The inappropriate intra-acinar activation of pancreatic digestive enzymes, especially trypsinogen, plays a central role in the development of acute pancreatitis (12, 13). An excessive increase in the intracellular calcium concentration can result in the over-activation of digestive enzymes in the pancreatic acinar cells, followed by autodigestion and inflammation of the pancreatic tissue (12, 13). The extracellular concentration of calcium in this patient may have been high enough to induce intracellular calcium-mediated signaling in pancreatic acinar cells, resulting in the excessive intra-pancreatic activation of digestive enzymes. Although hypercalcemia and/or hyperparathyroidism are considered as possible triggers of acute pancreatitis (1, 2), little is known about the clinical features of acute pancreatitis caused by hypercalcemia and/or hyperparathyroidism.

The acute onset of persistent and severe epigastric pain, often radiating to the back, is a typical symptom of acute pancreatitis. Patients with acute pancreatitis caused by hyperparathyroidism also complain of abdominal pain (6-11, 14, 15). However, our patient did not report abdominal pain at any point in the clinical course. This patient fulfilled the diagnostic criteria for Systemic Inflammatory Response Syndrome (16), including heart rate >90/min, respiratory rate >20/min, and white blood cell count >12,000/mm^3. Her quick Sequential Organ Failure Assessment score, an indicator of sepsis, was 2 points; although sepsis was suspected, septic shock did not occur (16). These findings suggested that her consciousness disturbance - caused by severe hypercalcemia secondary to hyperparathyroidism - masked the typical symptoms of pancreatitis. Alternatively,

her disturbed consciousness may have prevented her from reporting the abdominal pain. Painless pancreatitis has been reported in patients with post-endoscopic retrograde cholangiopancreatography hyperamylasemia (PEH) (17). In that report, CT findings of pancreatitis were noted in 37% of patients without abdominal pain who had been diagnosed with PEH. This suggested that painless pancreatitis can be hidden in patients with PEH. The findings in this study highlight the need to include pancreatitis in the differential diagnosis of patients with consciousness disturbance caused by hypercalcemia.

Conclusion

Hyperparathyroidism may cause acute pancreatitis. This report describes the case of a patient with acute pancreatitis with consciousness disturbance caused by hyperparathyroidism.

The patient provided her written informed consent for the use and publication of her personal information and imaging results.

The authors state that they have no Conflict of Interest (COI).

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