Pancreatitis with Intraabdominal Venous Thrombosis as an Initial Presentation of Parathyroid Adenoma: A Rare Clinical Presentation

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Patient: Female, 34-year-old
Final Diagnosis: Acute necrotizing pancreatitis with intra abdominal veins thrombosis secondary to parathyroid adenoma
Symptoms: Epigastric abdominal pain • radiated to the back • vomiting
Clinical Procedure: —
Specialty: Endocrinology and Metabolic • Surgery

Objective: Rare disease
Background: Benign parathyroid adenoma is a cause of hypercalcemia, which can lead to acute pancreatitis. Patients with acute pancreatitis are at risk for venous thrombosis. This report describes a 34-year-old woman with hypercalcemia due to parathyroid adenoma and acute pancreatitis associated with splenic vein and superior mesenteric vein thrombosis.

Case Report: A previously healthy 34-year-old woman presented with severe epigastric pain that radiated to the back, associated with vomiting. Her abdominal examination was soft and lax, with epigastric and left upper quadrant tenderness. Pancreatitis with splenic and superior mesenteric veins thrombosis was diagnosed. The diagnosis was confirmed by an elevated serum lipase level and contrast-enhanced computed tomography (CT) of abdomen. Her serum calcium level was elevated. However, further workup revealed elevated parathyroid hormone (PTH) levels and radiological imaging showed parathyroid adenoma. She was diagnosed with hypercalcemia-induced pancreatitis secondary to hyperparathyroidism with intraabdominal venous thrombosis. The patient was initially treated conservatively, and later underwent parathyroidectomy after her condition was stabilized. The patient is currently in good condition, after a 2-year follow-up period.

Conclusions: Acute pancreatitis and thrombosis secondary to primary hyperparathyroidism (PHPT) are rare, but can lead to potentially fatal complications, especially in patients without symptoms of PHPT. This report highlights the importance of recognizing that hypercalcemia associated with parathyroid adenoma can result in acute pancreatitis, leading to hypercoagulable states and inflammation of adjacent vessels, including the splenic and mesenteric veins. To the best of our knowledge, this is second case report of acute pancreatitis with intraabdominal venous thrombosis secondary to PHPT.

Keywords: Hypercalcemia • Hyperparathyroidism • Parathyroid Neoplasms • Thrombosis

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Introduction

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by an abnormally active parathyroid gland causing high parathyroid hormone, high serum calcium level, and low serum phosphorus level [1]. It is associated with increased morbidity and mortality [1]. Approximately 70% to 80% of patients present at an asymptomatic stage, while the remaining present with symptoms that classically involve the renal and skeletal systems [1].

In classical PHPT cases, patients traditionally present with reduced bone mineral density or fragility fractures, as well as kidney stones, nephrocalcinosis, or renal insufficiency [1,2]. In non-classical PHPT cases, patients present with cardiovascular, gastrointestinal, psychological, and cognitive symptoms. The cardiovascular system in patients with PHPT was found to be associated with left ventricular hypertrophy, aortic valve calcification, increased aortic stiffness, and increased intimal media thickness [1]. The gastrointestinal system is frequently manifested in PHPT patients, with constipation, heartburn, nausea, and pancreatitis. Psychological and cognitive symptoms reported in patients with PHPT include fatigue, depression, anxiety, decreased working memory and concentration, and irritability [1,2].

The incidence of PHPT-induced pancreatitis is very low (1.5%-8%), and it appears to be associated with hypercalcemia rather than with hyperparathyroidism itself [3,4]. The classical and non-classical manifestations of PHPT are well described, but little is published regarding PHPT-induced venous thromboembolism. We have found only one study from Argentina, which was presented as an abstract in the International Society on Thrombosis and Haemostasis and published in the Research and Practice in Thrombosis and Haemostasis reporting the incidence was 0.15% at 6 months and 1 year [5].

Hypercalcemia secondary to PHPT-induced pancreatitis is uncommon but is associated with significant mortality and morbidity [1,6,7]. Herein, this report describes a 34-year-old woman with hypercalcemia due to parathyroid adenoma and acute pancreatitis associated with splenic vein and superior mesenteric vein thrombosis.

Case Report

A previously healthy 34-year-old woman initially presented to the Emergency Department with severe abdominal pain at epigastric area that radiated to the back and was associated with anorexia and 3 episodes of vomiting for 1 day. The patient had no history of fever. She had no previous comorbidities, no history of alcohol consumption, and no previous history of gallstones or pathological fractures. She had no previous medical or family history of venous or arterial thrombosis.

On examination, her vital signs were within normal limits, she was afebrile, and the abdomen was soft and lax, with epigastric and left upper quadrant tenderness. Her other systemic examination findings were clinically unremarkable. Her blood investigation showed an elevated serum lipase level (1402 U/L, reference range (RR): 12-53 U/L). A plain radiograph of the abdomen was unremarkable.

The computed tomography (CT) scan of the abdomen showed a picture of acute pancreatitis, with peripancreatic fluid, moderate ascites, and pleural effusion. She also had splenic vein and superior mesenteric vein thrombosis, which was treated with warfarin (Figure 1). The diagnosis of acute pancreatitis was confirmed by an elevated serum lipase and CT findings.

On further investigation to determine the cause of pancreatitis, her serum calcium level was elevated at 4.82 mmol/L (RR: 2.08-2.65 mmol/L), corrected calcium was 5.00 mmol/L, albumin was 31 g/L, alkaline phosphatase was high at 125 U/L (RR: 46-116 U/L), and phosphorous level was low at 0.58 mmol/L (RR: 0.81-1.58). Other routine laboratory tests were within normal limits. Electrocardiogram showed a shortening of the QT interval. However, further workup was performed at that time and revealed an elevated PTH level (1390 pg/mL, RR: 18-80 pg/mL). The lipid profile was normal.

Ultrasound of neck was performed, and the finding was highly suggestive of a parathyroid adenoma (Figure 2).

The patient received a diagnosis of hypercalcemia-induced pancreatitis with focal venous thrombosis in mesenteric and splenic veins, secondary to primary hyperparathyroidism. The patient was treated conservatively with adequate hydration, calcitonin, zoledronic acid, denosumab, correction of abnormal electrolytes, and hemodialysis. However, we planned to perform a right inferior parathyroidectomy once the patient was stable.

Her condition worsened on day 9 of admission; therefore, a contrast-enhanced CT was performed to rule out any collection and to assess the pancreas. CT revealed severe diffuse necrotizing pancreatitis of almost the whole pancreas (body and tail) with extrapancreatic complications, including an increase in abdominal ascites and bilateral pleural effusions (Figure 3), as well as a lesion inferoposterior to the right thyroid lobe, suggestive of a parathyroid adenoma (Figure 4). She then underwent CT-guided aspiration of the pancreatic necrosis with pigtail insertion. Aspirated fluids from pigtail, urine, blood, and stool culture and sensitivity were all negative.

On day 16 of admission, the pigtail was removed, the patient’s condition improved, and she was discharged.
Right inferior parathyroidectomy was planned once the patient had fully recovered from pancreatitis. A follow-up CT of the pancreas 2 weeks after discharge showed a regressive course, as generalized inflammatory changes were observed in the pancreas, with fluid collection throughout the abdomen. The patient was scheduled for surgery 1 month after fully recovering from pancreatitis and successfully underwent a right inferior parathyroidectomy under general anesthesia. Intraoperatively, the right inferior parathyroid gland was grossly enlarged (3×1.5 cm), with cystic changes (Figure 5). Histopathology of the excised parathyroid gland reported a parathyroid adenoma without any evidence of malignancy (Figure 6).

Figure 1. Contrast computed tomography of the abdomen. Arrow shows superior mesenteric vein thrombosis.

Figure 2. Parathyroid ultrasound: Arrow shows evidence of a large right parathyroid hypoechoic solid mass measuring 3.5×1.2 cm with cystic changes.

Figure 3. Contrast computed tomography of the abdomen, with arrow showing severe diffuse necrotizing pancreatitis of almost the whole pancreas (body and tail).
Postoperatively, the PTH level decreased from 440.5 pg/mL to 10.6 pg/mL, and the patient’s calcium level was in the reference range. Thrombophilia screening tests were done after the acute stage and after stopping anticoagulant and all were negative. At the 2-year follow-up, her PTH level was normal (39.9 pg/mL, RR: 18-80 pg/mL), and calcium level was normal (2.33 mmol/L (RR: 2.08-2.65 mmol/L).

Discussion

Acute pancreatitis is one of the leading causes of hospital admissions worldwide. It can be a potentially fatal condition, with an overall mortality of up to 20% [8]. Hypercalcemia secondary to PHPT is a rare cause of pancreatitis, which has been reported in 1.5% to 8% of cases [3,4]. Moreover, less than 1% of patients with acute pancreatitis have PHPT [3].

The etiology beyond acute pancreatitis secondary to PHPT is described by 3 mechanisms. The first is the de novo activation of trypsinogen to trypsin induced by high levels of calcium, which causes autodigestion of the pancreas and subsequent pancreatitis. Second, a high calcium level leads to the formation of pancreatic calculi, ductal obstruction, and subsequent attacks of acute or chronic pancreatitis. Third are genetic risk factors, such as mutations in the cationic trypsinogen gene (PRSS1), N34S mutation in the serine protease inhibitor Kazal type I (SPINK1) gene, and mutations in the cystic fibrosis transmembrane conductance regulator gene. All these factors put patients with PHPT at risk of developing acute pancreatitis [9,10].

PHPT is commonly observed in postmenopausal women [11]. In contrast, our patient was a young woman in her early 30s. However, since PHPT is uncommon in a woman of childbearing age, it tends to be neglected in the differential diagnosis, especially in patients with atypical symptoms [12].

PHPT rarely occurs and often goes undiagnosed, due to a lack of symptoms; hence, most cases are diagnosed incidentally. The manifestations of PHPT in symptomatic patients often vary, due to hypercalcemia and its effects on target organs. Symptoms of PHPT include renal stones, osteopenia, depression, constipation, vomiting, potentially life-threatening hypercalcemia, and pancreatitis [11,13,14]. Our patient presented with abdominal pain radiating to the back, associated with anorexia and vomiting. Patients with PHPT are undiagnosed due to a lack of symptoms; thus, some patients initially present with acute pancreatitis [14]. In our case, the patient initially presented with acute pancreatitis and intraabdominal venous thrombosis.

Based on the 2012 revision of the Atlanta classification and definitions by international consensus, the diagnosis of pancreatitis is made by presenting any 2 of the following 3 criteria: (1) abdominal pain, consistent; (2) serum lipase or amylase greater than 3 times the upper limit of normal; and (3) characteristic findings of acute pancreatitis on cross-sectional abdominal imaging [15]. In the present case, the patient presented with persistent abdominal pain, and her serum lipase level was 3 times higher than the upper limit. Along with abdominal ultrasound, a picture of acute pancreatitis has also been reported.

Acute pancreatitis is usually associated with decreased serum calcium levels. According to the Ranson grading system, a low serum calcium level is important for prognosis. Therefore, hypercalcemia is rarely observed in patients with severe acute pancreatitis. This unusual condition should alert physicians to the presence of hyperparathyroidism or a malignancy [16].
To complete the diagnosis, PTH levels should be determined, and imaging of the parathyroid glands is important [16]. In the present case, the diagnosis of a parathyroid tumor was made using ultrasound, CT of the neck, and high serum PTH levels. Imaging modalities for the diagnosis of parathyroid adenoma are used to localize parathyroid adenoma. In the past, 4-gland parathyroidectomy with bilateral neck exploration was the criterion standard treatment. Recently, standard modalities for imaging parathyroid lesions include ultrasound, Technetium 99m-sestamibi, 4-dimensional parathyroid-CT, PET choline scan, and magnetic resonance imaging. Based on imaging findings, the surgeon can determine a suitable surgical intervention. However, this preoperative modality decreases the rate of complications, along with the need for lifelong thyroid hormone or calcium supplement therapy [17,18].

Once the abnormal gland is identified, surgical resection and histological examination of the tumor is the ultimate therapy, and parathyroidectomy can prevent the recurrence of
pancreatitis [4]. Generally, the recommended management of acute pancreatitis related to PHPT begins with conservative management. It is also important to stabilize the patient’s condition [4]. Several studies have reported that adequate fluid resuscitation, calcuiresis, calcitonin, furosemide, and bisphosphonate therapy act as a bridge to definitive surgery [19,20]. Gasparri et al reported that, with appropriate initial medical management before surgical excision in patients with the parathyroid crisis, the mortality rate decreased to 2.8% [21].

In the present case, hypercalcemia was corrected using intravenous fluids, forced calcuiresis, and hemodialysis. Acute pancreatitis, abdominal ascites, and bilateral pleural effusions were conservatively managed. However, her condition worsened on day 9 after admission. CT revealed severe diffuse necrotizing pancreatitis of almost the entire pancreas (body and tail) with extrapancreatic complications, including increased abdominal ascites and bilateral pleural effusions; therefore, a pigtail was inserted.

Although PHPT rarely presents in patients with acute pancreatitis, acute necrotizing pancreatitis is considered the worst and least common type of acute pancreatitis, with an overall incidence of 10% to 20%. It is associated with high mortality (34-95%) and morbidity (2-39%) [22,23]. In patients with acute necrotizing pancreatitis, mortality can occur in the first 2 weeks of onset and is most often due to systemic inflammatory response syndrome, which is an exaggerated inflammatory response associated with systemic organ dysfunction, immunosuppression, and organ failure [22].

The surgical management of acute necrotizing pancreatitis depends on the clinical situation of the patient and the response to conservative management. Delaying definitive intervention to enable necrotic collection to form a capsule is preferred. The first-line management for necrosis is either percutaneous drainage or endoscopic transmural drainage. Failure of these interventions can necessitate the use of more invasive interventions, either using traditional necrosectomy or minimally invasive techniques, including percutaneous endoscopic necrosectomy, video-assisted retroperitoneal debridement, and direct endoscopic necrosectomy [24].

In the present case, on day 16 of admission, the pigtail was removed, the patient’s condition improved, and she was discharged. However, right inferior parathyroidectomy was planned, once the patient fully recovered from pancreatitis. A follow-up CT of the pancreas 2 weeks after discharge showed a regressive course regarding generalized inflammatory changes in the pancreas and fluid throughout the abdomen.

Unfortunately, our patient also presented with venous thromboembolism. The CT scan showed superior mesenteric vein and splenic vein thrombosis, which was managed conservatively with bowel rest and warfarin. However, these findings can be explained by 2 factors: either it is secondary to hypercalcemia or complications of acute pancreatitis.

The hypercoagulable state in a patient with PHPT is not fully understood, whether secondary to hypercalcemia or primary hyperparathyroidism [7,25]. However, multiple mechanisms have been suggested, such as the effect of calcium in the vascular smooth muscle causing vasoconstriction or stimulation of multiple factors in the clotting system that boosts platelet aggregation. Furthermore, the ability of the kidneys to reabsorb sodium and water is altered by the hypercalcemic state, and non-compensated polyuria due to nausea and anorexia can cause dehydration and lead to a hypercoagulable state. In addition, a high calcium concentration has a cytotoxic effect and results in thrombosis [7,25].

Venous thrombosis can also be secondary to acute pancreatitis. Superior mesenteric vein thrombosis is very rare, with an incidence of 5% to 15% of all cases of mesenteric vessel occlusive disease. It is associated with high mortality rates and consequent catastrophic complications if not detected and managed early. The mechanism behind venous thrombosis in patients with acute pancreatitis is either venous compression or an imbalance between fibrinolysis and coagulation due to local inflammatory processes [26].

In 2 different systematic reviews and meta-analyses that were conducted recently, the treatment of venous thrombosis due to pancreatitis with anticoagulants improved the odds of recanalization. However, it did not increase the risk of hemorrhagic complications or overall mortality [27,28]. Mignini et al reported a case of a male patient with acute pancreatitis with mesenteric venous thrombosis secondary to PHPT [14].

Parathyroid malignancies could lead to the same presentation as reported by Zelano et al [29]. Therefore, there is role of histology in distinguishing these malignancies.

The definitive treatment for PHPT is surgical excision of the parathyroid adenoma [1]. Our patient underwent a successful right inferior parathyroidectomy after her condition was stabilized and was healthy after a 2-year follow-up period.

Conclusions

Hypercalcemia-induced pancreatitis secondary to PHPT can lead to serious health problems and potential complications. Early detection of the disease and its complications and the initiation of good management followed by parathyroidectomy should be considered to improve hypercoagulability and
reduce the risk of subsequent venous thromboembolism and recurrence pancreatitis, as well as other complications associated with PHPT. This report highlights the importance of recognizing that hypercalcemia associated with parathyroid adenoma can result in acute pancreatitis, leading to hypercoagulable states and inflammation of adjacent vessels, including the splenic and mesenteric veins.

**Department and Institution Where Work Was Done**

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**Ethics Statement**

Ethical approval was granted by the Ethics Research Committee at Armed Forces Hospital Northwestern Region, Tabuk, Saudi Arabia [ethics ID No.: KSAFH-RET-2024-568].

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