

A Case of Pancreatitis Associated with Hyperfunctioning Intrathyroidal Parathyroid Adenoma

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갑상선내 과기능성 부갑상선 선종에 의한 췌장염 1예

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Both intrathyroidal parathyroid adenoma and acute pancreatitis from hyperparathyroidism are rare disorders. We report a case of acute pancreatitis from hyperfunctioning intrathyroidal parathyroid adenoma in a 40-year-old man with severe abdominal pain. Serum chemistry values showed high amylase, lipase, calcium and intact parathyroid hormone level, and abdominal CT revealed acute pancreatitis. A 7 mm lesion was detected inside the left upper pole of thyroid on neck ultrasonography and confirmed to be a parathyroid lesion based on fine needle aspiration cytology. After exploratory parathyroidectomy, symptoms subsided. In patients who present with acute pancreatitis, hyperparathyroidism should also be considered if risk factors such as alcohol ingestion, gallstone, previous endoscopic retrograde cholangiopancreatography, and abdominal trauma do not exist. Exploratory parathyroidectomy should be performed in a case of acute pancreatitis from primary hyperparathyroidism.

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Introduction

Intrathyroidal parathyroid adenoma is an extremely rare case of the parathyroid gland lesions, caused by an embryologic abnormality (aberrant descent of the gland).¹⁾ Intrathyroidal parathyroid adenoma can be usually missed out to diagnose during preoperative imaging studies but diagnosed during surgery with postoperative pathologic findings.

A parathyroid adenoma manifesting acute pancreatitis was first described in 1957,²⁾ and hypercalcemia from hyperparathyroidism has been considered as an important cause of acute pancreatitis since then.

Here, we report a case of primary hyperparathyroidism due to intrathyroidal parathyroid adenoma that presented as acute pancreatitis.

Case

A 40-year-old man visited our emergency room (ER) with severe epigastric pain radiating to his back for 5–6 hours. He was not a heavy drinker and had not drunken alcohol prior to symptom development. He had been treated 5 times for acute pancreatitis over the past 1-year at a local clinic. Serum chemistry values were abnormal; amylase 4661 U/L (reference range: 28–100), lipase 21043 U/L (reference range: 13–60), and calcium elevated to 11.1 mg/dL (reference range: 8.6–10.2). Serum phosphate level 3.1 mg/dL (reference range: 2.7–4.5) was within normal range. Abdominal CT demonstrated diffuse fluid collection around pancreas and extensive edematous change of pancreatic parenchyma. There was no evidence of gallstone on CT. He did not have a history of endoscopic retro-

grade cholangiopancreatography (ERCP), abdominal trauma, and previous medication. The levels of carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA) were within normal range.

The patient was admitted at the department of gastroenterology and conservatively treated to stabilize his symptoms and serum chemistry imbalance. Additional evaluations were performed to determine the cause of acute pancreatitis. Although serum ionized calcium and intact parathyroid hormone (iPTH) results showed elevations to 6.29 mg/dL (reference range: 4.48–4.92) and 87 pg/mL (reference range: 14–72) respectively, renal function tests including blood urea nitrogen/creatinine and creatinine clearance were normal range. Furthermore, he did not have personal or family history of renal diseases. These results indicated the possibility of primary hyperparathyroidism, so technetium (Tc)-99m sestamibi scan and neck ultrasonography (USG) were performed to locate parathyroid lesion. Tc-99m sestamibi scan failed to detect specific uptake of parathyroid on its 3 hour-delayed image, but a 7 mm lesion was detected inside the left upper pole of thyroid by neck USG (Fig. 1). The lesion was embedded on the left upper posterior of thyroid, and it was difficult to differentiate thyroid nodular hyperplasia and intrathyroidal lesion. Fine needle aspiration (FNA) on the lesion was additionally performed. Sono-guided FNA cytological findings with stippled nuclear chromatin indicated the probable presence of a parathyroid lesion rather than thyroid lesion. Preoperative neck CT showed small mass in left posterior thyroid lobe and otherwise no visible mass in the whole neck and mediastinum.

Excision of the intrathyroidal parathyroid lesion was planned after symptom subsided. Preoperative serum chemistry values indicated calcium at 11.1 mg/dL (reference range: 8.6–10.2) and iPTH at 83.9 pg/mL (reference range: 14–72). Un-

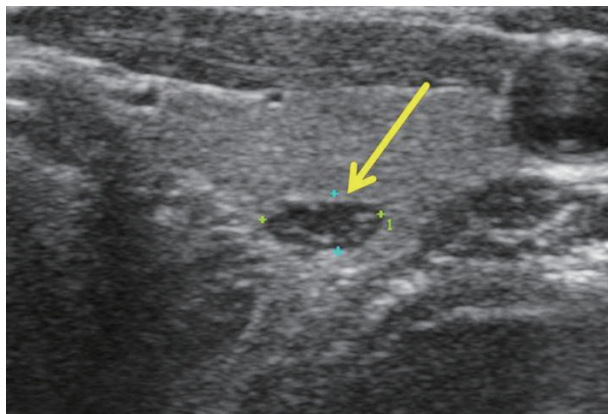


Fig. 1. Thyroid ultrasonography showing 7×7×3 mm heterogeneous hypoechoic nodule (arrow) in left posterior thyroid gland.

der general anesthesia, a 3 cm sized skin incision was made parallel to a skin crease on the anterior neck, and strap muscles and thyroid capsule were dissected and separated. Strap muscles were retracted to the lateral side while applying medial traction of thyroid gland, and the mass was palpated along the posterior surface of upper pole inside the left thyroid lobe. Palpable mass was not hard, and it did not appear to be invasive or adhesive to adjacent tissue. The mass was completely excised with a clear margin through an incision on the thyroid capsule and parenchyma (Fig. 2). The excised mass was measured as 7 mm, which concurred with preoperative USG view. Intraoperatively, serial serum iPTH levels were measured at 5, 10, and 15 minutes after excision and found to be 4.1 pg/mL, 3.9 pg/mL, and 3.0 pg/mL (reference range: 14–72) respectively. Frozen biopsy of the excised mass suggested parathyroid adenoma, and we were able to confirm that the hyperfunctioning parathyroid lesion had been completely removed. Final pathologic findings showed a definite diagnosis of typical parathyroid adenoma (Fig. 3). At 2 hours after surgery, serum cal-

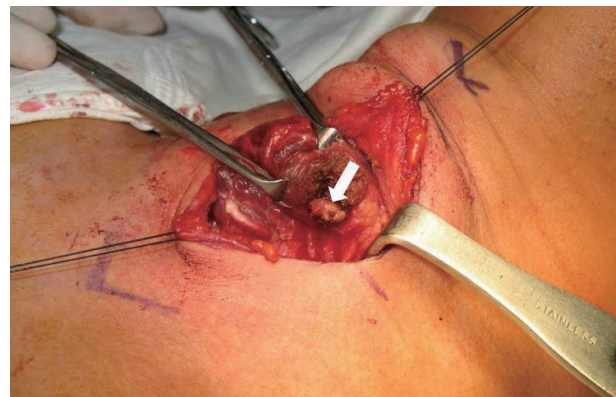


Fig. 2. Palpable mass (arrow) visible through incision on thyroid capsule and parenchyma.

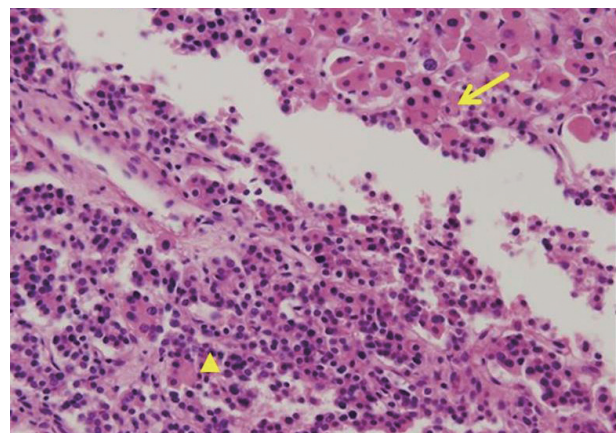


Fig. 3. Round nuclei with regular size in abundant eosinophilic cytoplasm of chief cells (arrow) and chief cells demonstrating solid sheet-like, acinar, follicle-like arrangement (triangle) (×400, H&E stain).

cium had reduced to 8 mg/dL (reference range: 8.6–10.2), and serum iPTH level was undetectable. On postoperative day 6, serum iPTH was normalized (26.5 pg/mL), and the patient was discharged from hospital with oral calcium medication. The patient did not have any hypocalcemic complications, such as numbness or tetany. However, the patient revisited our ER with severe epigastric pain at 1 week after discharge. On emergency abdominal CT and sonography, he was diagnosed as acute pancreatitis due to delayed stenosis of the intrapancreatic duct. Emergency ERCP was performed to insert a stent into the duct by a gastroenterologist. His symptom subsided immediately after stent insertion. The stent was removed two months after ERCP. At one year after the surgery, the patient showed normal calcium serum level with an iPTH level of 66 pg/mL (reference range: 14–72), and he had not experienced any recurrent episode of pancreatitis.

Discussion

Ectopism of the parathyroid glands occurs more frequently in the inferior glands than in the superior glands due to differentiation of the embryological developments of the parathyroid glands. Whereas the inferior parathyroid glands embryologically descend along a long virtual tract through the neck with descent of the thymus, the superior parathyroid glands descend via a shorter way compared to the inferior parathyroid glands.^{3,4)} Both the superior and inferior parathyroid glands can be positioned as the intrathyroidal type, but no proper embryologic explanation has been provided for this phenomenon. Ectopic parathyroid glands are located in the thymus (30%), mediastinum (22%), and thyroid (5%).³⁾

Intrathyroidal parathyroid adenoma rarely occurs in only 1.4–4% of all parathyroid adenomas.³⁾ Preoperative Tc-99m sestamibi scans can precisely detect parathyroid lesions, but some parathyroid lesions cannot be detected as our case because of the intrathyroidal location, small size, and a slightly marginal elevation in serum calcium and parathyroid hormone level. Based on these findings, we attempted to determine location of parathyroid lesion using various methods including Tc-99m sestamibi scan, neck USG, and neck CT.^{4,5)} In these days, the advanced techniques of Tc-99m sestamibi scan combined with single proton emission computerized tomography/computerized tomography and four dimensional CT have been introduced.^{6,7)}

In our case, parathyroid lesion inside the thyroid gland was confirmed on fine needle aspiration cytologic findings. Re-

cently there are some reports that FNA with PTH washout assay have a high reliability in localizing hyperfunctioning parathyroid tissue when the results show a greater value than serum PTH level.⁸⁾ If we performed PTH washout assay from needle aspirates, we could have more information that differentiates functioning adenoma from non-functioning simple hyperplasia.

Acute pancreatitis due to primary hyperparathyroidism was first described in 1957.²⁾ Some reports presented that 1–8% of all acute pancreatitis cases originated from primary hyperparathyroidism, and 1.5–13% of primary hyperparathyroidism cases manifested as acute pancreatitis.⁹⁾

In our case, we postulated that the hypercalcemia from hyperparathyroidism was the cause of acute recurrent pancreatitis because no typical predisposing factors for acute pancreatitis such as alcohol, gallstone, ERCP, trauma were found except hypercalcemia with hyperparathyroidism. However, there is another chance that acute recurrent pancreatitis results from pancreatic duct stenosis from the history that one event occurred at 1 week postoperatively and pancreatic duct stenosis was found through ERCP. But no other events occurred after this event through over 1 year. Hence we thought the one event of acute pancreatitis at postoperative 1 week might come from pancreatic duct obstruction caused by previous recurrent pancreatitis. Strictures of the pancreatic duct is generally known to be due to inflammation or fibrosis around the duct.¹⁰⁾

The pathophysiology of acute pancreatitis from hyperparathyroidism proceeds in three steps. Firstly, the calcium ion facilitates the conversion of trypsinogen to trypsin and stimulates the *de novo* activation of trypsinogen from mRNA on ribosomes, so hypercalcemia can induce trypsin hypersecretion. Secondly, calcium acts as a secondary messenger and triggers the exocytosis of cytokines, which induce the vasodilation of parenchymal vessels and the apoptosis of pancreatic parenchymal cells. Lastly, calcium levels become high enough to form a stone that obstructs the intrapancreatic duct.^{2,11)}

Although hyperparathyroidism seldom triggers acute pancreatitis, serum calcium and iPTH levels should be checked in a view of the possibility of parathyroid gland hyperfunction. Renal function also should be examined to exclude nephrogenic secondary hyperparathyroidism in a non-alcoholic patient with acute pancreatitis.

In our case, the patient was definitely indicated for surgical management because of the presence of severe pancreatitis resulting from hypercalcemia. However, proper indications in accordance to guidelines should be applied when approach-

ing asymptomatic primary hyperparathyroidism.¹²⁾

If an intrathyroidal type hyperfunctioning parathyroid lesion with surgical indication is suspected based on USG, exploratory parathyroidectomy should be performed even though there were no specific findings on Tc-99m sestamibi scan. During exploratory parathyroidectomy, serial rapid serum iPTH tests are necessary until the suspected excised mass is confirmed to be the only hyperfunctioning parathyroid adenoma or hyperplasia. When serial iPTH level does not decrease lower than 50% compared to preoperative iPTH level, another parathyroid must be explored to identify the hyperfunctioning parathyroid.¹³⁾

Palpation on suspected mass may be sufficient to find an intrathyroidal parathyroid mass, but intraoperative USG can also be applied to confirm the mass. When an intrathyroidal parathyroid mass cannot be located during surgery, surgeons should consider hemithyroidectomy on the side with higher suspicion of intrathyroidal parathyroid adenoma if it is certain that a hyperfunctioning parathyroid is present.¹⁴⁾

Similarly, if parathyroid carcinoma or multiple adenomas are suspected during operation, concurrent ipsilateral hemithyroidectomy should also be considered.

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