Primary Hyperparathyroidism Presenting as Recurrent Pancreatitis Due to Parathyroid Adenoma

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Abstract

Recurrent attacks of acute pancreatitis as initial manifestation of primary hyperparathyroidism is rare. We report two cases of young women presenting with recurrent attacks of pancreatitis due to parathyroid adenoma. After surgical excision of the parathyroid adenoma, symptoms of pancreatitis resolved, and serum parathormone and calcium levels returned to normal.

Keywords
- hyperparathyroidism
- recurrent pancreatitis
- parathyroid adenoma

Introduction

The etiology of pancreatitis is largely dominated by gall stones and alcohol. Primary hyperparathyroidism is also a cause of both acute and chronic pancreatitis. Hypercalcemia secondary to secretion of parathormone plays a major role in pathogenesis.

Case Report

Case 1

A 30-year-old female presented with complaints of abdominal pain and constipation for 1 month. Past history revealed multiple (three to four) episodes of abdominal pain with evidence of elevated serum amylase and lipase levels and was managed conservatively for pancreatitis. On examination, abdominal distension and epigastric tenderness were noted. USG abdomen showed gross ascites and bulky pancreas. Serum lipase and amylase levels were grossly elevated. Contrast-enhanced CT abdomen showed evidence of ill-defined peripherally enhancing collection involving body, tail of pancreas, which suggests necrotizing pancreatitis, gross ascites, and filling defect in splenic vein suggesting thrombosis. Multiple tiny renal calculi were seen in bilateral kidneys (►**Fig. 1A, B**). The bone window showed osteolytic lesions involving the right ala of sacrum and bilateral iliac wings (►**Fig. 1C**). In view of acute pancreatitis with multiple renal calculi and multiple bony lytic lesions, we suspected hyperparathyroidism to be an etiology and we did USG neck screening, which showed heterogeneously hypoechoic round lesion measuring 2.6 × 1.3 cm adjacent to lower pole of right lobe of thyroid with vascularity. Noncontrast CT neck showed hypodense lesion measuring 3 × 1.5 cm at the same location, suggesting parathyroid adenoma (►**Fig. 2A–C**).

Skeletal survey showed subperiosteal resorption involving the radial side of middle phalanges of 2nd, 3rd and 4th digits of right hand, multiple well-defined osteolytic lesions involving the skull, distal femur, ala of the sacrum and iliac wing, and end plate sclerosis of thoracic and lumbar vertebra (►**Fig. 3A–D**).

Biochemical findings revealed elevated parathyroid hormone (PTH) levels (1475 pg/mL), hypercalcemia (13 mg/dl), and hypophosphatemia (2 mg/dl). A diagnosis of primary hyperparathyroidism due to parathyroid adenoma, causing recurrent attacks of acute necrotizing pancreatitis, was made in view of the above findings.

The patient underwent an uneventful resection of the tumor-bearing right inferior parathyroid gland through a focused transcervical approach after safeguarding the recurrent laryngeal nerve (►**Fig. 4**). The patient made an uneventful recovery and was discharged with oral calcium supplements for the biochemical hypocalcemia that normalized in a couple of weeks. Postoperative serum PTH levels also normalized (12 pg/mL). The final histopathology confirmed the diagnosis of

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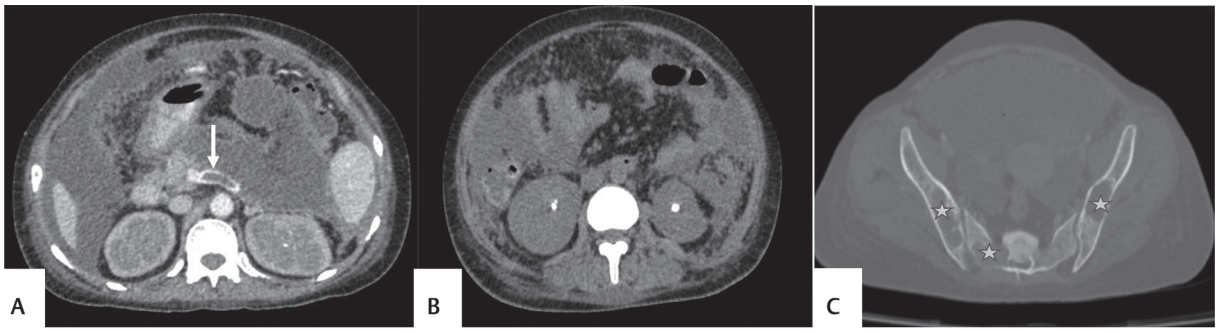

Fig. 1 (**A**) Contrast-enhanced CT abdomen, axial section shows ill-defined peripherally enhancing collection involving body and tail of pancreas, suggesting acute necrotizing pancreatitis with gross ascites and splenic vein thrombosis (arrow). (**B**) Plain CT abdomen, axial section shows multiple renal calculi seen in bilateral kidneys (**C**) Plain CT pelvis, axial section, bone window shows multiple osteolytic lesions involving right ala of sacrum and bilateral iliac wings (asterisk).

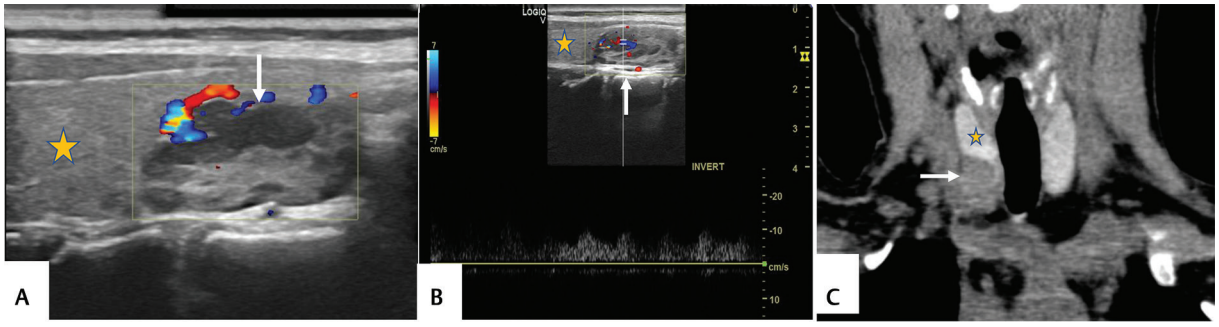

Fig. 2 (**A** and **B**) USG neck sagittal plain with color and spectral Doppler shows heterogeneously hypoechoic lesion (arrow) with vascularity adjacent to the lower pole of right lobe of thyroid (asterisk). (**C**) Plain CT neck coronal section shows hypodense lesion (arrow) at lower pole of thyroid (asterisk), suggesting parathyroid neoplasm.

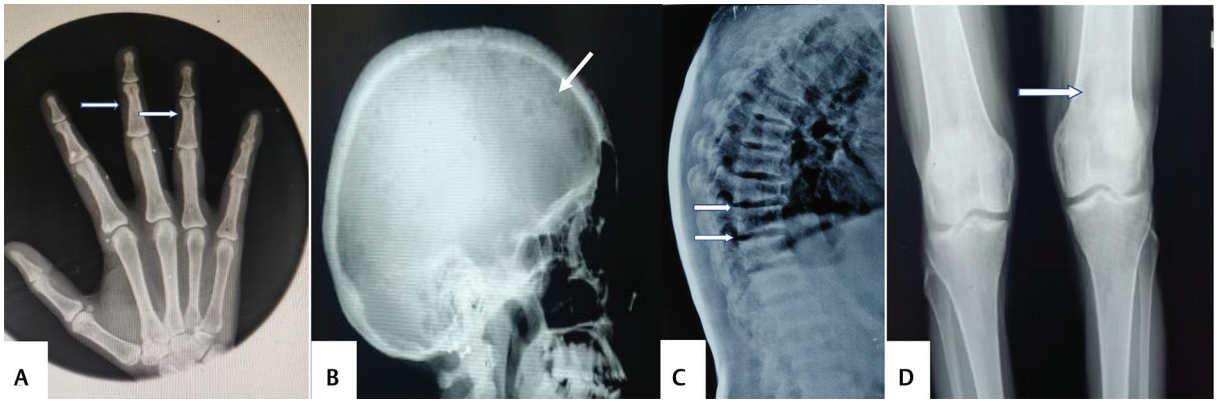

Fig. 3 (**A**) Plain X-ray coned down PA view of right hand which shows subperiosteal erosions seen in the radial aspect of middle phalanges of 2nd, 3rd and 4th digits (arrows). (**B**) Plain X-ray lateral view of skull shows multiple osteolytic lesions involving skull (arrow). (**C**) Plain X-ray lateral view of D-L spine shows thoracic and lumbar vertebral end plate sclerosis (arrows). (**D**) Plain X-ray bilateral knee joint AP view shows well-defined osteolytic lesion noted in the distal end of left femur, suggesting brown tumor (arrow).

clear cell parathyroid adenoma. Symptoms of acute pancreatitis resolved, and the patient is now on follow-up for 13 months without any recurrent episodes of pancreatitis.

Case 2

A 30-year-old female presented with complaints of abdominal pain, vomiting and altered sensorium for 1 week. Past history revealed several similar episodes of acute abdominal pain which were managed conservatively for pancreatitis. On examination, epigastric tenderness was noted. USG abdomen showed chronic calcific pancreatitis and increased echotexture of bilateral kidneys. Serum lipase and amylase levels were mildly elevated

Contrast-enhanced CT abdomen revealed pancreatic parenchymal and ductal calcifications with dilated pancreatic duct suggestive of chronic calcific pancreatitis, and lytic lesions were noted in iliac bones bilaterally (►**Fig. 5**). In view of recurrent attacks of pancreatitis and lytic lesions involving bones, contrast-enhanced CT neck evaluation was done, which showed heterogeneously enhancing mass lesion inferior to the left lobe of thyroid suggestive of parathyroid neoplasm (►**Fig. 6**). Biochemical findings revealed elevated PTH

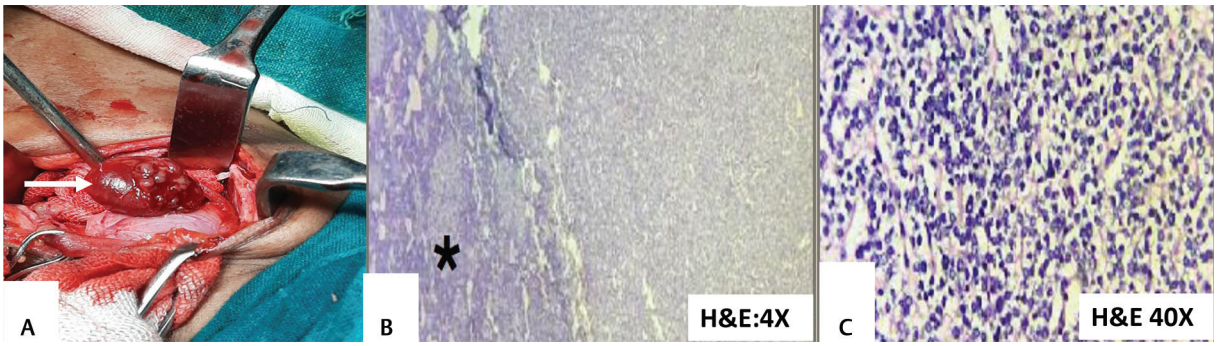

Fig. 4 (**A**) Intraoperative picture showing parathyroid adenoma being dissected (arrow) (**B**) Low-power 4X magnification image shows normal parathyroid gland on left side (asterisk) and tumor tissue on right side. (**C**) High-power 40X magnification image shows tumor tissue arranged in sheets composed of cells, which are monotonous population of round to polyhedral cells with very little pleomorphism suggestive of parathyroid adenoma.

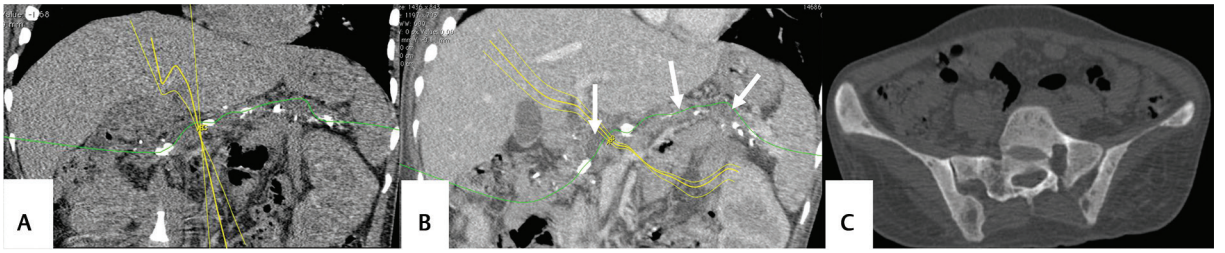

Fig. 5 (**A**) Plain CT abdomen, curved MPR image shows multiple pancreatic parenchymal and ductal calcifications (arrows). (**B**) Contrast-enhanced CT abdomen, curved MPR image shows ductal dilatation and ductal calcifications. (**C**) Plain CT pelvis, axial section, bone window shows multiple lytic lesions involving bilateral iliac bones suggestive of brown tumor.

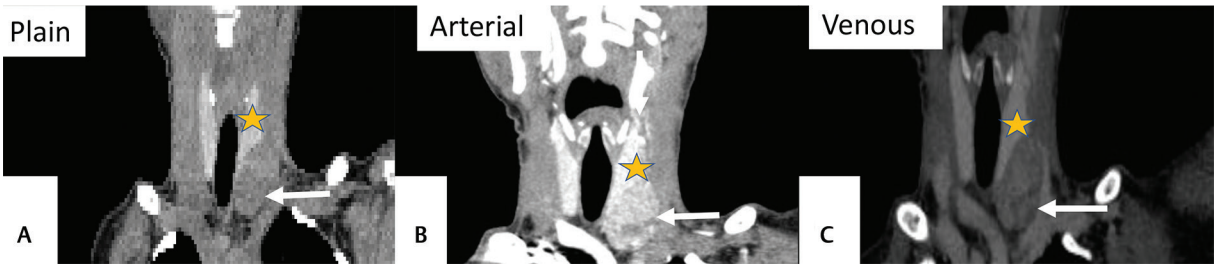

Fig. 6 (**A–C**) Plain and contrast CT neck, coronal section shows well-defined hypodense lesion inferior to left lobe of thyroid (asterisk), intensely enhancing on arterial phase and showing wash out in delayed phase (arrows).

levels (1193 pg/ml), hypercalcemia (21.7 mg/dl), and hypophosphatemia (1.5 mg/dl).

Incidentally, the patient also had galactorrhea with elevated serum prolactin levels for which MRI brain was performed which revealed pituitary microadenoma.

In view of the presence of both parathyroid adenoma and pituitary adenoma, the patient was further evaluated for multiple endocrine neoplasia (MEN) syndrome; however, she did not have symptoms of neuroendocrine tumors, nor did contrast-enhancing CT reveal any hyperenhancing lesion in pancreas.

A final diagnosis of primary hyperparathyroidism due to parathyroid adenoma, causing chronic calcific pancreatitis with incidental pituitary microadenoma, was made.

The patient underwent an uneventful resection of the tumor-bearing the left inferior parathyroid gland through a focused transcervical approach (►**Fig. 7**). The patient had an uneventful recovery and was discharged with oral calcium supplements for the biochemical hypocalcemia that normalized in a couple of weeks. Postoperative serum PTH levels also normalized (10 pg/mL). The final histopathology confirmed the diagnosis of clear cell parathyroid adenoma. Symptoms of acute pancreatitis resolved, and the patient is now on follow up for 11 months without any recurrent episodes of pancreatitis.

Discussion

The prevalence of acute pancreatitis in primary hyperparathyroidism is between 1.5 and 13 %.[1] In a patient with primary hyperparathyroidism, the risk of development of pancreatitis is 10 to 30 times more than the normal population, and in a patient with pancreatitis, the risk of detecting primary hyperparathyroidism is 33 times more than the normal.[2]

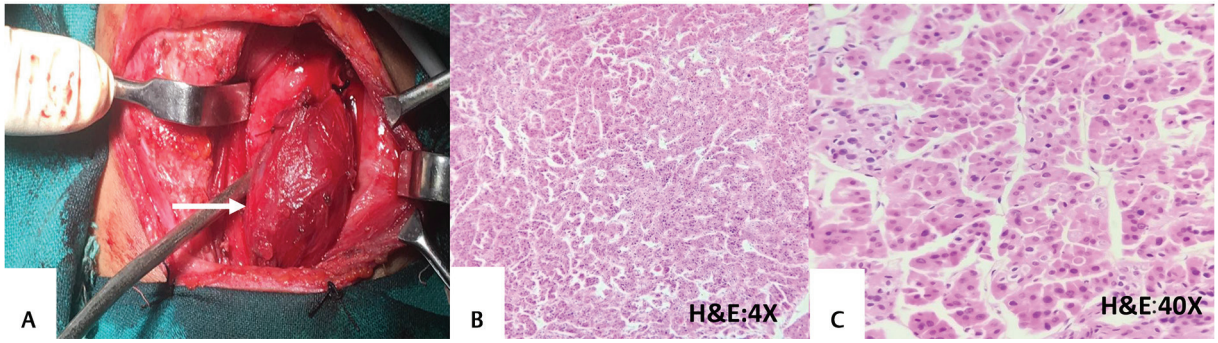

Fig. 7 (**A**) Intraoperative picture showing parathyroid adenoma being dissected (arrow). (**B**) Low-power 4X magnification image shows tumor is variably cellular divided by fibrous connective tissue. (**C**) High-power 40X image shows tumor is arranged in acinar, nests, and lobular patterns. Individual cells showed moderate-to-abundant eosinophilic cytoplasm with round-to-oval vesicular nuclei and few cells showing prominent nucleoli. These features are suggestive of parathyroid adenoma.

Serum parathormone levels normalize within minutes to hours following surgical excision. Postoperative hypocalcemia occurring after parathyroidectomy is called hungry bone syndrome.[3] It is due to extensive remineralization of bone, reflecting the deposition of calcium and phosphate within the bone parenchyma. Risk factors for hungry bone syndrome include old age, large tumor size, raised alkaline phosphatase (ALP) and blood urea nitrogen (BUN) and brown tumor.[4] Our index Case-1 had multiple brown tumor and elevated ALP, so we were able to correctly predict the occurrence of the postoperative hungry bone syndrome and manage effectively.

Hyperparathyroidism leads to hypercalcemia. Hypercalcemia would act by several mechanisms: increased level of calcium in pancreatic juice causes denovo activation of trypsinogen to trypsin, resulting in acinar cell damage and autodigestion of pancreatic parenchyma; activation of pancreatic enzymes through the lysosomal system and hydrolases; calcium precipitation and formation of protein plugs responsible for upstream ductal dilatation and subsequent pancreatitis. The direct toxic action of PTH on the pancreas is also mentioned in literature.[5] A genetic risk factor has also been found. Mutation of SPINK1 gene (serine protease inhibitor Kazal type I) and CFTR gene (cystic fibrosis transmembrane conductance regulator) was found more often in patients with primary hyperparathyroidism who developed an acute pancreatitis.[6] Hypercalcemia per se in addition to being an independent risk factor for precipitation of pancreatic cellular injury can also augment pancreatic disease in patients with ongoing pancreatic injury because of other causes like alcohol abuse, hyperlipidemia, viral infections, ischemia, and ductal hypertension. Recurrent acute pancreatitis can progress to chronic pancreatitis, as described by the necrosis–fibrosis theory. A south Indian study has proposed that the presence of hypercalcemia correlated to primary hyperparathyroidism (PHPT) among patients susceptible to tropical chronic pancreatitis (a form of chronic calcific pancreatitis), which may cause an unmasking of preclinical and subclinical disease[2]

Role of 4D CT in diagnosing parathyroid adenoma: The traditional modalities for parathyroid imaging are cervical US and nuclear scintigraphy. US enables precise anatomic localization and may be very accurate for eutopic parathyroid adenomas.[7] The spatial resolution of scintigraphy is lower than that of US, but scintigraphy will depict mediastinal parathyroid adenomas that are missed at US. Four-dimensional (4D) CT has advantages common to both US and scintigraphy. It is superior in detecting small lesions, multiglandular disease, and ectopic adenomas. It provides excellent anatomic detail for preoperative localization in eutopic and ectopic locations, localizing polar vessels. The multiple phases show uptake characteristics that help to differentiate parathyroid lesions from lymph nodes and thyroid nodules. The imaging features of parathyroid adenoma are intense enhancement in arterial phase, followed by rapid washout in delayed phases. Lymph nodes show progressively increasing enhancement after injection of contrast material, with peak enhancement at 90 seconds corresponding to the delayed phase. Thyroid tissue will have intrinsic high attenuation on noncontrast-enhanced images due to iodine content, intense enhancement in arterial phase with increasing contrast enhancement in arterial to delayed phases.

Brown et al reported that among instances in which an abnormal gland was not identified by sestamibi scanning, 4D CT correctly identified the abnormal gland in 80% of cases. Similarly, in patients undergoing reoperation, 4D CT scanning correctly identified the abnormal gland in 91% of cases, compared with 45% for sestamibi scanning.[8]

Conclusion

Our cases demonstrate importance of high-index of suspicion of primary hyperparathyroidism in patients presenting with recurrent attacks of pancreatitis without any risk factor and with hypercalcemia. Timely diagnosis, appropriate preoperative localization techniques and focused surgical intervention help to resolve complications and improve outcome.

Conflict of Interest
None declared.

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