Primary hyperparathyroidism presenting with acute pancreatitis and asymptomatic bone involvement

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Summary

A 15-year-old female patient presented to the emergency room with recurrent vomiting for two weeks associated with abdominal pain. She had two similar attacks in the previous three months both of them were diagnosed as pancreatitis in two different hospitals. On admission, her serum calcium and parathyroid hormone levels were very high. CT scan revealed left inferior parathyroid adenoma. Investigations to rule out possible multiple endocrine neoplasia were all negative. The patient was managed by intravenous fluids and furosemide to lower her serum calcium level. Then, left inferior parathyroidectomy was done. Postoperatively, the patient had hungry bone syndrome with severe hypocalcaemia and was managed by intravenous calcium infusion for five days in the intensive care unit. Later, she was kept on oral calcium and vitamin D supplementation. She became symptom-free and her serum calcium improved gradually.

KEY WORDS: hypercalcemia; acute pancreatitis; primary hyperparathyroidism; hungry bone syndrome.

Introduction

Primary hyperparathyroidism (PHPT) may present with skeletal manifestations or recurrent nephrolithiasis. It can also be asymptomatic, detected only on routine laboratory screening. In western countries, the clinical pattern of PHPT has shifted more towards the asymptomatic presentation (1). But, in developing countries PHPT usually presents with severe skeletal manifestations; vitamin D deficiency could be a leading cause for aggressive osteitis fibrosa cystica (2). Acute pancreatitis is rather a rare presentation of PHPT. Although hypercalcemia seems to be the major risk factor, mutations in different genes have also been proposed (3).

Case report

A 15-year-old female patient presented to the emergency room with recurrent vomiting for two weeks associated with abdominal pain. She had two similar attacks during the previous three months. In both times, she was diagnosed and treated, in a different hospital, as a case of pancreatitis. She denied any history of severe bone pain or fracture. No similar conditions were reported in her family. She had low grade fever, normal blood pressure, and upper abdominal tenderness. Laboratory investigations revealed that serum lipase was 1395 U/L (normal range 30-110 U/L) and amylase was 140 U/L (normal range 7-60 U/L). Her serum calcium was found to be 3.77 mmol/L (normal range 2.15-2.6 mmol/L) and serum parathyroid hormone was 1629 pg/ml (normal range 12-72 pg/ml). Vitamin D level was 8.4 ng/ml (normal range 15-50 ng/ml). Lipid profile, blood glucose and renal function tests were all within normal limits. CT scan of the abdomen revealed bulky pancreas with peri-pancreatic collection (11.4x9.1 cm). It also showed osteopenia and lytic areas in the left iliac bone, the femoral neck bilaterally, and the right pubic bone. No gall bladder stones were found. CT scan of the neck with intravenous contrast (Figure 1) revealed left inferior parathyroid adenoma (3.5 x 1.7 x 1.2 cm). Investigations to rule out possible multiple endocrine neoplasia (MEN) were all negative. These investigations included checking serum levels of gastrin, insulin, prolactin, and IGF-1 in addition to plasma ACTH and metanephrines. Assessment of urinary free cortisol excretion was also done. Ultrasonographic examination showed no renal stones. Urinary calcium excretion and bone mineral density (BMD) were not assessed. Genetic tests were not performed. All first degree relatives had normal serum calcium levels.

The patient was diagnosed to have primary hyperparathyroidism with hypercalcemia-induced pancreatitis. Intravenous fluids and furosemide managed to lower serum calcium to 2.85 mmol/L. Left inferior parathyroidectomy was done. Postoperatively, serum calcium dropped to 2.6 mmol/L within 30 minutes and then gradually to 1.6 mmol/L. PTH dropped to 12 pg/ml, then went up to 126 pg/ml after 24 hours. The patient was kept for 5 days in the intensive care unit and maintained on intravenous calcium infusion (8 g/day) to treat hungry bone syndrome. Oral calcium (3 g/day) was started, with gradual withdrawal of intravenous calcium. The patient was also given alfacalcidol 2 mcg/day. She became symptom-free with normal amylase and lipase levels. Histopathological examination of the resected parathyroid gland confirmed the diagnosis of a parathyroid adenoma (3.2 x 1.5 cm) which was well demarcated from normal tissue with no capsular invasion. It also showed absence of fat cells, lobular pattern or evidence of malignant change. Three months after parathyroidectomy, serum calcium became 2.15 mmol/L and PTH was back to normal. Oral calcium replacement has been reduced to 1.8 gm/day and alfacalcidol to 1 mcg/day.
Discussion

The association between pancreatitis and PHPT is controversial. Bai et al. reviewed the association between both conditions in the literature. They reported that the published cohorts of patients were subject to bias; because serum calcium screening was not universally performed among all control patients. They also concluded that hypercalcemia may contribute to pancreatitis in these cases, along with genetic or environmental insults (4). Hypercalcemia can cause activation of trypsinogen to trypsin, resulting in autodigestion of the pancreas. It can also lead to the formation of pancreatic calculi, ductal obstruction, and subsequent attacks of acute or chronic pancreatitis (5). Acute pancreatitis is a very uncommon presentation of PHPT. The recurrence of pancreatitis before establishing the diagnosis makes the reported presentation a rare one. Absence of bone pain, despite severe skeletal involvement, adds to the rarity of the case. Complete recovery after surgical removal of the parathyroid adenoma establishes the causal relationship. The Mayo Clinic experience between 1950 and 1975 found that out of 1153 patients with PHPT, only 17 (1.5%) had coexisting pancreatitis (6). Other factors of possible etiologic significance in pancreatitis, such as gallstones or alcohol abuse, were present in 11 of the 17 patients (6). Misgar et al. reported the case of a 32-year-old man who was diagnosed to have PHTP during the fourth attack of pancreatitis. But the patient did not have any skeletal manifestations and his postoperative period was uneventful (7).

PHPT can be part of MEN, types 1 and 2A. In MEN-1, PHPT is usually due to multiglandular hyperplasia of the parathyroid glands; however solitary adenomas have also been observed (8). In MEN-2A, the pathology of the parathyroid glands includes hyperplasia, adenoma or a combination of the two (9). The reported patient had negative laboratory screening for both MEN types 1 and 2A. As she is only 15 years old, genetic tests are strongly recommended and long term follow up would be mandatory.

In developing countries, PTHP can have severe bone involvement. Deficiency of vitamin D could be a contributing factor (2). The term hungry bone syndrome has been coined to profound and prolonged (more than four days postoperatively) hypocalemia, after parathyroidectomy for severe hyperparathyroidism. The syndrome has been reported in 25-90% of patients with radiological evidence of hyperparathyroid bone disease vs only 0-6% of patients without skeletal involvement. Treatment is aimed at replenishing the severe calcium deficit by using high doses of calcium supplemented by high doses of active metabolites of vitamin D (10). The presented case had vitamin D deficiency and osteitis fibrosa cystica. Both condition increased the risk of postoperative hungry bone syndrome. Replacement treatment was successful, and the patient had very good recovery.

Conclusions

- Primary hyperparathyroidism can present with pancreatitis (though rare).
- In those patients, parathyroidectomy can cure both hyperparathyroidism and pancreatitis.
- Postoperative hungry bone syndrome should be anticipated in patients with severe osteopenia.

Conflict of interest

None declared.

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