Pancreatitis—Primary Hyperparathyroidism Association: Case Report and Literature Review

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INTRODUCTION

Pancreatitis is known to be associated with primary hyperparathyroidism (pHPT). However, the relationship of cause and effect between the two diseases continues to be debated in the medical literature in determining whether one leads to the other.

CASE REPORT

We report a 49-years-old Malay man who presented in July 1997 to the University of Malaya Medical Center, Kuala Lumpur. He had one-day history of severe upper abdominal pain and vomiting. The vital observations were normal but there was tenderness in the upper abdomen. Past history revealed occasional episodes of loin pains and passing stones per urethra. He admitted to be a smoker but had never consumed alcohol.

Investigations revealed serum amylase of 2,285 IU/L (n=25 < 150), mild hyperglycemia and crystalluria. Serum calcium level was 2.65 mmol/L (n=2.20–2.60). Ultrasound examination showed a normal gallbladder without any stones. A calculus was noted in the right kidney. CT scan showed inflammation of pancreatic tail and a suspected stricture of pancreatic duct. Somehow on this occasion the hypercalcemia was not pursued. At the suggestion of the gastroenterologists, an ERCP was done which showed normal common bile and pancreatic ducts. The symptoms soon settled on conservative management and he was discharged home.

His next review was in a urology clinic where he presented with features of acute right epididymoorchitis which was investigated and successfully treated with antibiotics. In November 1997 and in February 1998 he had two further admissions with clinical features of acute pancreatitis with serum amylase levels of 1,410 and 1,147 IU/L respectively. On both occasions he quickly settled spontaneously and requested for discharge. Once again, routine calcium of 2.80 mmol/L did not raise any alarm. It wasn’t until May 1998, nearly ten months after his first presentation and after a third admission with acute pancreatitis (serum amylase: 1,354 IU/L) that the hypercalcemia was noted and acted upon. On this admission the serum calcium was 2.89 mmol/L and serum phosphate, 0.94 mmol/L (n=0.9–1.5). He was also hyperglycemic, his blood glucose being 13.6 mmol/L. Repeat checks confirmed persistent hypercalcemia (calcium=3.09 mmol/L), hypophosphatemia (phosphate=0.7 mmol/L), a normal albumin (43 g/L) and a urinary calcium of 5.5 mmol/L (n=2.2–7.5).
Parathyroid hormone level (iPTH) level was 99.8 pg/ml (n=11.0)

Fasting lipid levels and the thyroid hormonal assay. The intact was normal as was the blood urea, electrolytes, creatinine and other reason. The main challenge has come from Bess (3) and colleagues from Mayo clinic in 1980. Reviewing 1,153 patients with proven pHPT they found only 17 patients with pancreatitis. They suggested that the association of HPT and pancreatitis was due to bias in patient selection or just chance alone since the incidence of pancreatitis in their series is too low.

These objections by Bess and his colleagues have consistently been challenged with counter arguments. Even before the Mayo clinic report, Kelly (4) in 1968 published an experimental study, demonstrating that persistent hypercalcemia increases the calcium content of the pancreatic juice. This lead to accelerated intrapancreatic conversion of trypsinogen to trypsin, the latter causing pancreatic damage.

Sitges-Sera (5) and co-authors in 1988, have also stressed the point that hypercalcemia per se is behind the causation of pancreatitis. They highlighted the association of pancreatitis with non-hyperparathyroid causes of hypercalcemia. Hypercalcemic conditions like parenteral nutrition, calcium infusion, myeloma, disseminated breast cancer or severe hyperthyroidism are all associated with pancreatitis. Presenting their own 10 cases in support they have suggested that pancreatitis is more likely to develop in patients who exhibit moderate to severe hypercalcemia. According to Sitges-Sera those patients with asymptomatic hyperparathyroidism and/or with mild hypercalcemia are less prone to develop pancreatitis.

Carnille (6) and colleagues have made an interesting narration on the issue from France in 1998. They reviewed 1,435 consecutive patients who were operated on for hyperparathyroidism. Of these, 1,224 patients had a biochemically proven pHPT, the remaining 211 had renal hyperparathyroidism (RHPT). They found that a total of 40 patients (3.2%) with pHPT had pancreatitis. Out
of these, 18 had acute pancreatitis; the remaining having subacute or chronic inflammation. This rate of pancreatitis was higher than in their random hospital population. Surgical cure of pHPT was followed by the spontaneous healing of 17 out of 18 patients with acute pancreatitis. A single diseased gland was found in 27 (out of 40 patients with pancreatitis), which is in favour of primary parathyroid disease being responsible for, and not a consequence of pancreatitis. In 78% of cases, pancreatitis preceded the diagnosis of pHPT and that no pancreatitis was recorded either in the RHPT group or after parathyroidectomy. Their laboratory data suggest that pancreatitis is an effect of hypercalcaemia and not of high intact parathyroid hormone levels (iPTH) levels per se. Their conclusion was that (i) the Pancreatitis-pHPT association is not incidental; (ii) pancreatitis is the consequence and not the cause of pHPT; (iii) hypercalcaemia seems to be a major factor in the development of pancreatitis in pHPT patients; and (iv) cure of pHPT leads to the healing of acute pancreatitis.

A controversial aspect of the Pancreatitis-HPT association is the suggestion that pancreatitis may be caused by parathyroid surgery or at least should be accepted as an uncommon complication of it. Supporters of this theory, Reeve and Delbridge, (7) had postulated in 1982 that the mechanism was the release of parathyroid hormone and an acute rise in serum calcium consequent on operative manipulation of a parathyroid tumour. In their experience, this complication was much more common when thyroid lobectomy or bilateral subtotal thyroidectomy was performed in addition to parathyroidectomy.

This has been contested by Robertson (8) and associates from the Leicester Royal Infirmary. They reported a study in 1995 to test the hypothesis that up to 35% of patients may experience hyperamylasaemia after parathyroidectomy indicating subclinical inflammation of the pancreas. A series of 26 patients undergoing parathyroidectomy were studied by preoperative and post operative biochemical analysis and CT scan of the pancreas after operation. However postoperatively, there was no evidence in any patient of acute pancreatic inflammation or hyperamylasaemia. They postulated that any amylase elevation in other reports might reflect an increase in salivary isoamylase as a result of extensive neck dissection rather than reflecting a subclinical pancreatitis.

Finally, Shepard (9) from Tasmania in 1996 has also disagreed with the theory of post-parathyroidectomy pancreatitis. Reviewing the literature on the subject, Shepard's suggests that it is the surgical stress rather than manipulation of the parathyroid gland, which is responsible for excessive parathyroid hormone release in patients after parathyroidectomy.

In conclusion, acute pancreatitis is one of the symptoms of primary hyperparathyroidism, often caused by a parathyroid adenoma and curable by its excision. Calcium and parathyroid profiles should be scrutinized in all fresh cases of acute pancreatitis even though primary hyperparathyroidism is a rare cause.

REFERENCES