Original Article

Grand Round

Hypercalcemia Due to Hyperparathyroidism Leading to Acute Pancreatitis

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Pancreatitis is a common non bacterial inflammatory disease caused by activation, interstitial liberation and auto digestion of pancreas by its own enzymes. Common causes of acute pancreatitis are gall stones and alcohol. Much is known about the causes of pancreatitis but huge experimental data available about understanding of its pathogenesis is still incomplete. Hyperparathyroidism and other disorders accompanied by hypercalcaemia are occasionally complicated by acute pancreatitis. It is thought that the increased calcium concentration in pancreatic juice resulting from hypercalcaemia may prematurely activate proteases. In this article a case acute pancreatitis resulting from hpercalcaeia due to parathyroid adenoma in a young patient is presented. Hyperparathyroidism was suspected when despite severe pancreatitis calcium level remained high and parathormone level was grossly raised

Key words: Hypercalcemia, Acute Pancreatitis, Hyperparathyroidism

Introduction

Hyperparathyroidism is one of the hormonal conditions that may be an etiological factor in pancreatitis. However the relationship of cause and effect between the two diseases continues to be debated in the medical literature. Besides, other causes of acute pancreatitis like gallstone disease and alcoholism are far more common. For this reason the appearance of a raised serum calcium level, in the routine biochemical profiles of a patient first presenting with acute pancreatitis, does not raise much alarm. However, the precise frequency with which pancreatitis occurs in association with hyperparathyroidism is not known. Mixter, Keynes and Cope (1962) found sixty-two cases of these diseases co existing and reported that pancreatitis occurred in eleven out of 155 patients with hyperparathyroidism.[1] It appears that either the coexistence of these two diseases is not as common in the United Kingdom as in the United States of America or that pancreatitis is not investigated so thoroughly to exclude hyperparathyroidism.

Case Report

A 30-year-old man was admitted on 8 September 2012 to PIMS (Pakistan Institute of Medical Sciences) Islamabad as an emergency with a sudden onset of colicky abdominal pain which radiate to his back. He gave no history of indigestion, vomiting, change of bowel habit or change in color of his stools or urine. He smoked fourteen cigarettes per day for ten years and admitted to a moderate alcohol intake. On examination he was an ill looking man with a pulse rate of 100/min, blood pressure was 110/70 mmHg, respiratory rate 16/min, he was afebrile, and his tongue was dry and coated. The thyroid gland was not enlarged. The abdomen was non distended but there was guarding and tenderness across the upper abdomen. The results of the main investigations performed were: hemoglobin 11.9%; white blood count 15.000 mm3; serum amylase 700 units, lipase was 1080 units and urea and electrolytes were within normal limits. The serum calcium was 11.4mg/dl (normal range 8.5 to 10.5 mg/dl). An X-ray of the abdomen was normal, ultrasound of abdomen showed cholelithiasis and bilateral nephrolithiasis. C.T scan of abdomen showed absccess

and inflammation at tail of pancreas (**Figure 1)**. The hypercalcemia was ignored on this occasion.

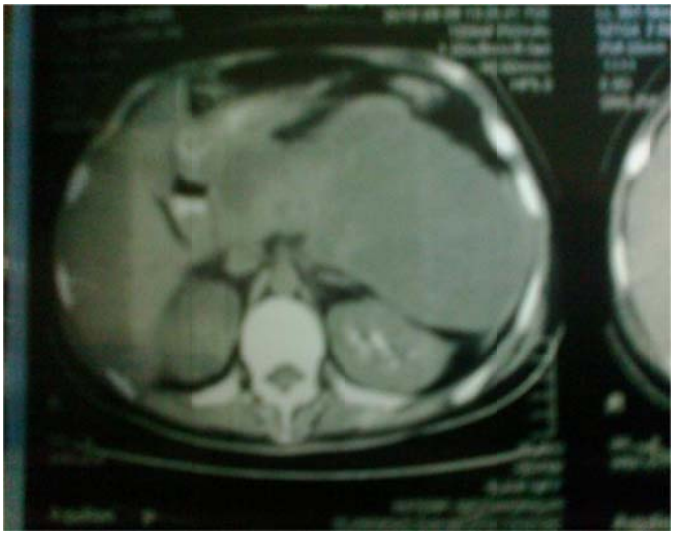

Figure 1. Absccess and inflammation at tail of pancreas

Patient underwent Open cholecystectomy and Pancreatic Abscess was drained. Post op patient was stable remained in hospital for 20 days and was discharged in stable condition.

Patient was readmitted on 15 October 2012 with complaints of fever for 7 days, constipation for 3 days and pain abdomen for three days. On examination abdomen was soft but there was tenderness in upper abdomen. Pulse was 84/min, Respiratory rate: 14/min, Blood pressure: 110/70 mmHg and temperature was 98.5 F. WBCs 14400/microliter, Hb 8.3g/dl, Alkaline phosphatase 459 U/L (40-130), S.Calcium12.1 mg/dl (8.4-10.2), S.Phosphorus 1.5 mg/dl (2.3-4.7), S.Amylase 108 U/L. USG abdomen and pelvis Relatively echogenic kidneys, especially on right side, bilateral nephrolithiasis and small fluid in Morrison pouch. C.T scan of abdomen showed that on comparative analysis with previous study there is significant regression in pancreatic and peri-pancreatic fluid collections; three small fluid pockets are still visible and there is interval regression in peri pancreatic fat stranding. Most important thing we noticed now was the hypercalcemia because in most of pancreatitis patients there is hypocalcaemia. So we did the PTH (parathramone) level which turned out very high 632 pg/ml (normal 23.8-107.4). USG neck showed normal sized thyroid but solid hypo echoic mass posterior to lower pole of left lobe of thyroid most likely parathyroid Adenoma. **(Figure 3 A & B)** Parathyroid scan (**Figure 2**) was done by employing Dual Phase 99mTc-MIBI scintigraphy and it revealed moderate focal tracer retention in the region of lower pole of left lobe of thyroid with washout showed a left inferior parathyroid adenoma.

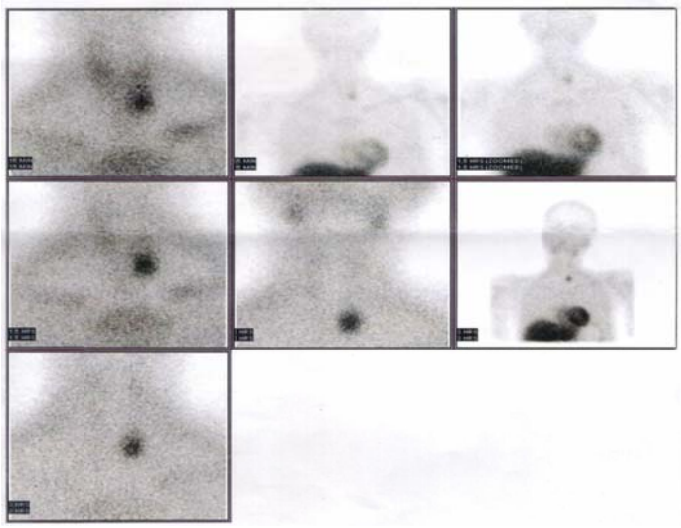

Figure 2. Parathyroid scan

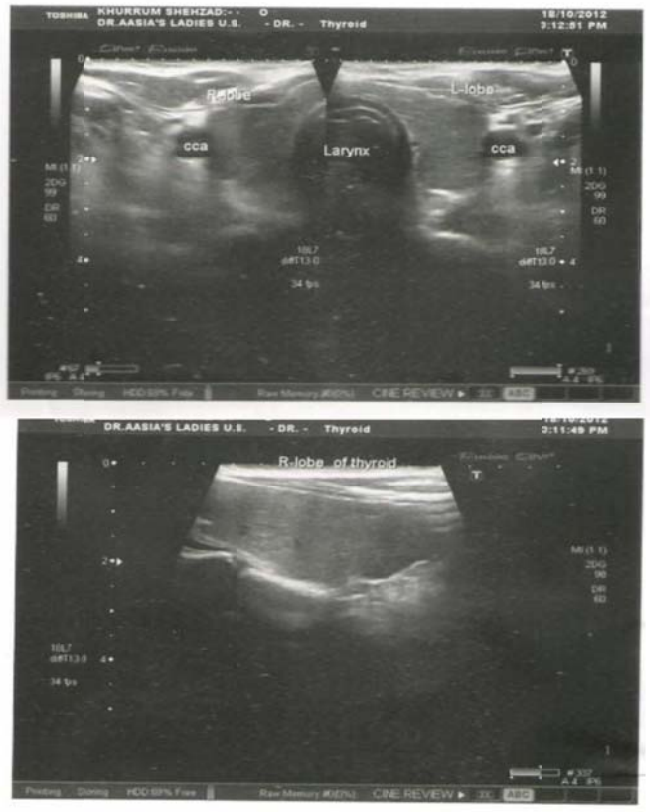

Figure 3 A & B. Ultrasound picture of parathyroid Adenoma

The patient then underwent an open bilateral neck exploration, which showed a left inferior parathyroid adenoma**.(Figure 4 A & B)**

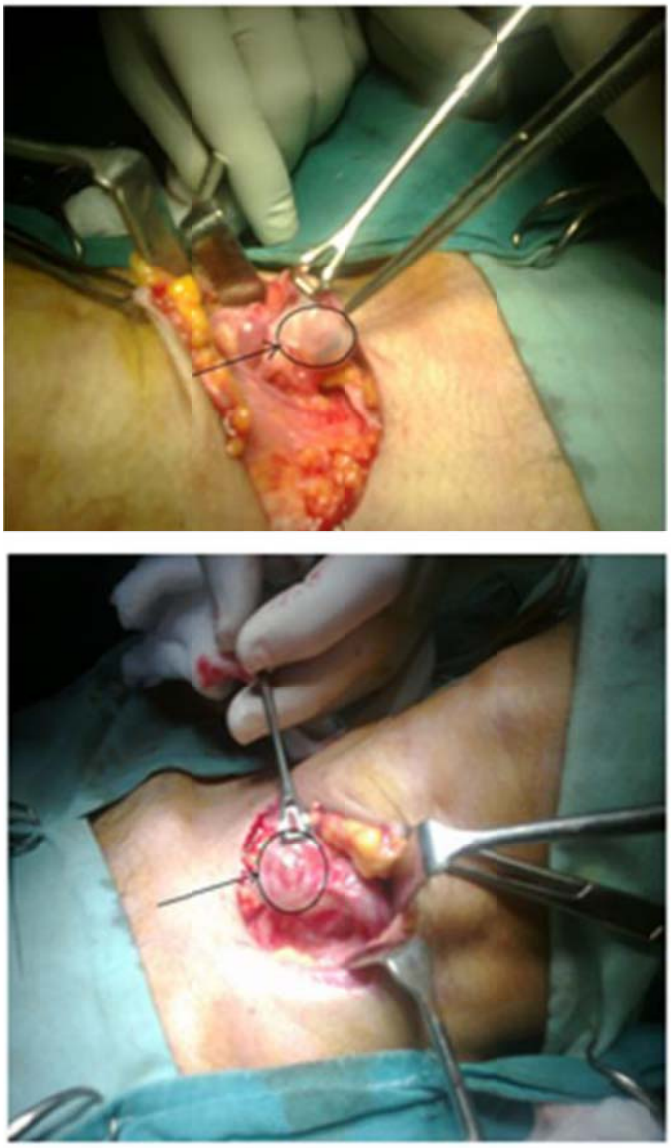

Figure 4 A & B. surgical Demonstration of Parathyroid adenoma

Histopathology of adenoma showed "Encapsulated lesion composed of trabaculae and nests of cells with intervening richly vascular stroma. The cells exhibit round nuclei with salt and pepper chromatin and eosinophilic cytoplasm. Peripheral compressed rim of parathyroid tissue is also seen. Postoperatively patient's serum calcium came down before patient was discharge in stable condition.

Discussion

Pancreatitis related to hyperparathyroidism (HPT) was first reported in 1947 by Martin and Canseco in the Journal of American Medical Association.[2] But it was 10 years later that pancreatitis as a feature of primary HPT became well known through the writing of Cope in the Annals of Surgery in 1957.[1] Since then, individual cases and series have been reported periodically in the belief that pancreatitis is just one of the manifestations of pHPT (primary h perparathyroidism) and that recurrent pancreatitis can be cured by treating the cause of pHPT. However not everyone accepts this. Some suggest that the association of pancreatitis with pHPT is incidental or in fact pancreatitis may be the result of parathyroid surgery for some other reason. The main challenge has come from Bess and colleagues from Mayo clinic in 1980(3). Reviewing 1153 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 was too low. These objections by Bess and his colleagues have been challenged with counter arguments. Even before the Mayo clinic report, Kelly in 1968 published an experimental study in the Archives of Surgery[4], demonstrating that persistent hypercalcemia increases the calcium content of the pancreatic juice leading to accelerated intrapancreatic conversion of trypsinogen to trypsin, the latter causing pancreatic damage. Sitges-Sera' and co-authors in 1988, have also stressed the point that hypercalcemia per se is behind the causation of pancreatitis.[5] They highlighted the association of pancreatitis with non-hyperparathyroid causes of hypercalcemia like parenteral nutrition, calcium infusion, myeloma, disseminated breast cancer or severe hyperthyroidism. Carnille and colleagues reported from France in 1998 after reviewing 1435 consecutive patients operated for hyperparathyroidism. Of these, 1224 patients had biochemically proven pHPT, the remaining 211 had renal hyperparathyroidism (RHPT). They found that a total of 40 patients (3.2%) with pHPT had pancreatitis, 18 having an acute attack. This rate of pancreatitis was higher than in their random hospital population. Spontaneous healing of 17 out of 18 patients with acute pancreatitis followed surgical cure of pHPT. A single diseased gland was found in 27 (out of 40patients with pancreatitis), which is in favor 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.[6] Ballon et al. (1972) described a case in which a parathyroid adenoma was incriminated as causing severe relapsing pancreatitis in a persistently normocalcaemic patient.[7] The mechanism for the causation of the pancreatitis was obscure in the face of persistent normo calcaemia and they observed that the coincidental association of diseases must be considered. The association of hypercalcaemia or pancreatic calcification and pancreatitis should direct attention to studies diagnostic of hyperparathyroidism. Indeed, in acute fulminating pancreatitis, Bockus (1950) points out that if the blood calcium is not depressed after the first 2 days, hyperparathyroidism should be suspected.[8]

Conclusion

Acute pancreatitis is one of symptoms of primary hyperparathyroidism, caused by a parathyroid adenoma and is curable by its excision. Hypercalcemia and hyperparathyroidism should be scrutinized in all fresh cases of acute pancreatitis even though primary hyperparathyroidism is a rare cause. Any oversight will result in diagnostic delays.

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