

Primary Hyperparathyroidism Presenting as Pancreatitis : A Retrospective Study in India

ABSTRACT

Aim : To study the association between primary hyperparathyroidism and acute or chronic pancreatitis.

Methods: Case records of all the patients underwent surgical treatment for Primary hyperparathyroidism (PHPT) during the period April 2015 to March 2020 were analysed. Clinical presentation, biochemical investigations, imaging studies and outcome of surgery were studied in detail.

A total of 54 patients diagnosed to have PHPT underwent parathyroid adenoma excision during 5 years period (2015 – 2020). Abdominal pain, elevated serum amylase and lipase by 3 times of normal, radiological features of pancreatitis were taken as parameters to diagnose pancreatitis. Out of the 54 patients, 8 patients (14.8%) were presented only with pancreatitis. None of the patient had any other risk factor for pancreatitis. All 8 patients underwent parathyroidectomy. Seven patients had single parathyroid adenoma and one patient had two adenomas. After successful parathyroidectomy none of the patient had recurrence of pancreatitis during a follow up period of 6-42 months.

Conclusion: Incidence of pancreatitis in PHPT is 14.8%, which is significantly high compared to western studies. Presence of hypercalcemia during pancreatitis needs further evaluation to rule out hyperparathyroidism especially in the absence of any other risk factor for pancreatitis.

Keywords: Primary hyperparathyroidism, pancreatitis, Parathyroid adenoma

Introduction

Primary hyperparathyroidism (PHPT) commonly presents with bone and renal stone disease in India (1) in contrary to the western world where the disease is diagnosed in asymptomatic patients (2). Normocalcemic PHPT with or without symptoms is another presentation in the western world (2). Several publications have shown the association between hypercalcemia of PHPT and pancreatitis. The prevalence of pancreatitis in PHPT is high in India and it varies from 6.9% (3) to 16% (4) .Where as it ranges from 1.5% (5) to 8.1% (6) in the western population.

In this retrospective study, clinical presentation of PHPT, frequency of pancreatitis in PHPT, biochemical investigations, imaging studies, management, outcome of surgery and follow up were investigated in detail.

Materials and Methods

Case records of all the patients underwent surgical treatment for Primary hyperparathyroidism during the period April 2015 to March 2020 were analysed. Clinical presentation was studied in detail. High serum calcium and Parathyroid hormone (PTH) levels were taken as biochemical criteria for the diagnosis of PHPT.

Abdominal pain, elevated serum amylase and/or lipase atleast 3 times the upper normal level, radiological study(CT scan or Ultrasonography of abdomen) showing the changes of

pancreatitis were the three criteria considered. Acute pancreatitis was diagnosed when the patient presented with any two of these criteria (7).

Chronic abdominal pain, Computed tomography or magnetic resonance imaging showing pancreatic calcification, ductal dilatation and atrophy were considered to diagnose chronic pancreatitis (8).

Data of PHPT patients presented with pancreatitis were analysed in detail. Serum creatinine, 25 hydroxy vitamin D, Alkaline phosphatase were also included in the statistics. High resolution ultrasonography of neck and Technitium 99 sestamibi scan were performed in all patients to localize the parathyroid mass.

All the patients underwent focussed parathyroidectomy with Intraoperative PTH (IoPTH) monitoring. Greater than 50% PTH drop criteria which predicts the postoperative calcium levels accurately (9) was used to confirm the success of surgery.

Protocol for Intraoperative PTH monitoring

Four blood samples were taken during surgery for PTH assay. The timing of sampling was as follows; Preincision (before making cervical incision), Preexcision (just before clamping the blood supply of abnormal gland), 5 minutes and 10 minutes post excision of hyper secreting parathyroid tissue. Drop of 10 minutes post excision PTH levels by >50% from the highest value (preincision or preexcision) indicates successful surgery.(9).

Data were statistically analysed using Libre office 7.0 software

Results and Interpretation

Total Number of patients underwent parathyroidectomy for PHPT was 54, gender ratio M:F was ~ 3 : 7 (16 males and 38 females), Age of the patients varied between 26 to 64 years. Presentation and symptom analysis were as follows: (Table 1, Fig. 1.)

Table 1. Presentation and symptom analysis of patients.

Presentation and Symptom	Total number of patients	Percentage
Bone pain	36	66.6%
Myalgia	17	31.4%
Weakness/ fatigue	32	59.2%
Fracture	2	3.7%
Nephrolithiasis	17	31.4%
Nephrocalcinosis	11	20.3%
Nausea/ Vomiting	12	22.2%
Abdomen pain	14	25.9%
Constipation	6	11.1%
Psychiatric manifestation	7	12.9%
Hypercalcemic crisis	4	7.4%
Asymptomatic	0	0

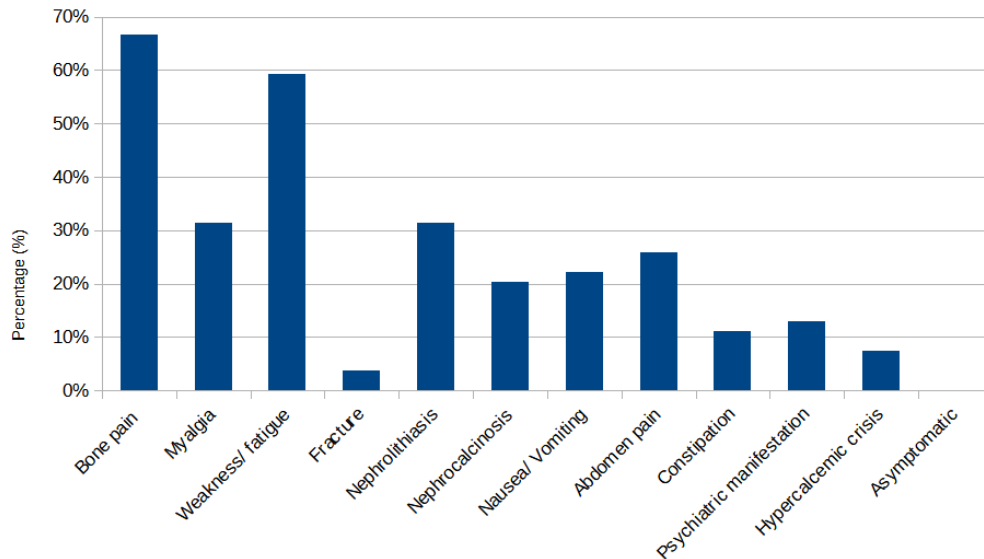


Fig 1. Graphical distribution of presentation and symptom analysis.

Total number of patients presented only with pancreatitis were 8, which constitutes 14.8% of the total PHPT patients. M:F ratio was ~ 3:7. Age distribution (mean \pm standard deviation) was 35.25 ± 7.78 years. Seven patients had 2 episodes of acute pancreatitis and one patient had 3 episodes of pancreatitis before diagnosing PHPT.

All of them had no other cause for pancreatitis like alcoholism, gall stones, hypertriglyceridemia or diabetic ketoacidosis (10). None of the patient had any radiological changes to diagnose chronic pancreatitis (8).

Table 2. Biochemical investigations of PHPT patients with pancreatitis

Biochemical parameter	Observed value (Mean \pm SD)	Reference range
Serum calcium	12.19 \pm 0.64	8.5 -10.2 mg/dl
Intact PTH	518.93 \pm 235.24	15-68.3 pg/ml
Inorganic Phosphate	2.91 \pm 0.52	2.5-4.5 mg/dl
Creatinine	1.08 \pm 0.41	0.57-1.11 mg/dl
25 hydroxy vitamin D	31.44 \pm 13.35	Deficiency < 10 ng/ml
Alkaline Phosphatase	242 \pm 165.73	44-147 IU/l

Localization studies of PHPT patients with pancreatitis

Ultrasonography of neck showed single parathyroid mass in 7 patients and one patient had suspicious second lesion. Tc ⁹⁹ Sestamibi scan showed single lesion in all 8 patients.

Management of PHPT patients with Pancreatitis

Focussed parathyroidectomy was performed in all eight patients under Intra operative PTH monitoring. Seven patients had Io PTH drop of more than 50% after excision of a single parathyroid mass. One patient did not fulfil the criteria hence bilateral neck exploration was performed. Two lesions were excised from that patient to achieve >50% drop in Io PTH. Serum calcium levels were dropped to normal range in all patients in the early postoperative period. No patient developed hungry bone syndrome.

Histopathology showed parathyroid adenoma in all patients

No patient had recurrence of pancreatitis during the follow up period of 6-42 months and the serum calcium levels were also remained in the normal range.

Discussion

Primary Hyperparathyroidism is still a symptomatic disease in India (1, 11). The common symptoms of PHPT in this study group were bone pain and weakness/fatigue. One interesting observation was none of the patients were asymptomatic (Table 1).

Our study shows 14.8% (8 patients) of the PHPT patients have presented only with acute pancreatitis. All of them have elevated serum calcium in the range of 12.19 ± 0.64 (mean \pm SD). The results of this study are comparable to other studies published from India (4, 12, 13). All 8 patients underwent successful parathyroid adenoma excision. None of our patient had recurrence of pancreatitis during a follow up period of 6-42 months and the serum calcium levels were also remained in the normal range.

The association of Pancreatitis and PHPT has been studied extensively and contradicting reports have been published. Some studies suggesting the causal association between PHPT and pancreatitis (14, 15, 16) and others refuting the same (17).

J Jacob et al, 2006, have observed that patients with PHPT have 28 fold increased risk for developing pancreatitis compared to patients without PHPT. They concluded that there is a causal association between PHPT and pancreatitis and correlated that to high Serum calcium values (14).

B Carnaille et al, 1998, studied the association of PHPT and pancreatitis. They have proved that hypercalcemia is the cause for pancreatitis and the association of PHPT and pancreatitis was not incidental. Treating PHPT resulted in healing of pancreatitis. They also observed that there was no increased risk for pancreatitis in patient with renal hyperparathyroidism, where Serum calcium values were not elevated (15).

Several mechanisms have been proposed for calcium induced pancreatic acinar cell injury. One is High extracellular calcium levels lead to sustained elevation of cytosolic calcium signals. These abnormal cytosolic calcium signals induce pathological activation of intra acinar trypsinogen and nuclear factor kappa B, which in turn resulting in morphological changes of acute pancreatitis (18). Second is the combination of hypercalcemia and genetic mutation. Changes in Serine protease inhibitor kazal type 1 (SPINK 1) gene or cystic fibrosis transmembrane conductance regulator (CFTR) by mutation increase the risk of pancreatitis in PHPT (19). Third is calcium salts precipitate on the protein plugs in the pancreatic juice and cause obstruction of the small and large duct of the pancreas (20).

Prompt diagnosis and treatment of PHPT prevents further attacks of pancreatitis (15). In this study no recurrence of pancreatitis was observed in the follow up period of 6-42

months. PHPT induced Necrotising pancreatitis can be fatal too (21). Hence checking serum calcium level in all patients with pancreatitis is always prudent and further evaluation to rule out PHPT in patients without other risk factors for pancreatitis is also advisable. A review article by Harrison X bai et al, 2012, also emphasized the need for checking serum calcium in pancreatitis (22).

Conclusion

Our study shows that 14.8% of Primary Hyperparathyroidism patients present only with pancreatitis and surgical excision of the parathyroid adenoma prevents the further attacks of pancreatitis.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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