Parathyroid Cancer Causing Acute Severe Pancreatitis

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Abstract
Parathyroid carcinoma is a rare disease and accounts for less than 1% of all cases of primary hyperparathyroidism. Many times, parathyroid carcinoma is detected only after surgery. Parathyroid carcinoma as a cause of acute pancreatitis is uncommon. We report this case of acute severe pancreatitis associated with parathyroid carcinoma. Hypercalcemia was found during workup for acute pancreatitis which was due to primary hyperparathyroidism. During surgery, there was a suspicion of parathyroid carcinoma and en bloc resection was done followed by adjuvant radiation therapy. It is important to treat the precipitating factor for acute pancreatitis. Surgery is the mainstay of treatment for parathyroid carcinoma.

Introduction
Parathyroid carcinomas account for less than 4% of parathyroid diseases.¹ They principally present with elevated serum calcium and PTH levels. Initial presentation very often is with a “hypercalcemic crisis”.

We report this case of acute severe pancreatitis associated with parathyroid carcinoma. Hypercalcemia was found during workup for acute pancreatitis which was due to primary hyperparathyroidism. During surgery, there was a suspicion of parathyroid carcinoma and en bloc resection was done followed by adjuvant radiation therapy.

Case Report
A 43-years-old gentleman, textile-mill worker, presented in emergency with severe epigastric pain. Generalized weakness, reduced appetite and recurrent vomiting were present for the past 45 days. He also complained of severe, dull continuous pain in the epigastrium radiating to the back for one week which was aggravated on consuming food and was partially relieved on bending forward, associated with dyspepsia, constipation and weight loss. His urine output was reduced.

On examination, he was dehydrated with persistent vomiting, afebrile and tachycardia with normotension. Abdominal examination demonstrated distension with epigastric tenderness. Blood investigations revealed leukocytosis (12,000/cu mm) with polymorphonuclear leucocytosis, elevated pancreatic enzymes- serum lipase (8605 U/L) and serum amylase (2435 U/L), hypercalcemia (14.7 mg/
In the current case, elevated serum parathyroid hormone (PTH) (948.7 pg/ml) and serum alkaline phosphatase level (217 U/L). Serum triglycerides were normal.

Ultrasound (USG) of the abdomen revealed a bulky pancreas with peri-pancreatic fat stranding, normal gallbladder, intra-hepatic biliary radicles, common bile duct and normal sized kidneys. There was no free fluid in the abdomen. Based on the history, clinical examination, blood investigations and USG, he was diagnosed to have acute severe pancreatitis secondary to PTH-dependent hypercalcemia.

He was treated aggressively with intravenous fluids, analgesics, antiemetics and proton pump inhibitors. The serum calcium levels were persistently high despite adequate hydration and diuresis, hence steroid was added. Serum calcium levels dropped but still continued to remain above the normal range. Acute pancreatitis resolved with conservative management. Localization studies were done for parathyroid, anatomical localization in form of USG neck revealed a large extrathyroidal mass at the upper pole of the left thyroid lobe measuring 2.8x2.6x1.5 cm. Functional localization by Tc99m Sestamibi was concordant with USG and showed high uptake in same area (Figure 1).

As the tumor was palpable, in an elderly male and presentation was hypercalcemic crisis, a presumptive diagnosis of parathyroid carcinoma was made. Bilateral neck exploration for parathyroid glands was done which showed tumor was arising from left superior parathyroid gland and other 3 glands were normal in size, location and color. The tumor was densely adhered to left lobe of thyroid and en bloc resection of left sided parathyroid mass (left superior parathyroidectomy with left hemithyroidectomy) and central compartment lymph node dissection with left cervical thymectomy was done. The gross specimen (parathyroid+hemithyroidectomy) weighed 18 grams. The parathyroid tumor was 3.0x1.7x2.7 cm in size (Figure 2).

Histopathology showed that parathyroid mass was a parathyroid carcinoma and was comprised of neoplastic cells, arranged in nests and separated by broad fibrous bands with sparse mitoses and some intranuclear inclusions with areas of coagulative tumor necrosis. There was no perineural invasion or lymphovascular emboli but adipose tissue at periphery of tumor was invaded. Tumor was also adhered to thyroid but not infiltrating it. All lymph nodes and thymus were free of disease (Figure 3). Postoperatively, patient had normalization of serum PTH and serum Calcium denoting successful outcome of surgery. He was discharged on 4th postoperative day after stabilization of serum Calcium on oral Calcium and Vitamin D supplements. He is asymptomatic at 4 months follow up and adjuvant local radiotherapy is going on.

Discussion

Parathyroid carcinomas account for less than 4% of parathyroid diseases. They principally present with elevated serum calcium and PTH levels. Initial presentation very often is with a “hypercalcemic crisis”. Metastatic invasion of regional lymph nodes or distant sites can confirm the diagnosis preoperatively. A diagnosis can also be suggested intraoperatively on the basis of tumor invasion into surrounding structures. An intraoperative diagnosis of carcinoma based on frozen section findings is rather controversial because of the overall difficulty of rendering the diagnosis. Histopathologic features include a high mitotic rate and a capsular, vascular or perineural invasion. Other findings include cellular pleomorphism, atypia and atypical mitoses. The abnormal mitotic figures are distinctive, though not pathognomonic. Postoperative recurrence rates are high with significant 2-year mortality rate between 46% and 65%.

As the condition is rare, leading authorities including the American Joint Committee on Cancer (AJCC) have not published any staging recommendations.4

Acute pancreatitis secondary to primary hyperparathyroidism (PHPT) is infrequent. It was first described by Cope et al.5 Work-up for PHPT should be routinely performed to detect the etiology of non-gallstone pancreatitis secondary to hypercalcemia. The prevalence of PHPT is estimated to be between 1.5% and 7%. Based on the available epidemiological data, a direct causal relationship between PHPT and acute pancreatitis appears to be doubtful. It is a known fact that hypercalcemia of any etiology can potentially, albeit rarely lead to acute pancreatitis. Other rare causes of hypercalcemia leading to pancreatitis include total parenteral nutrition, metastatic bone disease, vitamin D toxicity, sarcoidosis and infusion of intravenous calcium in high doses perioperatively during cardiopulmonary bypass.

The suggested pathophysiological mechanisms that cause pancreatitis in hypercalcemia include I) Deposition of calcium in the pancreatic duct causing pancreatic duct obstruction;
II) Activation of trypsinogen within the pancreatic parenchyma due to hypercalcemia leading to autodigestion of the pancreas; and III) Genetic variants in SPINK1 (serine protease inhibitor Kazal type 1) and CFTR (cystic fibrosis transmembrane conductance regulator) genes along with hypercalcemia that increase the risk of acute pancreatitis in patients with PHPT.

Acute pancreatitis is usually associated with a decrease in serum level of calcium and this is mainly related to decreased serum albumin levels. Based on the Ranson grading, low serum calcium levels has prognostic significance and is a marker of severity because it is carried bound to albumin-rich intravascular fluid that extravasates to the peritoneum. Hence, it is not common to observe hypercalcemia in a patient with severe acute pancreatitis. Presence of hypercalcemia in pancreatitis should always alert treating physicians about presence of underlying hyperparathyroidism or malignancy.

Parathyroid hormone levels should be tested and if hormone is elevated and imaging of the parathyroid glands should be conducted.

In our case, the diagnosis of a parathyroid mass was made by USG neck followed by 99mTc-Sestamibi scintigraphy. Surgical resection of the mass is definitive treatment as parathyroidectomy protects from recurrence of pancreatitis. Post-operative hypocalcemia is common and warrants calcium supplementation.

**Conclusion**

A multi-specialty coordinated approach between gastroenterologists, radiologists and surgeons is imperative in treating this rare phenomenon of acute pancreatitis caused by hypercalcemia secondary to a parathyroid carcinoma.

**References**