Epigastric pain with elevated serum calcium, lipase, and amylase

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A 57-year-old man presented to the emergency department because of epigastric pain for 2 days. His serum lipase, amylase, and calcium levels were markedly elevated, but the lipopro-

tein profile was within normal limits. Diagnostic studies are shown below (Figures 1–4).

For diagnosis and discussion, see the following page.

Figure 1. Computed tomography (CT) image shows the pancreas (arrowheads) to be diffusely enlarged and surrounded by a moderate amount of peripancreatic edema (arrows).

Figure 2. CT image demonstrates a mass (arrowhead) in the right side of the neck. The mass produces extrinsic pressure on the right lateral lobe of the thyroid (arrows).

Figure 3. Ultrasound image made in the axial plane shows a well-delineated, inhomogeneous mass (arrows) lateral to the inferior pole of the right lateral lobe of the thyroid.

Figure 4. Delayed sestamibi image shows that the tracer has washed out of the thyroid. There is retention of tracer (arrows) in the right side of the neck.

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DIAGNOSIS: Acute pancreatitis secondary to hypercalcemia produced by a parathyroid neoplasm.

DISCUSSION

Common causes of acute pancreatitis include alcohol abuse, biliary tract disease, pancreas divisum, drugs, trauma, viral infection, and hyperlipidemia. A more uncommon but long-associated cause of pancreatitis is hyperparathyroidism. In one study of 1475 patients with acute pancreatitis, hyperparathyroidism accounted for only 5 cases (0.4%) (1). However, in patients with hyperparathyroidism and resulting hypercalcemia, pancreatitis occurs 10 to 20 times more often than in the general population. The most frequent etiology is adenoma, followed by hyperplasia or parathyroid carcinoma. In this case, the large size of the parathyroid mass and the histologic features suspicious for lymphatic invasion, while not diagnostic, were worrisome for malignancy.

The mechanism of hypercalcemia as a cause of pancreatitis is controversial and poorly understood. Some propose that stones obstruct the pancreatic ducts, although only a small percentage of patients with hyperparathyroid-associated pancreatitis indeed have intraductal stones. Others theorize that the increased serum calcium directly increases pancreatic enzyme output and release of gastrin and cholecystokinin-pancreozymin. Alternatively, some believe necrosis of acinar and ductal pancreatic cells is linked to increased permeability of the pancreatic duct due to hypercalcemia. Activation of trypsinogen to trypsin by excessive calcium also has been suggested as a possible cause of pancreatitis (1–3).

CT is the key imaging modality used for management of acute pancreatitis and, together with the clinical Ranson criteria, helps in staging severity. Four major pathologic categories have been designated: acute interstitial pancreatitis or edematous pancreatitis (as in this case), necrotizing pancreatitis, hemorrhagic pancreatitis, and suppurative pancreatitis. Complications include phlegmon, ascites, fluid collections or pseudocysts, abscesses, pseudoaneurysms, and hemorrhage. Direct imaging of the pancreas is important in demonstrating such complications as well as the extent of pancreatic parenchymal necrosis. The degree of necrosis is determined by the relative amount of pancreatic parenchymal enhancement with intravenous contrast. One study found that patients without pancreatic necrosis have no increased mortality risk and 6% morbidity, whereas those with extensive necrosis ($\geq 50\%$) have 29% mortality and 94% morbidity (4). CT findings in mild, uncomplicated pancreatitis (as in this case) include increase in gland size; peripancreatic inflammation surrounding a normal-sized pancreas; diffuse enlargement with shaggy, irregular borders; and heterogeneous appearance. The sensitivity of CT for detecting acute pancreatitis is 77% to 92% (4). Approximately a third of cases with acute pancreatitis will, in fact, have a normal CT appearance despite clinical symptoms and elevated serum pancreatic enzymes. MRI is much less commonly used in evaluating acute pancreatitis but can be useful in examining pseudocyst and hemorrhagic complications as well as imaging in certain specific clinical settings.

The appearance of parathyroid adenoma on CT is an oval or round soft tissue mass seen on 1 or 2 slices, with a thin plane of fat separating it from the thyroid or the esophagus. Enhancement is seen in 25% of masses, with the largest masses enhancing more frequently. Calcification, hemorrhage, and cysts are rarely seen. CT sensitivity for adenoma detection is 70% to 81% (5).

The classic sonographic appearance of a parathyroid adenoma is a 1-cm, hypoechoic or anechoic mass in a cranio-caudal orientation behind the thyroid and often seen adjacent and medial to the carotid artery. Primary parathyroid hyperplasia is more difficult to image sonographically. Parathyroid carcinoma can look like adenoma on ultrasound, but some lesions invade the surrounding soft tissue and make distinction from thyroid malignancy difficult. The sensitivity of ultrasound for detecting parathyroid disease ranges from 55% to 77% (5).

Newer parathyroid scintigraphy with intravenous technetium Tc 99m sestamibi with single-photon emission CT was used in studying this patient. It allows parathyroid imaging by demonstrating washout from the normal thyroid tissue with retention in the hyperfunctioning parathyroid. Sensitivity is 88% to 100% and increases with glandular size. With dual-tracer technetium Tc 99m pertechnetate/thallous chloride Tl 201 subtraction imaging, ^{201}Tl is taken up by the thyroid and parathyroid tissues, but only pertechnetate is taken up by normal thyroid tissue, allowing visualization of the parathyroid glands by subtraction. Sestamibi has many advantages over the older dual-tracer scintigraphy in its physical properties, technical features, and ease of study interpretation (5).

Pancreatitis is uncommonly linked to hyperparathyroidism, but the pancreatitis is often severe when the two are associated. Despite many case reports and studies suggesting that parathyroidectomy has cured and prevented the recurrence of pancreatitis, the cause-and-effect relationship remains controversial (6, 7). Other data and experimental evidence have shown that surgical cure of hyperparathyroidism and hypercalcemia does not correlate with remedy of pancreatitis symptoms (7). Only time will tell if parathyroidectomy will successfully prevent recurrent pancreatitis in this patient, whose symptoms were linked to hypercalcemia resulting from his hyperfunctioning parathyroid neoplasm.

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