

# The Surgical Patient

## An unusual cause of pancreatitis in a young man

Michael Binstock, MS, PA-C; Steven Sweet, BS;  
Rhonda Fishel, MD, FACS

**H**yperparathyroidism (HPT) has long been a common reason for referrals to endocrinologists and general surgeons. Although patients often have no symptoms, clinicians should be familiar with the signs, symptoms, laboratory findings, and other disease processes that might indicate HPT. Usually the diagnosis is straightforward, but in the case discussed in this article, HPT manifested in a most unusual way.

### CASE

A 20-year-old African-American male presented as an outpatient for surgical consultation with a 3-day history of nausea, vomiting, and epigastric abdominal pain. The patient had a history of hypertension and gastroesophageal reflux disease for which he took atenolol and a proton pump inhibitor. He

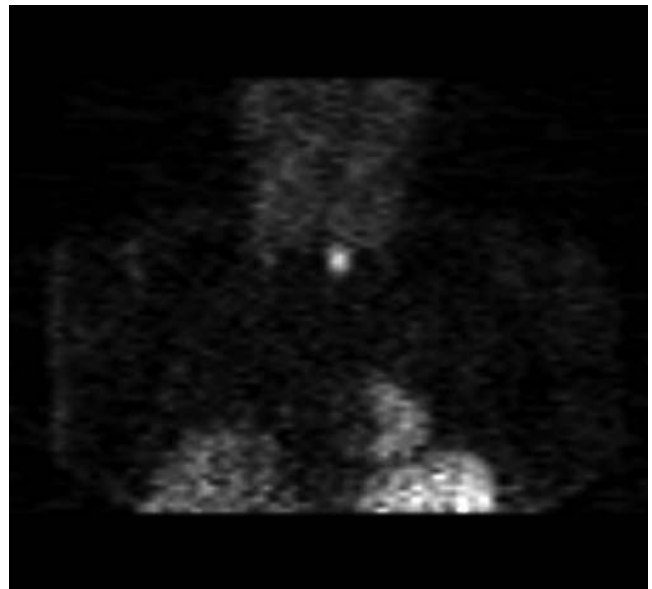
was allergic to penicillin, strawberries, and seafood. There was no surgical history, and the patient denied use of alcohol and illicit drugs. A review of systems was noncontributory, and the results of a physical examination were entirely normal except for moderate obesity and epigastric tenderness to light and deep palpation. The results of laboratory tests were normal, except numbers were elevated for serum calcium at 13.9 mg/dL (normal [n], 8.4-10.2 mg/dL), amylase at 1,163 U/L (n, 25-125 U/L), and lipase at 783 U/L (n, 10-140 U/L). Abdominal CT showed fluid collection around the pancreas compatible with pancreatitis (see Figure 1).

Initially, the pancreatitis was treated with IV normal saline solution, analgesics, and complete bowel rest. The abdominal pain resolved, and the serum amylase and lipase levels were brought within normal range. Nevertheless, the patient's serum calcium levels remained elevated.

Further workup revealed that the parathyroid hormone (PTH) level was 781 pg/mL (n, 12-65 pg/mL) and that the



**FIGURE 1.** Contrast abdominal CT indicates fluid surrounding the pancreas.

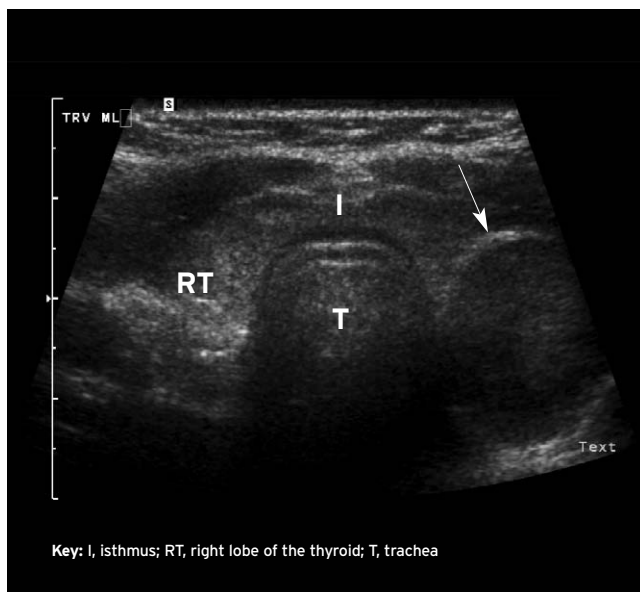


**FIGURE 2.** A technetium-99m sestamibi scan reveals a left inferior parathyroid adenoma.

ionized calcium level was 2.2 mmol/L (n, 1.12-1.32 mmol/L). Imaging studies were performed to localize any areas of hyperactivity within the parathyroid glands. A technetium-99m sestamibi scan was positive in the area of the left lower thyroid gland (see Figure 2). Ultrasonography (US) of the neck demonstrated a mass correlating with the findings on the sestamibi scan (see Figure 3). Taken together, these findings suggested primary HPT that was probably due to a parathyroid adenoma. Additional tests for multiple endocrine neoplasia types 1 and 2 (MEN1, MEN2) revealed nothing remarkable.

**Operative course** The patient underwent unilateral neck exploration with resection of the enlarged left lower parathyroid gland. Before gland removal, an intraoperative intact PTH level was elevated at 2,500 pg/mL. The specimen weighed approximately 5.66 g (n, 40-50 mg); frozen section of the mass revealed hypercellular tissue consistent with parathyroid adenoma. Twenty- and 40-minute postdissection intact PTH levels were 101 pg/mL and 38 pg/mL. The drop in PTH level suggested that no other hyperplastic parathyroid glands were present. The surgeon was satisfied that the patient had single glandular disease and that the dissection of the parathyroid adenoma was adequate.

**Postoperative course** The patient was monitored postoperatively for surgical complications. He showed no signs of bleeding at the incision site; numbness; tingling of the buccal mucosa, distal forearms, or distal extremities; or recurrent laryngeal nerve trauma. On laboratory tests, ionized calcium levels were within normal limits. He was seen in the office for follow-up 6 days after surgery. At that time, his serum calcium level had declined to 6.6 mg/dL, so calcitriol and calcium supplements were prescribed to keep his calcium levels within an acceptable range.



**FIGURE 3.** A sonogram of the neck demonstrates the location of the parathyroid adenoma.

## DISCUSSION

The parathyroid glands regulate calcium and phosphorus by releasing variable amounts of PTH, which raises serum calcium levels while lowering serum phosphorus levels. Secretion of PTH is mainly controlled through the interaction of calcium with specific calcium-sensing receptors on the membrane of the parathyroid cells.<sup>1</sup>

HPT is a syndrome of relative excessive release of PTH. Normally, the activity of the parathyroid glands is regulated by the level of ionized (free) calcium in the bloodstream.<sup>1</sup> A decreased level of ionized calcium will stimulate the synthesis and secretion of PTH from the parathyroid. PTH activates osteoclasts, which resorb calcium from bone. PTH also increases blood calcium levels by stimulating renal tubular reabsorption of calcium and increasing the conversion of vitamin D into 25-hydroxy vitamin D, which is essential for calcium absorption in the small bowel and bones.<sup>1,2</sup> HPT can be classified into primary, secondary, and tertiary types.

**Primary HPT** is usually the result of a single parathyroid adenoma (80%), which is responsible for the hypersecretion of PTH. Hyperplasia of two or more parathyroid glands occurs less commonly (20%), with carcinoma of the glands occurring very rarely.<sup>3</sup>

**Secondary HPT** can be due to any condition that depresses serum calcium levels and leads to a compensatory hypersecretion of PTH.<sup>4</sup> The most common causes are renal failure, inadequate dietary intake of calcium, and vitamin D deficiency.<sup>5</sup> This form of HPT results from a physiologic or pathophysiologic parathyroid response to hypocalcemia in an attempt to maintain calcium homeostasis.<sup>6</sup> The serum PTH level is elevated, while the calcium level may be normal or low.

**Tertiary HPT** is rare and occurs because of prolonged hypocalcemia (usually secondary to chronic renal failure) that causes parathyroid gland hyperplasia. Typically, patients who have undergone renal transplant will continue to have autonomous oversecretion of PTH by the parathyroid glands, which results in hypercalcemia.<sup>7</sup>

HPT is often unrecognized, manifesting in up to 0.1% of all adult patients examined in the clinical setting.<sup>5</sup> Primary HPT is a disease of the adult population; it occurs in three times as many women as men<sup>5</sup> and has an increased incidence in persons older than 50 years (see Table 1, page 34). Studies regarding HPT in racial groups are lacking, but a retrospective chart review shows that the incidence of African-Americans presenting with primary HPT is approximately 14%.<sup>8</sup> Sporadic parathyroid adenomas and hyperplasia of the glands account for most cases of HPT. Familial syndromes, including those caused by MEN1 and MEN2, are relatively uncommon.

**Clinical presentation** In this case, the patient presented with pancreatitis caused by an underlying parathyroid adenoma but with no other signs or symptoms suggesting HPT. This was unusual, as only about 2% of patients with HPT present with pancreatitis.<sup>5</sup> Although some persons with HPT are asymptomatic and may learn that they have the condi-

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tion through routine blood work,<sup>9</sup> approximately 75% to 80% of those with primary HPT will present symptomatically.<sup>8,10</sup> Complaints are often related to underlying osteoporosis, nephrolithiasis, constipation, peptic ulcer, pancreatitis, gallstones, depression, lethargy, neuromuscular weakness and fatigue, or aortic and/or mitral valve calcifications.

**Diagnosis** The hallmark of HPT is persistent *hypercalcemia*, defined as serum calcium levels greater than 10.5 mg/dL or ionized calcium levels greater than 1.12 mmol/L.<sup>5</sup> Elevated PTH levels confirm the diagnosis, and further laboratory testing is unnecessary because other causes of hypercalcemia rarely are associated with elevated PTH levels.<sup>6</sup> Findings of hypophosphatemia, decreased renal tubular reabsorption of phosphorus, hypercalciuria, and characteristic radiographic changes support the diagnosis of primary HPT but are not prerequisites.<sup>2</sup> Patients with secondary HPT may have normal or decreased levels of serum calcium with elevated PTH. A medical or family history of renal disease would suggest the diagnosis. Tertiary HPT is diagnosed when PTH levels are resistant to vitamin D/calcium suppression therapy after renal transplant.<sup>6,7,11</sup>

**Treatment** Before surgical treatment, it should be determined whether other electrolyte abnormalities, particularly of BUN and creatinine, are present. Severe hypercalcemia should be corrected with IV normal saline, and patients with normal renal function should be given IV diuretics to remove excess serum calcium.<sup>11</sup> Persons with advanced primary HPT or tertiary HPT can benefit from parathyroidectomy. Hyperplastic parathyroid glands require resection of all but one of the glands. Patients with secondary HPT require treatment of the disease causing the elevated levels of PTH. The goal of medical management is to normalize calcium levels. Supplementation of vitamin D and calcium is necessary. Patients with end-stage renal disease also need phosphate binders to decrease hyperphosphatemia. Patients with tertiary HPT, after correction of serum calcium levels, may require resection of the parathyroid glands.

Newer medical therapies such as bisphosphonates and calcimimetics are still experimental.<sup>12</sup> Parathyroidectomy can be accomplished with greater than a 95% success rate with mini-

mal morbidity.<sup>7,12,13</sup> Parathyroidectomy is the only curative treatment for HPT at this time.<sup>12</sup> Both symptomatic and asymptomatic patients may be candidates for surgery. Generally accepted indications for surgery include a history of a life-threatening episode of hypercalcemia, reduction in creatinine clearance by more than 30% of expected value for age, presence of kidney stones by history or radiography, 24-hour calcium excretion elevation greater than 400 mg, or reduction of bone mass more than 2 standard deviations below normal.<sup>7</sup>

**Operative approaches** The standard bilateral exploration has long been the choice for parathyroidectomy and allows all the parathyroid glands to be visualized.<sup>14</sup> However, with the advent of preoperative localization techniques, the unilateral approach has become more widely accepted among surgeons.<sup>13,14</sup> It provides a better cosmetic effect, and patients who undergo the unilateral exploration consume less oral calcium and have a lower incidence of biochemical and early severe symptomatic hypocalcemia compared with patients explored bilaterally.<sup>14,15</sup> However, this approach requires preincision and postexcision PTH assay testing as well as preoperative localization.

The two most useful studies for localization are US and technetium-99m sestamibi scanning.<sup>13</sup> These tests have a sensitivity of 94% when used in conjunction, but only for patients with disease in a single parathyroid gland.<sup>13</sup> For patients with multiglandular disease, the sensitivity is significantly decreased. Intraoperatively, serum PTH levels should be drawn immediately before excision and at 20 and 40 minutes after excision of a parathyroid adenoma or debulking of hyperplastic parathyroid glands.<sup>16</sup> Parathyroidectomy has been adequate if the PTH level is reduced to less than 50% of the preoperative baseline level. If the PTH levels do not drop sufficiently, the surgeon must revert to bilateral neck exploration to search for multiple adenomas, hyperplastic parathyroid glands, or an ectopic parathyroid gland.<sup>15-17</sup>

Postoperatively, the serum PTH level will fall to less than normal in 70% of patients who have undergone parathyroidectomy.<sup>5</sup> This can cause hypocalcemic parasthesias and possibly lead to tetany. Ionized calcium levels must be

**TABLE 1. Patients with primary hyperparathyroidism**

	Age	Gender	Race	Presenting symptoms	Causes of primary HPT
Most patients with primary HPT	>50 y	Female to male, 3:1	Predominantly Caucasian	<ul style="list-style-type: none"> <li>• Abdominal pain</li> <li>• Bone pain</li> <li>• Fatigue</li> <li>• Kidney stones</li> <li>• Psychosis</li> </ul>	<ul style="list-style-type: none"> <li>• Familial HPT (MEN1, MEN2)</li> <li>• Parathyroid adenoma</li> <li>• Parathyroid hyperplasia</li> </ul>
The patient in this case	20 y	Male	African-American	Pancreatitis	<ul style="list-style-type: none"> <li>• No evidence of MEN1 or MEN2</li> <li>• Parathyroid adenoma</li> </ul>

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checked frequently. Liquid or chewable calcium carbonate should be given to prevent hypocalcemia. Patients who continue to have hypocalcemia require calcitriol to enhance calcium absorption.<sup>12</sup>

## CONCLUSION

In medicine, things are not always what they appear to be. Pancreatitis was diagnosed in our patient, but when his serum calcium levels did not drop after treatment, further investigation revealed the root of his problem. Pancreatitis secondary to HPT is rare, and still rarer in African-Americans. Most patients are female and older than 50 years. Our patient was atypical, illustrating how important it is to exercise good clinical judgment and to closely monitor and carefully interpret laboratory and diagnostic studies. In this case, that approach allowed for the proper diagnosis and the appropriate treatment of this patient. [JAAPA](#)

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**Michael Binstock** practices general and trauma surgery at The Sinai Hospital of Baltimore in Baltimore, Maryland. **Rhonda Fishel** is a general/trauma/critical care attending at The Sinai Hospital of Baltimore. **Steven Sweet** is a student in the CCBC-Towson Physician Assistant Program in Baltimore. The authors have indicated no relationships to disclose relating to the content of this article.

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**Steve Wilson, PA-C, department editor**

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