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Case Report

Hypercalcemic Crisis Caused by a Parathyroid Mass Requiring Thoracoscopic Resection

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ABSTRACT

Objective: To describe the presentation, work up, and treatment of a giant parathyroid adenoma presenting as hypercalcemic crisis that ultimately weighed 57 g and extended into the mediastinum, requiring hand-assisted thoracoscopic resection.**Methods:** The patient is a 68-year-old man with a prior history of parathyroidectomy, who initially presented with a severe hypercalcemia of 16.3 mg/dL and a parathyroid hormone (PTH) level of 2692 pg/mL on routine labs.**Results:** Diagnostic and staging work up revealed a 7.2-cm mass extending from just superior to the sternal notch into the right posterior mediastinum to the carina, causing esophageal displacement. No evidence of local invasion or distant metastasis was observed on further imaging, and cytology demonstrated hypercellular parathyroid tissue. The PTH level of the aspirate was >5000 pg/mL. The patient subsequently underwent a right hand-assisted video-assisted thoracoscopic resection of the intrathoracic mass. Final pathology identified a 7.0-cm, 57-g parathyroid adenoma, without any pathologic findings suspicious for malignancy. However, the endocrine surgery team plans for annual laboratory assessment to ensure no recurrence.**Conclusion:** Primary hyperparathyroidism is most commonly caused by a single adenoma. However, in the setting of severe hypercalcemia and elevated PTH, one must have a high suspicion for malignancy, and care should be taken to remove the mass en bloc. For extremely large adenomas extending into the mediastinum, a minimally invasive, hand-assisted, thoracoscopic approach is a safe and effective method of resection.© 2021 AAACE. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders and is characterized by the overproduction and secretion of parathyroid hormone (PTH). Women are found to have more prevalence of PHPT than men, with a ratio of approximately 4:1, and its peak incidence is found in the early years after menopause.¹ Hypercalcemic crisis is an uncommon, although not rare complication of PHPT. Hypercalcemic crisis has no uniform standard definition; however, a generally accepted definition in the literature

is an albumin-corrected serum calcium level >14 mg/dL.² Most patients are symptomatic, although symptoms can be mild depending on the degree, acuity of onset, and underlying etiology.

Approximately 80% to 85% of PHPT cases are caused by a single parathyroid adenoma, whereas a small percentage of patients will have multiple adenomas (2%–5%) and an even smaller percentage will have parathyroid carcinoma.^{3–5} Parathyroid adenomas are often relatively small, typically <2 cm in size, and averaging 1 g in weight. Large or giant parathyroid adenomas are typically considered to be approximately >3.5 g in weight.^{6–8} Here, we present a patient who was ultimately found to have a parathyroid adenoma of 7 cm in size and 57 g in weight, requiring hand-assisted thoracoscopic resection.

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The patient is a 68-year-old man, with a significant past medical history of parathyroidectomy in Mexico in 2011. Records were obtained from this surgery. They were notably in Spanish, although

Abbreviations: PHPT, primary hyperparathyroidism; PTH, parathyroid hormone. This paper was accepted as an abstract for oral presentation at the Indiana Chapter of the American College of Surgeons 67th Annual Scientific Meeting, scheduled to take place in Noblesville, Indiana in 2020, but the meeting was canceled due to the coronavirus 2019 pandemic.

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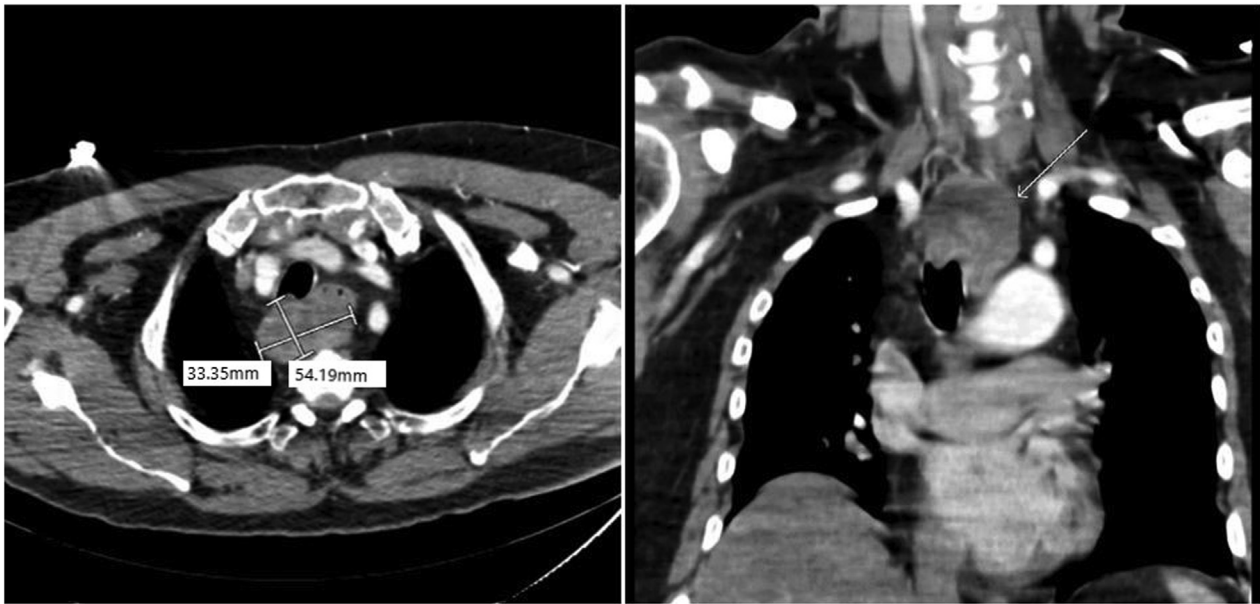


Fig. 1. Representative axial and coronal contrast-enhanced computed tomography scans of the patient's posterior mediastinal mass. Ruler markings and arrow indicate the mass.

translation was attempted. However, there was no documentation as to which parathyroid gland had been removed, as the operative report was not available. The pathology report did describe a parathyroid adenoma without atypia that had been excised along with a “cystic structure.”

In 2019, the patient presented for routine laboratory tests and was found to have a calcium level of 16.3 mg/dL (his serum albumin was normal at 4.2 g/dL). The patient reported difficulty hitting the high notes, although was otherwise largely asymptomatic. He denied experiencing any fatigue, abdominal pain, nausea, vomiting, constipation, or changes in mental status or personality. After his test results, he was admitted to a local hospital for immediate treatment. Additional laboratory results were significant for PTH, ionized calcium, alkaline phosphatase, magnesium, creatinine, creatinine clearance, and vitamin D levels of 2692 pg/mL, 1.93 mmol/L, 165 mg/dL, 1.3 mg/dL, 1.65 mg/dL, 44 mL/min/1.73 m², and 24.7 ng/mL, respectively. He received intravenous fluid resuscitation, furosemide, calcitonin, and a bisphosphonate, which successfully lowered his serum calcium and ionized calcium to 11.6 mg/dL and 1.51 mmol/L, respectively. He was subsequently transferred to our tertiary referral center for further evaluation and management.

Upon transfer, the patient underwent a neck ultrasound, which demonstrated 2 thyroid nodules measuring 1.4 and 0.4 cm in size, although without parathyroid gland enlargement. This was followed by single-photon emission computed tomography/computed tomography, which revealed a 7.2-cm right-sided mass extending from the lower neck into the posterior mediastinum in the pretracheal groove to the carina, causing esophageal displacement (Fig. 1). The mass had only mild, nonspecific sestamibi uptake (Fig. 2). Given the concern for esophageal invasion, an endoscopic ultrasound with fine needle aspiration was performed, revealing a well-defined mass of hypercellular parathyroid tissue on cytology. The PTH level of the aspirate was >5000 pg/mL. No distant disease was detected on positron emission tomography/computed tomography. Other laboratory tests typical in the work up for PHPT, such as 24-hour urine calcium, were foregone given that suspicion for familial hypocalciuric hypercalcemia was low, and the severity of the patient's hypercalcemia with his reduced creatinine clearance met criteria for a definitive surgical management.^{9,10}

The patient subsequently underwent a right hand-assisted video-assisted thoracoscopic resection of the mass. The lesion was first identified and mobilized thoracoscopically off of the esophagus, with no evidence of invasion. As the dissection was continued into the thoracic inlet, further safe mobilization became more challenging; thus, the anterior port was extended into a mini-muscle sparing thoracotomy. A hand was placed through the new thoracotomy incision under direct thoracoscopic visualization, and the rest of the mass was safely mobilized and removed. The patient's intraoperative PTH level appropriately decreased following the resection, and his PTH level decreased to 13 pg/mL postoperatively, indicating operative cure (Table). Final pathology identified a 7.0-cm, 57-g parathyroid adenoma without vascular or perineural invasion or atypia, no mitoses, and a Ki-67 of 2% (Fig. 3).

The patient was closely monitored for signs of hungry bone syndrome, and as per routine postoperative protocol of our institution, he received ergocalciferol for vitamin D deficiency as well as prophylactic calcium supplementation.^{11,12} While he did not experience symptoms of hypocalcemia, his calcium carbonate dose was increased to 1500 mg twice daily after his calcium level decreased to 8.4 mg/dL on postoperative day 2. His calcium levels were successfully maintained due to this oral regimen. Furthermore, he received oral magnesium and phosphorus supplementation in the immediate postoperative period for his transiently and mildly low serum levels. Otherwise, his postoperative course was uncomplicated, and he was discharged on postoperative day 3, with the continuation of calcium and ergocalciferol supplementation for his vitamin D deficiency.

On 6-month follow-up, the patient had recovered well from surgery. His PTH level was slightly elevated at 73 pg/dL; however, this elevation was likely secondary to a mild vitamin D deficiency, and he remained eucalcemic (Table). At 18-month follow-up, he was normocalcemic with normalization of his PTH and vitamin D levels. Unfortunately, the patient's health care funding situation was such that he could not afford genetic testing. Despite no pathologic evidence of carcinoma, he was recommended and scheduled for annual laboratory assessment with endocrine surgery to ensure no recurrence.

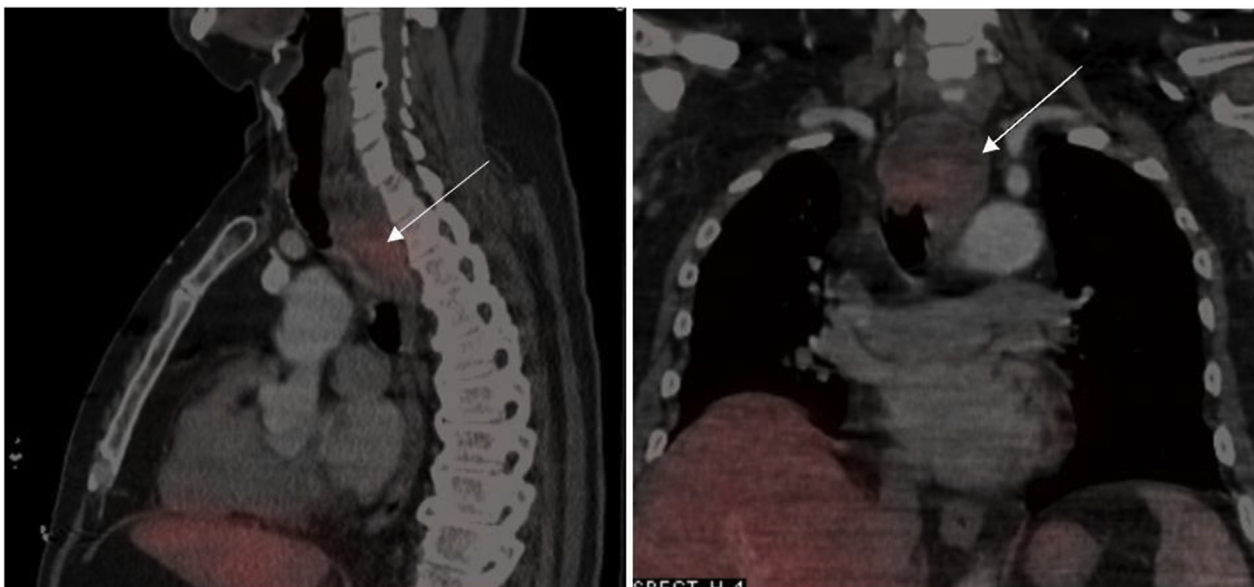


Fig. 2. Representative sagittal and coronal computed tomography scans with overlaid single-photon emission computed tomography scans with Tc-99m sestamibi radiopharmaceutical. The posterior mediastinal mass, as indicated by the arrows, show mild nonspecific increased sestamibi avidity.

Table
Patient’s Laboratory Values on Presentation, Pre-, Intra-, and Postoperatively and at Follow-Up

Time point	Calcium (mg/dL)	Ionized calcium (mmol/L)	Parathyroid hormone (pg/mL)
Initial presentation	16.3^a	1.93	2692
Preoperatively	11.0	1.52	1370
Intraoperatively			
Prior to resection	1492
5 min after resection	665
10 min after resection	381
15 min after resection	312
Postoperatively			
Postoperative day 0	10.1	1.29	13
Postoperative day 3	8.4	...	45
6-mo follow-up	9.5	1.09	73^b
18-mo follow-up	9.6	...	25.5 ^c

^a Bold font indicates value higher than the normal reference range.

^b Patient also had a mild total vitamin D deficiency at the 6-month follow-up (26.2 ng/mL, laboratory normal 30–100 ng/mL), likely contributing to this mild elevation.

^c Patient’s vitamin D level normalized at the 18-month follow-up (33 ng/mL, laboratory normal range 30–100 ng/mL).

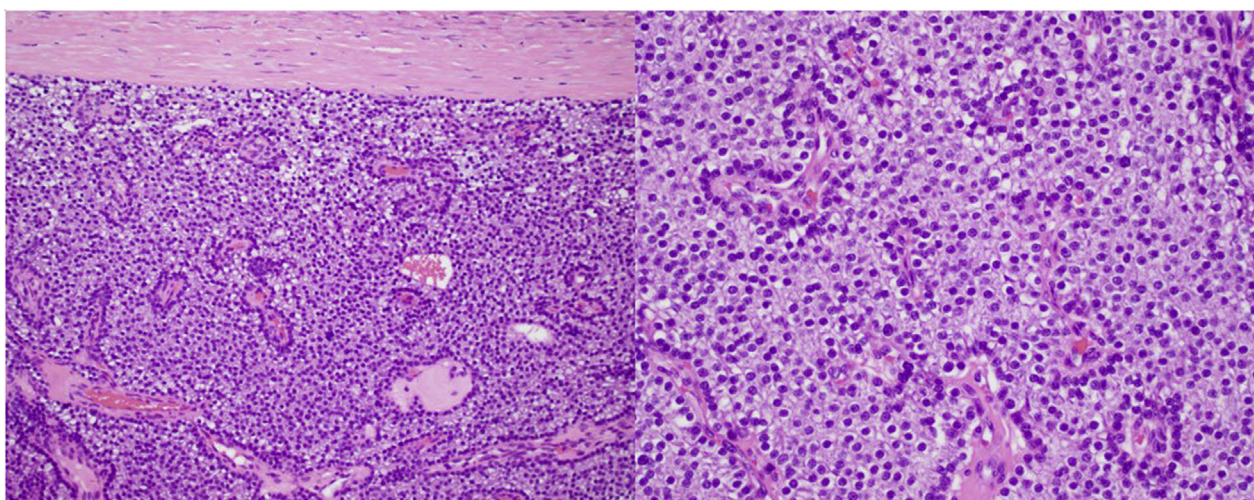


Fig. 3. Sample slides from the final pathologic specimen of the resected parathyroid mass. Hyperplastic chief cells with round nuclei and little granular cytoplasm are most prominently seen with reduced stromal adipocytes.

Discussion

Giant parathyroid adenomas are typically defined as those >3.5 g in mass. Due to the rarity of such large adenomas, the clinical significance of their increased size has not been well classified. Spanheimer et al⁸ compared 15 giant parathyroid adenomas out of 300 consecutive cases, of which the largest was 29.93 g in size, to those <3.5 g and found that patients with giant adenomas presented with higher mean preoperative calcium and PTH levels, and were less likely to have a multiglandular or symptomatic disease. Another series conducted in France studied 26 patients with giant parathyroid adenomas, ranging up to 40 g in size, although found no symptoms specific to giant adenomas.⁷ Unfortunately, limited sample sizes will likely continue to restrict the power of studies exploring giant parathyroid adenomas; however, further characterization of the clinical and pathologic significance of such adenomas will still be impactful in guiding the workup and management of large neck masses.

The adenoma we describe measured 7 cm in its largest dimension and weighed 57 g. To our knowledge, this is the first reported case describing an adenoma of this scale. Most reports of such a “huge” parathyroid adenoma only describe tumors of approximately weighing 40 g at most.^{13,14} Even more seldom are parathyroid adenomas that extend from the neck deep into the mediastinum. In one such case in the literature, the mass was removed transcervically.¹⁵ Other cases of thoracoscopic resections have been reported; however, the masses were purely located in the mediastinum, more consistent with an ectopic parathyroid adenoma.^{16–18} The extension from the neck into the posterior mediastinum presents a unique dilemma for surgical resection, possibly prohibiting safe dissection with either a pure transcervical or thoracoscopic approach. Our case is probably the first to demonstrate that hand-assisted thoracoscopic resection is a safe and effective adjunct to the removal of such masses, while still retaining the benefits of a minimally invasive approach.

Importantly, in the setting of hypercalcemic crisis and hyperparathyroidism, malignancy must be carefully considered in the differential diagnosis. Parathyroid carcinomas, though uncommon, can often present similarly to giant parathyroid adenomas, especially in the absence of local invasion and distant metastases. Patients with parathyroid carcinoma typically present with symptoms or complications of profound hypercalcemia, such as target end organ damage.¹⁹ In contrast, patients with giant parathyroid adenomas present more frequently with asymptomatic hypercalcemia, similar to our patient.^{7,8} It has been postulated that patients with large parathyroid masses and profound hypercalcemia but no distinct symptomatology may be more likely to have a benign pathology; however, this speculation has not been formally investigated to date.⁶ Regardless, since there is no definitive way to rule out malignancy prior to resection, the surgeon must have a high index of suspicion, and care should be taken to remove the mass en bloc.

Histologic differentiation between parathyroid adenomas and carcinomas is also challenging. However, certain findings on histopathology are more suspicious of malignancy, like dense fibrous bands, frequent mitotic figures, vascular or perineural invasion, or increased Ki-67.^{6,20} In the absence of these features, as in our patient's case, the final suspicion for parathyroid carcinoma is very low. However, since there have been few reports of long-term follow-up of patients with giant parathyroid adenomas and since there is currently no consensus or guideline on the monitoring of

these patients, it is reasonable to continue a long-term follow-up of such patients to monitor for recurrence.

Conclusion

In summary, we report a rare case of a giant parathyroid adenoma occupying both the lower neck and the posterior mediastinum presenting as a hypercalcemic crisis. We demonstrate, perhaps for the first time, that a minimally invasive, hand-assisted, thoracoscopic approach is a safe and effective method of removing such mass. We recommend long-term laboratory follow-up for such patients to ensure no evidence of recurrence.

Disclosure

The authors have no multiplicity of interest to disclose.

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