

Functional Large Parathyroid Carcinoma Extending into the Superior Mediastinum

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Mediastinal parathyroid carcinoma is very rare regardless of whether it is functioning, and it is sometimes problematic in both diagnosis and treatment. We herein report a case of primary hyperparathyroidism (PHP) associated with large parathyroid carcinoma extending into the superior mediastinum successfully removed by a transcervical approach, with a review of recent literature. A 61-year-old male with a six-year history of PHP and urinary stone disease presented with an abnormal mediastinal mass in a chest X-ray. His serum level of intact parathyroid hormone (PTH) was markedly elevated to 1,220.0 pg/mL (normal range: 10.0–65.0 pg/mL), though calcium and phosphorus levels were within normal limits. Chest computed tomography demonstrated a large mass in the superior mediastinum, displacing the trachea to the right and reaching the aortic arch, posteriorly adjacent to the thoracic vertebra. Transcervical extirpation of the tumor was performed. The resected specimen measured 50×85×38 mm and weighed 56.8 g. Histopathological examination revealed a capsular invasion of the tumor cells, and a diagnosis of parathyroid carcinoma was made. On the 8th postoperative day, the patient was discharged uneventfully with a decreased serum level of PTH (59.0 pg/mL), and no recurrent disease or exacerbation of hyperthyroidism was observed 36 months after surgery. (Ann Thorac Cardiovasc Surg 2008; 14: 112–115)

Key words: parathyroid carcinoma, mediastinum, hyperparathyroidism, surgery

Introduction

Functional parathyroid carcinoma in the mediastinum is a very rare entity. Although primary hyperparathyroidism (PHP) is commonly associated with parathyroid adenoma or hyperplasia, parathyroid carcinoma accounted for only 2% of PHP in a recent report.¹⁾ When mediastinal involvement occurs, the diagnosis and treatment of PHP sometimes becomes problematic. We report here a patient with a large parathyroid carcinoma extending to the aortic arch from the left lower pole of the thyroid that was successfully treated with surgery via a transcervical

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approach. A review of the literature is also provided.

Case

A 61-year-old male with a six-year history of PHP and urinary stone disease presented with an abnormal mediastinal mass in a chest X-ray (Fig. 1). A thumbnail-sized mass was palpated above the sternal notch in a thyroid position. Serum levels of intact parathyroid hormone (PTH), calcium, and phosphorus were 1,220.0 pg/mL (normal range: 10.0–65.0 pg/mL), 7.6 mg/dL (7.0–10.0 mg/dL), and 2.1 mg/dL (2.9–4.3 mg/dL), respectively. No bone pain or abdominal symptoms were noted, and renal dysfunction was not demonstrated. No tumor markers were elevated preoperatively. Chest computed tomography (CT) demonstrated a large mass in the superior mediastinum, displacing the trachea to the right (Fig. 2). The tumor reached the aortic arch, posteriorly adjacent to the thoracic vertebra. ^{99m}Tc-²⁰¹Tl sub-



Fig. 1. Chest X-ray demonstrated an abnormal mediastinal mass displacing the trachea and a bulge in the left upper mediastinum (arrows).

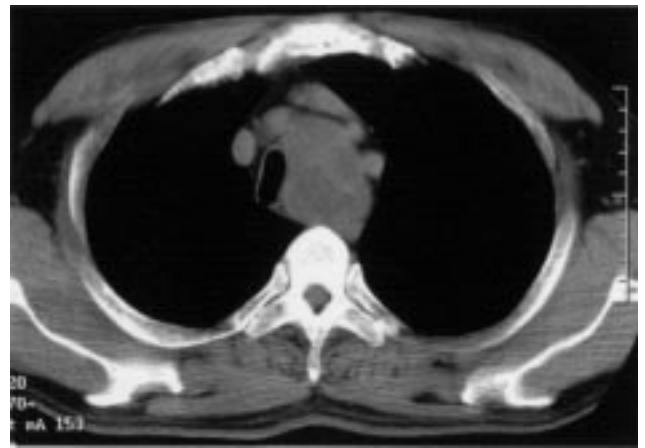


Fig. 2. Chest computed tomography showed a large mass in the superior mediastinum extending to the aortic arch. The trachea was compressed laterally, and proximal brachial cephalic arteries were displaced.

traction scintigraphy demonstrated an abnormal uptake in accordance with the tumor (Fig. 3). A mediastinal extension of a functional parathyroid tumor was suspected. Transcervical extirpation of the tumor via a neck collar incision was therefore performed.

The tumor was fed by the left inferior thyroid artery, and no feeding artery was found from the mediastinal organs. The tumor was separated from surrounding mediastinal tissue by a fibrous capsule. The invasion of neighboring organs was absent, and extirpation was successful without additional sternotomy. Calcium gluconate (2.55 g) was injected intraoperatively after removal of the tumor. The resected specimen was a large soft tumor measuring 50×85×38 mm and weighing 56.8 g, with multicystic lesions containing old bloodlike fluid (Fig. 4). Histopathological examination revealed small round tumor cells growing in a trabecular or glandular form (Fig. 5). The tumor was lobulated by dense fibrous trabeculae. Invasion into the capsule and hyaline band were partially observed, and diagnosis of parathyroid carcinoma was made. Serum calcium decreased to 4.0 mg/dL postoperatively, and the patient received 3 µg a day of oral alfacalcidol, a synthetic analogue to active vitamin D, and 6 g a day of oral calcium lactate. On the 8th postoperative day, the patient was discharged uneventfully with a de-

creased serum level of PTH (59.0 pg/mL), and no recurrent disease or exacerbation of hyperthyroidism was observed 36 months after surgery.

Discussion

The mediastinal parathyroid gland is found in 3% to 19% of the population²⁾ and in 11% of cases with PHP.³⁾ However, the true incidence of mediastinal parathyroid carcinoma in PHP remains unknown. In the largest series reported by Wang and co-workers, 1,200 patients surgically treated for PHP, none presented with a mediastinal parathyroid carcinoma, functioning or otherwise.²⁾

Sandelin and associates reported that in 95 cases of parathyroid carcinoma, the median tumor weight was 4.420 g (1.050–40 g), and the median tumor diameter was 25 mm (range 5–50 mm)⁴⁾ In comparison, our case was comparatively large; however, the largest functioning mediastinal parathyroid carcinoma reported in English literature weighed 1,200 g.⁵⁾ The second largest measured 12×9×8 cm and weighed 450 g, reported by Chiofalo and co-workers.⁶⁾

In patients with PHP, a preoperative diagnosis of parathyroid carcinoma is very difficult because the clinical manifestations are almost the same as those of benign disease. Most symptoms occur because of an excess secretion of PTH by the malignancy, as with PHP associated with benign adenoma or hyperplasia, rarely because of invasion or compression of the surrounding organs.⁷⁾ However, several clinical features suggest malignancy rather than benign disease: (1) a markedly high serum

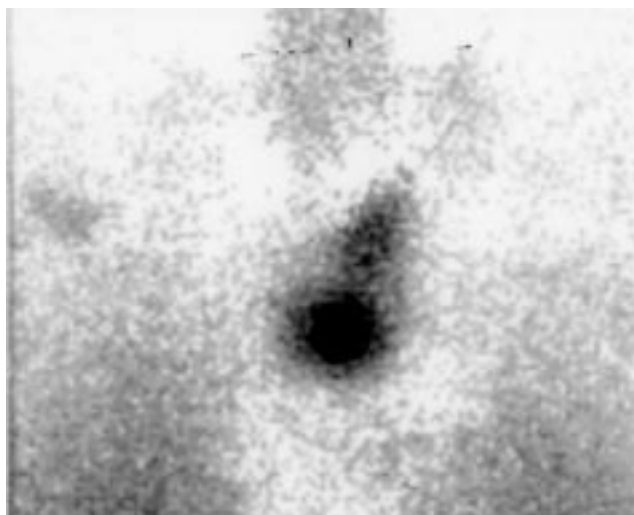


Fig. 3. ^{99m}Tc - ^{201}Tl subtraction scintigraphy demonstrated abnormal uptake in accordance with the mediastinal tumor.

level of PTH ranging from 3 to 10 times above the normal limit, (2) a high serum calcium level generally above 14 mg/dL, and (3) the presence of a palpable neck mass (large mass lesions are unusual in the case of benign PHP).⁷⁻⁹⁾

An association between parathyroid malignancy and long-term hemodialysis has been reported,¹⁰⁾ and in patients with chronic renal failure, secondary hyperparathyroidism may occur. However, symptoms resulting from hypercalcemia are insignificant because hemodialysis reduces serum calcium levels.

In our case, the serum calcium level was normal, and symptoms resulting from hypercalcemia were not apparent, except for the patient's history of renal stone disease. His PTH level was remarkably high at 18 times the normal upper limit. A neck mass was palpated, but most of the mass was in the mediastinum.

Furthermore, a histological diagnosis of parathyroid carcinoma is also difficult because malignancy is not clearly distinguishable from benign adenoma by histopathological features.⁷⁾ Schantz and Castleman established the following pathological criteria for the diagnosis of this malignancy:¹¹⁾ (1) a thick dense fibrous capsule and/or trabeculae that divides the tumor into (2) sheets of cells arranged in a lobular pattern, (3) the presence of mitotic figures, and (4) capsular and/or vascular invasion. However, each feature could also be observed in a benign disease. Moreover, immunohistochemical staining, electron microscopy findings, and DNA content analysis are not helpful in the differentiation of parathyroid malignancy



Fig. 4. The gross specimen showed a large pyriform soft tumor measuring 50×85×38 mm and weighing 56.8 g, with multicystic lesions containing old bloodlike fluid.

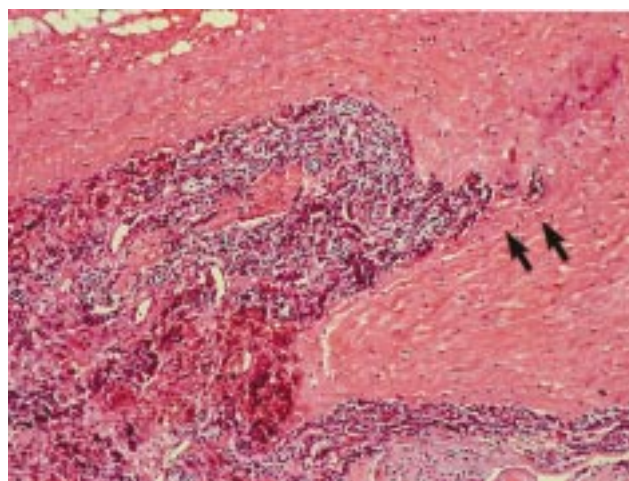


Fig. 5. Histopathology revealed atypical small round tumor cells in sheet form. An invasion of the thick fibrous capsule was also observed (arrows).

from benign disease.^{7,12)} Thus parathyroid carcinoma should be definitively diagnosed only by a demonstration of invasive growth into the capsule, blood vessels, or surrounding structures, or indeed, by the malignant clinical features such as local recurrence or metastasis. Therefore intraoperative frozen sectioning is useless in the sur-

gical diagnosis of parathyroid malignancy.

The best treatment option is complete surgical resection, which should be carried out without rupture or spillage of the tumor.^{7,9,12)} Most cases are resectable via a cervical approach.²⁾ The parathyroid glands arise from the third and fourth branchial pouches during the fifth week of embryogenesis. The glands from the fourth branchial pouches will normally come to lay posterolaterally to the thyroid as the superior parathyroid and may migrate into retro- and paraesophageal regions from the neck down to the level of the carina. On the other hand, the inferior parathyroid glands arise with the thymus from the third pouches and descend into the lower neck, and they may migrate into the anterior mediastinum, including the thymus itself, the aortic arch, and great vessels in the upper mediastinum. Thus most mediastinal parathyroid glands are accessible via a transcervical pathway. Sternotomy provides a wider operative field for mediastinal exploration in the case of a missing functional gland and is the best method for total thymectomy in the case of migrated parathyroid tissue in the thymus. Video-assisted thoracoscopy is another alternative for the mediastinal exploration of smaller and lateral lesions. In our case, the parathyroid malignancy was adherent to the lower pole of the left thyroid and extended into the mediastinum, reaching the aortic arch but without invading the surrounding organs. The blood supply was only from the neck. Thus the tumor was believed to have arisen near the left thyroid, subsequently growing into the mediastinum, influenced by negative intrathoracic pressure in the mediastinum and by gravity. The tumor is then thought to have grown larger than its origin, giving it its pyriform shape.

The prognosis of parathyroid malignancy is variable, and recurrence occurs in about 40% of cases.⁴⁾ Local tumor implants are the most common type of recurrence and usually occur within 3 years.^{4,7)} The lung is the second most common site of recurrence. Lymph node involvement, however, is infrequent, as reported by Sandelin and co-workers in 3 of 95 cases.⁴⁾ They also reported that the 5- and 10-year survival rates of patients with parathyroid malignancy are 85% and 70%, respectively. Moreover, although repeated surgery for recurrent disease may prolong survival, surgery is not a cure.^{4,7)}

In cases with mediastinal recurrence, the exact localization and surgical resection is problematic. In surgical explorations of functional mediastinal parathyroid, 36% are unsuccessful.²⁾ ²⁰¹Thallium or ^{99m}Technetium 2-methoxyisobutyl-isonitrile (MIBI) scintigraphy may be useful for preoperative diagnosis, but not for intraopera-

tive exploration. In such cases, the recently introduced radionuclide-guide method, which uses a handheld gamma scintillation probe may be useful.¹³⁾

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