Primary hyperparathyroidism due to giant parathyroid tumor - Adenoma or Carcinoma?

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ABSTRACT: Parathyroid adenomas account for most cases of primary hyperparathyroidism (PHPT). Certain symptoms and biochemical abnormalities alert the surgeon to their presence, since these benign tumors are rarely evident on physical examination. Moreover, because they are usually very small, preoperative localization using sestamibi scanning or ultrasonography is required to avoid bilateral neck exploration. Parathyroid adenomas rarely attain huge proportions. We report a case of a parathyroid adenoma measuring 7.5 x 5.5 x 4 cm and weighing 89 g; to our knowledge one of the greatest masses reported in the literature. The tumor was located behind the left thyroid lobe and expanded anterior to the thorax and the esophagus in the prevertebral space. At surgery, the parathyroid tumor was successfully removed on block with the left lobe of the thyroid gland and nodal clearance. No signs of malignancy were observed by both morphological and histopathological analyses.

Key Words: Giant parathyroid adenoma, Primary hyperparathyroidism, Parathyroid carcinoma.

INTRODUCTION

Although parathyroid disease is relatively uncommon, parathyroid adenomas account for more than 80% of all cases of primary hyperparathyroidism (PHPT). The clinical expression of PHPT has undergone a number of significant changes in the last 50 years. A 10-fold increase in disease incidence was recorded after identifying an association with nephrolithiasis in 19341, and a further 4-fold increase was noted in the United States when routine biochemical screening was introduced in the 1970s2. Since then, there has been a 3-fold decline in prevalence attributed to hormone replacement therapy in postmenopausal women3, cessation of therapeutic head and neck irradiation4, and improvements in vitamin D nutrition5. Giant parathyroid adenomas are very rare, the most frequent etiological association being that seen with irradiation, for example, in survivors of the atomic bomb6. On the other hand, parathyroid carcinomas account for 1% to 3% of PHPT6. Patients usually present with a severe form of hyperparathyroidism at diagnosis, such as bone disease, renal disease, or hypercalcaemic crisis, in contrast to the relatively asymptomatic presentation of benign parathyroid disease7. Problems encountered include difficulty in establishing accurate preoperative diagnosis and intraoperative recognition, local invasion of adjacent structures in the neck, local recurrence that require re-operation, metastatic disease commonly to the lung and liver, and death from uncontrollable hypercalcaemia8.

We report a case of a giant parathyroid tumor with carcinoma diagnosis highly suspected pre- and intraoperatively. Finally, the histopathologic diagnosis was an adenoma, representing to our knowledge one of the largest masses documented in the literature.

Case Report

A 56-year-old woman with a 12-year history of neph-
rolithiasis was referred to our Hospital for bone metabolism evaluation. She complained of progressive fatigue, low back pain, and inability to walk because of neuromuscular weakness. The patient’s history was otherwise unremarkable. There were no associated abdominal colic, neuropsychiatric disturbances or hypertension. Physical examination revealed a large palpable mass in the lower part of the left side of the neck. On the basis of clinical findings and ultrasound examination, it was initially misdiagnosed as a thyroid nodule. Biochemical investigations confirmed euthyroidism with thyroid-stimulating hormone and free thyroxine (T4) levels of 3.7 mIU/l and 15.2 μg/dl, respectively. With a clinical suspicion of hyperparathyroidism, the investigations revealed significant hypercalcemia (1.9 mmol/l) with an elevated parathyroid hormone (PTH) level of 1800 pg/ml, a serum phosphate concentration of 2.1 mg/dl, hypercalciuria (24 hr urine calcium 357 mg), and elevated serum alkaline phosphatase (412u/l; normal range 78-289). Bone marrow examination detected osteitis fibrosa and bone cysts, consistent with the classical bone disease of hyperparathyroidism. The skull x-ray showed punched out lesions typically described as salt and pepper appearance. Sestamibi scan revealed a left-sided hyperfunctioning parathyroid adenoma in the lower pole of the thyroid gland (Figure 1).

Thus, the patient underwent unilateral neck exploration with intraoperative parathyroid hormone measurement. Parathyroidectomy of the tumor was performed, en block with left hemithyroidectomy and central (paratracheal) compartment lymph node clearance. Macroscopically, the tumor consisted of a gray-white tissue mass with cut sections demonstrating multiple blood-filled cysts, ranging from 0.7 to 3 cm in greatest dimension. None of the nine lymph nodes showed metastatic involvement. Following the excision, the parathormone levels dropped from 2500 pg/ml (pre-excision level) to 368 pg/ml in 10 min and to 125 pg/ml after 20 min. In the immediate postoperative period the patient developed hypocalcaemia that required treatment with intravenous calcium therapy. Follow-up at 3 and 6 months revealed normal serum calcium and intact PTH. The histopathological examination confirmed the diagnosis of a giant benign parathyroid adenoma (7.5 x 5.5 x 4 cm), weighing 89 gr (Figure 2, 3).

**DISCUSSION**

Most cases of PHPT are caused by parathyroid ad-
Giant Parathyroid Adenoma

enomas (in more than 85% of cases), which trigger an increase in basal secretions and in the amplitude of PTH pulses\(^9\). Although PTH secretion is still modulated by plasma calcium levels, a decreased sensitivity of parathyroid cells to extracellular calcium has been found in vivo and in vitro\(^10\). This induces an increased set-point, defined as the calcium level at which PTH secretion is inhibited by 50%, and a shift to the right of the inverse sigmoidal relationship between PTH secretion and the calcium concentration. Recent data suggest that the severity of PHPT is determined by a strict set of measurements, including the set-point, the cell number, and the secretory output per cell\(^10\). Gland weight is recognized as the best available index of parathyroid tumor cell number\(^1\). Furthermore, many studies have established a direct relationship between gland weight and serum PTH and calcium levels\(^11,12,13\). Similarly, it has been found that an increased glandular mass correlates with the severity of PHPT and the subsequent risk of transient postoperative hypocalcemia\(^14\). We measure intact PTH (iPTH), which is a single polypeptide chain, 84 amino acids long, with a molecular weight of 9500Da. We choose to measure iPTH as opposed to fragmented PTH, because it enables us to directly assess the secretory capacity of the parathyroid glands. The usual weight of a parathyroid adenoma ranges from 70 mg to 1 g, although there are sporadic reports of tumors weighing more than 20 g\(^10\). Giant parathyroid adenomas are extremely rare. There are sporadic reports of large adenomas retaining masses of 110 g\(^4\), but the adenoma from our patient, which weighed 89 g, represents one of the greatest masses ever reported in the literature.

Other causes of PHPT include multigland hyperplasia (in 5% to 10%), and carcinoma (less than 1%)\(^6\). Carcinoma results in severe PHPT and complications from recurrence and metastatic spread. Hence, its detection is vital to the overall management of patients. However, differentiating carcinoma from benign parathyroid disease is difficult in the preoperative and intraoperative stages, and even after histopathologic evaluation\(^8,14\). The principle features distinguishing parathyroid carcinoma from adenoma are thick fibrous bands, mitotic activity, capsular invasion and vascular invasion. Fibrous bands were present in 90 percent of parathyroid carcinomas\(^7\).

Often, the diagnosis is made in retrospect, as in recurrences. Parathyroid carcinomas are generally larger and firmer than parathyroid adenomas. The clinical manifestations of hyperparathyroidism are usually more severe, and serum levels of calcium, PTH and alkaline phosphatase are significantly higher than in patients with adenoma. Patients with parathyroid carcinoma have a high incidence of renal dysfunction, osteoporosis and gastrointestinal symptoms\(^6,15\). Preoperative and intraoperative suspicion is important in planning the effective treatment. Fine needle aspiration cytology should not be performed in patients undergoing initial neck exploration because of the risk of seeding tumor cells. The optimal surgical treatment is en bloc resection with ipsilateral thyroid lobectomy and removal of any enlarged or abnormal lymph nodes. Particular, attention must be given to avoid rupture of the tumor during surgery, because of the very high risk of local seeding and persistent or recurrent disease\(^6,16,17\).

Most of the parathyroid cancers are diagnosed after surgery and often only after reoperation for local or distant recurrence; many patients have a good clinical course despite the type of the initial operation; others have recurrent or persistent hypercalcemia and severe metabolic complications that can be difficult to control and often result in death\(^6,17\). The outcome of these patients depends on the biologic features and on the management of the recurrent
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ΠΕΡΙΛΗΨΗ: Ο πρωτοπαθής υπερπαραθυρεοειδισμός οφείλεται στην παρουσία παραθυρεοειδικού αδενώματος στα περισσότερα των περιπτώσεων. Συγκεκριμένα κλινικά και εργαστηριακά συμπτώματα υποδηλώνουν την παρουσία τους, ενώ από την χοληθή όγκου ανευρίσκονται με τη φυσική εξέταση. Επιρροάζεται, το συνήθως μικρό μέγεθος τους επιβάλλει τη δυνάμεια προσγειωτικού αντικαταστάτικου ελέγχου με στατιστική εξέλιξη με συστοιχία ή υπερηχογραφία για τον ακριβή εντοπισμό τους και την απορρίψη της χλανάριας εμπιστοσύνης διεξέρευσης του προληπτικού. Το αδενώματος των παραθυρεοειδών οφείλονται από τον μεγάλο μέγεθος τους παρουσίας διαστάσεων. Παρουσιάζουν την περίπτωση παραθυρεοειδικού αδενώματος διαστάσεων 7.0 x 5.0 x 4.0 cm και βάρους 89 gr. Σύμφωνα με τη μελέτη της διεθνούς βιβλιογραφίας, η περίπτωση μας αποτελεί μία από τις μεγαλύτερες σε μέγεθος βλάβες του όγκου αναφερθέντων στους στοιχείους του, ενώ επικεντρώνται προς το παρελθόν και τον αυτοκατασκευασμένο χώρο. Ο όγκος του παραθυρεοειδικού αποφεύγει επιτυχώς, ενώ ταυτόχρονα διενεργήθηκε σύστοιχη λοβέξη με και αυθεντική της ψυχαγωγία, με λειτουργικό καθαρισμό της περιοχής. Η μακροπρος και ιστοπαθολογοανατομική εξέταση του παρακεντάμενου δεν επαρκεία στοιχεία κατόχων.

Δέξες Κλειδά: Παραθυρεοειδικό αδένωμα, Πρωτοπαθής υπερπαραθυρεοειδισμός, Καρκίνωμα των παραθυρεοειδών.
REFERENCES


