Radiological considerations and surgical planning in the treatment of giant parathyroid adenomas

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ABSTRACT

Giant parathyroid adenomas constitute a rare clinical entity, particularly in the developed world. We report the case of a 53-year-old woman where the initial ultrasonography significantly underestimated the size of the lesion. The subsequent size and weight of the adenoma (7cm diameter, 27g) combined with the severity of the hypercalcaemia raised the suspicion for the presence of a parathyroid carcinoma. This was later disproven by the surgical and histological findings. Giant parathyroid adenomas are encountered infrequently among patients with primary hyperparathyroidism, and appear to have distinct clinical and biochemical features related to specific genomic alterations. Cross-sectional imaging is mandated in the investigation of parathyroid adenomas presenting with severe hypercalcaemia as ultrasonography alone can underestimate their size and extent. This is important since it can impact on preoperative preparation and planning as well as the consent process as a thoracic approach may prove necessary for certain cases.

KEYWORDS

Parathyroid adenoma – Giant – Primary hyperparathyroidism – Surgery – Imaging – Consent

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Primary hyperparathyroidism (pHPT) is the third most common endocrine disorder and the leading cause of hypercalcaemia among ambulant patients. It primarily affects women with a female-to-male ratio of 4:1 and a peak incidence around the fifth decade of life.¹ In the majority (80–85%) of cases, it results from a single parathyroid adenoma while parathyroid hyperplasia (15%) and carcinoma (<1%) represent rarer causes of pHPT. Giant parathyroid adenomas have variable definitions in the literature but the most commonly used is that for adenomas exceeding 3.5g in weight.^{2,3}

Case History

A 53-year-old woman was referred to the endocrinology department for investigation and management of newly diagnosed hypercalcaemia. She reported suffering from fatigue as well as generalised bone and muscle pain over the preceding three months. Her past medical history included controlled hypertension.

A 2–3cm left neck mass was palpable on cervical examination. The remainder of the physical examination was unremarkable. Laboratory evaluation was consistent with pHPT as she suffered from severe hypercalcaemia (adjusted

serum calcium: 15.9mg/dl, normal range: 8.4–10.5mg/dl) associated with exceedingly high parathyroid hormone (PTH) levels measuring 4,038pg/ml (normal range: 10–65pg/ml). In view of the severe hypercalcaemia, the patient was admitted to hospital and started on intravenous fluids followed by a bisphosphonate infusion. Within two days of hospitalisation, the adjusted serum calcium had normalised.

In order to investigate the pHPT, neck ultrasonography was initially performed. This revealed a lobular, well defined hypoechoic lesion situated behind the left lower pole of the thyroid gland and measuring 2.85cm in diameter (Fig 1). The severity of the hypercalcaemia made parathyroid carcinoma an important differential diagnosis. Sestamibi imaging or single photon emission computed tomography were not considered as based on the clinical presentation, biochemistry and ultrasonography findings, it was not the nature of the tumour that was in question (consisting of functioning parathyroid tissue) but its anatomical extent. Consequently, cross-sectional imaging in the form of magnetic resonance imaging (MRI) was performed instead. MRI findings were typical of a left inferior parathyroid adenoma but showed it to measure 7.0cm × 3.7cm × 2.7cm as it extended deep into the mediastinum down to the origin of the left common carotid artery (Fig 2).

Figure 1 Ultrasonography demonstrating a lobular (arrows indicating lobules), well defined hypoechoic lesion situated behind the left lower pole of the thyroid gland

Figure 2 T2 weighted coronal magnetic resonance imaging illustrating a left inferior parathyroid adenoma (arrow) extending deep into the mediastinum down to the origin of the left common carotid artery

Following normalisation of the patient's adjusted serum calcium, consent was obtained for a targeted parathyroidectomy. She was informed that a manubriectomy and/or sternotomy may become necessary owing to the size and extent of the mass and its potential adherence to intra-thoracic vessels. Surgery was performed on the fifth day of hospitalisation. The parathyroid adenoma was successfully removed transcervically without the need for a manubrial or sternal split. Intraoperative PTH monitoring confirmed a successful parathyroidectomy (PTH_{15 mins}: 349.8pg/ml, PTH_{25 mins}: 228.7pg/ml). Operative findings revealed a well defined lobular mass, weighing 27g and measuring 7cm in diameter (Fig 3). Histopathological examination confirmed a chief cell parathyroid adenoma (Fig 4).

The patient's postoperative course was uneventful, and her serum calcium and PTH levels normalised rapidly. In order to prevent hypocalcaemia, she was discharged on calcium and vitamin D replacement therapy for two weeks. She is currently normocalcaemic and asymptomatic nine months following surgery on no supplementation.

Discussion

Normal parathyroid glands weigh 30–50mg.¹ Pathological parathyroid glands, excised from patients with pHPT, show great variability in size and have a median estimated weight of 650mg.⁵ The term 'giant parathyroid adenoma' is used in the literature to describe sporadic cases of parathyroid adenomas with a glandular mass greater than the median estimated. Various weight cut-offs have been used, the largest being 3.5g.^{2,3}

Spanheimer *et al* analysed data retrospectively from 300 cases of pHPT, and determined the preoperative

Figure 3 Intraoperative (arrow) and immediately postoperative photographs revealing a well defined lobular mass

Figure 4 Histological features of the giant parathyroid adenoma (haematoxylin and eosin stain, 100x magnification): The lesion consists of chief cells (arrow), among which there are many delicate vessels (A). In some areas, nodules of water clear cells (arrow) are present (B).

characteristics and postoperative course of 15 giant parathyroid adenomas weighing more than 3.5g.³ Patients with giant parathyroid adenomas were more likely to have single gland disease as well as greater mean preoperative calcium and PTH levels compared with those with non-giant adenomas. No differences were recorded with regard to gland location, accuracy of imaging modalities, or persistent or recurrent pHPT. However, giant parathyroid adenomas were associated with higher rates of postoperative hypocalcaemia. These results are in agreement with those from an earlier study reporting on 26 giant parathyroid adenomas also defined as weighing >3.5g.²

Spanheimer *et al* concluded that giant parathyroid adenomas might represent a distinct clinical entity.³ Indeed, in a study published by Sulaiman *et al* in 2012, the genetic characterisation of sporadic parathyroid adenomas weighing >4g revealed specific genomic features that correlated positively with PTH levels and therefore parathyroid hyperfunction.⁴

The present case was that of a true giant parathyroid adenoma, both in terms of its size and weight, associated with severe hypercalcaemia and extremely high PTH levels. These features raised the suspicion of malignancy and necessitated urgent surgery.

Our case highlights several important principles of good surgical practice that will allow optimal preoperative preparation and planning:

- > Giant parathyroid adenoma is not a diagnosis confined to the developing world despite the majority of case reports originating from those countries.⁵ This case serves as a reminder to surgeons in the developed world (where these lesions are exceedingly rare) that giant parathyroid adenomas can be encountered there too.
- > Although parathyroid tumours attaining such large size and causing severe hypercalcaemia as well as

extremely high PTH levels are more likely to represent a parathyroid carcinoma,¹ this presentation can also be the manifestation of a benign giant parathyroid adenoma. This will be important both during (surgical approach) and after excision (length of follow-up period and planning of adjuvant therapy if indicated).

- > As a giant parathyroid adenoma can reach 7cm in diameter and still be barely palpable on cervical examination, the importance of cross-sectional imaging is reiterated in the investigation of parathyroid adenomas presenting with severe hypercalcaemia and extremely high PTH levels. Ultrasonography alone may underestimate the size of the adenoma as only part of it may be visualised transcervically. Preoperative cross-sectional imaging will delineate the anatomy of the entire adenoma, and will therefore facilitate surgical planning, prevent unplanned conversion to a thoracic approach and optimise the consent process by ensuring all the necessary information (including surgical approach and risks) is provided to the patient prior to surgery.

Conclusions

Giant parathyroid adenomas are an exceedingly rare finding in the developed world where most patients seek medical attention early and access to imaging is readily available. Despite its rarity, this case illustrates that giant parathyroid adenomas can be encountered in the developed world too, and that when patients present with severe hypercalcaemia and extremely high PTH levels, cross-sectional imaging should complement ultrasonography (even if the adenoma has been visualised clearly on ultrasonography). Computed tomography and/or MRI provide superior anatomic detail to ultrasonography. In addition, they allow visualisation of the mediastinum (which is limited with ultrasonography). In this way, a giant parathyroid adenoma extending into the mediastinum will be excluded or (in the unlikely event that this is the case) it will allow for optimal preoperative preparation and planning.

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