Non-functioning parathyroid adenoma: a rare differential diagnosis for vocal-cord paralysis

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ABSTRACT

INTRODUCTION Adenomas of the parathyroid gland typically present with symptoms of hyperparathyroidism, manifested by fatigue, bone pain, abdominal pain, weakness, dyspepsia, nephrolithiasis and skeletal bone disease. Here, we describe, for the first time, a case of a non-functioning benign tumour of the parathyroid gland presenting as vocal-cord paralysis.

CASE HISTORY A 49-year-old male presented with a 10-week history of dysphonia and the feeling of having 'something stuck in my throat'. History-taking elicited no other associated symptoms. Flexible nasal endoscopy demonstrated paralysis of the left vocal cord. Computed tomography of the neck revealed a cystic lesion, 18mm in diameter adjacent to the oesophagus. After more rigorous tests, a neck exploration, left hemithyroidectomy, excision of the left paratracheal mass and level-VI neck dissection was undertaken, without incident to the patient or surgical team. Histology was consistent with a parathyroid adenoma.

CONCLUSIONS This case emphasises the importance of including adenomatous disease of the parathyroid gland in the differential diagnosis despite normal parathyroid status as a cause of vocal cord palsy.

KEYWORDS

Parathyroid adenoma – Hyperparathyroidism – Vocal cord

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Adenomas of the parathyroid gland typically present with symptoms of hyperparathyroidism, manifested by fatigue, bone pain, abdominal pain, weakness, dyspepsia, nephrolithiasis and skeletal bone disease.¹ Parathyroid adenomas (PAs) presenting as vocal-cord paralysis (VCP) are rare.¹ Patients with functioning PAs have been reported to have elevated levels of calcium and parathyroid hormone (PTH).^{1–4} In context of parathyroid disease, patients who present with VCP and have normal laboratory investigations carry a high suspicion of a malignant parathyroid carcinoma that has invaded the recurrent laryngeal nerve (RLN).² Here, we describe, for the first time, a case of a non-functioning benign tumour of the parathyroid gland presenting as VCP.

Case History

A 49-year-old male presented initially to the Ear, Nose and Throat (ENT) department with a 10-week history of dysphonia and the feeling of having 'something stuck in my throat'. History-taking elicited no other associated symptoms. The only reported past medical history was of renal calculi. Clinical examination of his neck was unremarkable. Flexible nasal endoscopy demonstrated paralysis on the left vocal cord. Computed tomography of the neck revealed a cystic lesion, 18mm in diameter adjacent to the oesophagus. It extended around the posterior left lateral margin of the

trachea and was inseparable from the oesophagus medially (Fig 1). The lesion had well-defined margins, and arose from the proximal-third of the oesophagus, just below the level of the thyroid gland. Initially, this lesion was presumed to be an oesophageal diverticulum or duplication cyst. However, upper gastrointestinal endoscopy was normal.

Ultrasound of the neck was carried out. A hypoechoic, lobulated, well-defined mass of dimension 20 × 11 × 23mm caudal to the lower pole of the left thyroid lobe and adjacent to the oesophagus (but which appeared separate from both) was revealed. Minimal colour Doppler flow at the cranial aspect of the mass was noted. Superficial to this mass was an additional, similar-looking lesion (12 × 8 mm) that was probably a nodule. Lateral cervical lymph nodes were not enlarged. Bilateral thyroid, submandibular and parotid salivary glands appeared to be normal. These findings were in accordance with a left inferior parathyroid mass and, in view of left VCP, a parathyroid carcinoma was suspected.

It was felt that fine needle aspiration cytology (FNAC) would not be appropriate due to three main reasons. First was the risk of disruption of the mass and seeding of cancerous tissue within the needle tract. Second, FNAC could not be used to differentiate between an adenoma and carcinoma because tumour invasion cannot be assessed upon cytology. Finally, FNAC can result in fibrosis of the specimen, making resection more difficult. In addition, the fibrotic reaction

Figure 1 CT of the neck showing a cystic lesion adjacent to the oesophagus

that occurs can mimic malignancy on histology, in particular adenomas that have undergone multiple aspirations.⁶

Serum blood tests were within normal limits, specifically PTH (5.4 (range, 1.3–7.3) pmol), calcium (2.23 (2.2–2.6) mmol/l), thyroid-stimulating hormone (1.30 mU/l), free thyroxine (15.8 (10–21) pmol/l), and free triiodothyronine (5.8 (3.5–6.5) pmol/l). Full blood count, coagulation screen, liver-function tests, urea and electrolytes were also unremarkable.

Discussion within the multidisciplinary team concluded that neck exploration, left hemithyroidectomy, excision of the left paratracheal mass and level-VI neck dissection should be undertaken.

Surgical Method

Under general anaesthetic with the patient positioned supine in neck extension, a curvilinear collar incision was made within a skin crease 2cm above the sternal notch. A hard paraoesophageal mass within the serosa of the cervical oesophagus, wedged between the trachea and oesophagus involving the left RLN, was identified. Sharp dissection mobilised the mass, and sacrifice of the left RLN, left hemithyroid, and level-VI neck nodal dissection was done *en bloc*. Procedure duration was 185 minutes.

Histology and Outcome

The parathyroid mass had a multi-cystic, haemorrhagic appearance with ill-defined borders, and contained haemorrhagic fluid (Fig 2). The specimen was composed predominantly of clear cells interspersed with foci of chief cells. Cells

Figure 2 Gross specimen of the resected parathyroid mass showing a multi-cystic, haemorrhagic appearance with ill-defined borders

were arranged in groups and trabeculae, and showed foci of prominent cystic degeneration, haemorrhage and fibrosis. The tumour did not show significant atypia or mitotic activity. There was no evidence of vascular or perineural invasion. However, malignancy was suspected because the tumour demonstrated irregular infiltration into surrounding soft tissue, so it was sent to a second tertiary centre for expert analyses. The centre concluded that the specimen was an adenoma based on the following data: low levels of Ki-67, negative for PGP9.5 and galectin-3, and positive for parafibromin. Furthermore, the irregular pattern of parenchyma within the background stroma suggested 'pseudo' invasion secondary to degenerative fibrosis rather than 'genuine' invasion. All identified lymph nodes (10) were negative for tumour.

The patient recovered well and was discharged on the second postoperative day. He is awaiting ENT assessment for medialisation of the vocal cords.

Discussion

Here we report, for the first time, a patient presenting with VCP and a parathyroid mass seen on imaging yet levels of PTH and calcium in serum were within normal ranges. Tumours of the parathyroid glands are classified into four groups; adenoma, hyperplasia, cystic changes and carcinoma.⁵ Most cases of primary hyperparathyroidism are found to be PAs.¹ Therefore, a painless, non-functioning parathyroid mass raises the suspicion of a parathyroid carcinoma.⁵ Furthermore, the presentation of gradual-onset VCP suggests malignant invasion of the RLN, which raises further the suspicion of a carcinoma.²

Studies have reported VCP to be a rare presentation of a PA, but the patients in those studies had functioning PAs.^{1–4} Primary hyperparathyroidism is seen in 20–30/100,000 people, and most cases are due to PAs. Hyperparathyroidism is

manifested by fatigue, bone pain, abdominal pain, weakness, dyspepsia, nephrolithiasis and skeletal bone disease.¹ Our patient had suffered a single episode of nephrolithiasis several years previously but, at presentation, levels of calcium and PTH were normal. VCP raises the suspicion of malignancy due to a PA, but could also be due to a thyroid carcinoma, squamous cell carcinoma of the larynx or oesophagus, and metastatic disease.⁴ Alternative causes include iatrogenic damage, collagen vascular diseases, or neurological disorders.¹

Angelos and colleagues described a 68-year-old male who presented with a sudden-onset hoarse voice and painful neck but whose laboratory investigations were normal.³ However, he had been investigated previously for hyperparathyroidism before sudden-onset VCP, and was waiting to undergo elective parathyroidectomy. Angelos and colleagues concluded that the sudden-onset VCP was secondary to a haemorrhage within the adenoma that caused sudden expansion of the capsule, which applied pressure on the RLN to elicit pain. The haemorrhage damaged surrounding adenomatous tissue, which soon normalised serum levels of calcium and PTH.

The VCP mechanism in our patient was not known but acute haemorrhage seemed unlikely because: (i) there was no history of hypercalcaemia; (ii) dysphonic symptoms had been ongoing for 10 weeks; (iii) pain had not been reported. It was assumed from preoperative images and VCP that the mass could be a carcinoma. Intraoperative examination showed the mass to encase the RLN. An intraoperative frozen section did not seem to be useful because: (i) of our suspicion of a parathyroid carcinoma; (ii) it would hamper nerve preservation; (iii) subsequent complex histological testing and resultant disruption of the mass (with potential implantation of malignant parathyroid tissue) would reduce the chance of complete resection of the tumour.

Several causes for VCP from PAs have been suggested. As mentioned above, sudden-onset paralysis can be secondary to a haemorrhage within the PA.^{3,4} Similarly, abscess formation within the PA could cause expansion and place pressure on nerves.^{3,4} Alternatively, if VCP onset has been more gradual and signs of infection are absent, the aetiology could be stretching of the RLN due to the close proximity of the PA.⁴ This scenario seemed to be most likely in our patient.

A non-functioning PA can be classified as a 'primary' or 'secondary' dysfunction. The latter would occur if the PA produced high levels of PTH but haemorrhage or infection has damaged the remaining PA and/or part of the parathyroid

gland, thereby causing atrophy and normalisation of the PTH level.⁵ Primary dysfunction would be due to a low production of PTH or inhibition of release of PTH into the blood supply (possibly due to ischaemia).⁵ Primary dysfunction occurs if the patient has never suffered from high levels of PTH. In our patient, the mechanism was not clear. He had suffered previously from renal calculi, which suggests that he may have had hypercalcaemia at some point. However, the renal calculi could have been incidental because there had not been any report of hypercalcaemia or hypercalcaemia in this patient previously.

Stretching, pressure, inflammation or oedema can lead to neuropraxia and eventual axonotmesis of a nerve.⁴ In our patient, the extent of damage to the RLN was not known because it was resected. Parathyroid carcinoma was the diagnosis suspected preoperatively and, given its high recurrence (~50%), complete resection may not have been achieved unless the RLN had been divided and taken with the specimen. In cases where the RLN has not been sacrificed, recovery has occurred within 1 week, suggesting only neuropraxic damage and a good prognosis.¹⁻⁴

Conclusion

Our patient presented with VCP and a parathyroid mass, but there were no clinical signs of hyperparathyroidism. There are different reasons why PAs cause VCP and why PAs are non-functioning. This case emphasises the importance of including adenomatous disease in the differential diagnosis despite normal parathyroid status. Unfortunately, the diagnosis of a PA was confirmed after RLN sacrifice. Surgeons should remain cautious for potential cases of a parathyroid carcinoma, and complete resection reduces the high prevalence of recurrence.

References

1. Givens DJ, Hunt JP, Bentz BG. Uncommon presentations of parathyroid adenoma. *Head Neck* 2013; **35**: E265–E268.
2. Iwasaki K, Usami A, Oida I *et al.* Sudden recurrent laryngeal nerve paralysis due to apoplexy of parathyroid adenoma. *Auris Nasus Larynx* 1999; **26**: 101–104.
3. Angelos P, Thompson NW, Giordano TJ. Spontaneous vocal cord paresis and return to normocalcemia: an unusual presentation of parathyroid adenoma with concomitant abscess. *Surgery* 1997; **121**: 704–707.
4. Lee JC, Barkdull GC, Weisman RA. Parathyroid adenoma as a cause of vocal fold paralysis. *Arch Otolaryngol Head Neck Surg* 2009; **135**: 712–713.
5. Sekine O, Hozumi Y, Takemoto N *et al.* Parathyroid adenoma without hyperparathyroidism. *Jpn J Clin Oncol* 2004; **34**: 155–158.
6. Norman J, Politz D, Bowersky I. Diagnostic aspiration of parathyroid adenomas causes severe fibrosis complicating surgery and final histologic diagnosis. *Thyroid* 2007; **17**: 1,251–1,255.