Synchronous symptomatic parathyroid carcinoma and parathyroid adenoma with incidental follicular thyroid carcinoma

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ABSTRACT

We describe the case of an 89-year old Caucasian woman admitted with confusion and severe clinical manifestations of acute hypercalcaemia. There was no history suggestive of any malignancy and initial management included correction of the hypercalcaemia with intravenous fluid therapy. Sestamibi parathyroid scintigraphy and neck ultrasonography demonstrated a 4cm left-sided thyroid lesion and a nearly 2cm right-sided thyroid lesion. The patient underwent a total thyroidectomy and parathyroidectomy. Histology confirmed a concomitant parathyroid adenoma, parathyroid carcinoma and follicular thyroid carcinoma. To our knowledge, this is the first reported case in the literature.

KEYWORDS

Parathyroid carcinoma – Follicular thyroid carcinoma

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Introduction

Parathyroid carcinoma (PC) is a rare cause of primary hyperparathyroidism (pHPT), accounting for approximately 1% of patients.¹ The majority of PCs actively hypersecrete parathyroid hormone (PTH), with patients presenting with hypercalcaemia. While thyroid disease is not uncommon in pHPT, concomitant thyroid cancers and PCs are extremely rare.² We describe the first reported case of a parathyroid adenoma (PA), PC and coexistent follicular thyroid carcinoma (FTC) in an elderly patient.

Case history

An 89-year-old woman of Caucasian ethnicity was admitted to our hospital with dehydration and acute confusion. She had recently presented to the memory clinic with symptoms of short-term memory loss and confabulations for a three-month period. Other symptoms of recent onset were recurrent abdominal colic, polyuria, polydipsia and constipation. Her past medical history included hypertension, hyperlipidaemia, osteoporosis with a compression fracture of the 11th thoracic vertebra, a left hip replacement and aortic regurgitation. Physical examination revealed a palpable thyroid lump on the left side. Biochemical investigations demonstrated hypercalcaemia (3.22mmol/l), suppressed phosphate levels (0.76mmol/l) and elevated levels of PTH (15.7pmol/l), in keeping with pHPT; otherwise, her complete

blood count, 25-hydroxyvitamin D levels, thyroid function tests and urinary calcium levels were grossly normal. She was initially managed with intravenous hydration and subcutaneous calcitonin while being further investigated.

Dual phase technetium (^{99m}Tc) sestamibi scintigraphy revealed prominent uptake in a 4.1cm x 2.9cm x 3.0cm lesion in the early phase, localised in the upper to middle poles of the left thyroid lobe (Fig 1A). This image is characteristic of a hyperfunctioning parathyroid gland. There were no other sestamibi avid lesions seen in the neck or mediastinum. Ultrasonography of the neck showed the presence of a hypoechoic solid-cystic nodule with internal vascularity and peripheral coarse calcification in the left thyroid lobe (Fig 1B), and a benign right-sided thyroid nodule posteriorly, measuring 1.5cm x 1.4cm x 1.6cm, with no Doppler hypervascularity or malignant features seen (Figures 1C and 1D).

Fine needle aspiration (FNA) of the left thyroid nodule was not performed preoperatively in view of the technical challenge in differentiating between benign and malignant parathyroid disease in cytological specimens. Furthermore, FNA can cause tumour rupture and seeding, which may preclude curative resection. Given the radiologically benign nature of the right thyroid lesion, no FNA was performed.

Following informed consent, the patient underwent a planned left thyroidectomy and left inferior parathyroidectomy with intraoperative neuromonitoring. Intraoperatively, the

left inferior parathyroid gland was enlarged and firm in nature. Following the excision of the left inferior parathyroid gland, intraoperative PTH levels remained significantly raised at 71.1pmol/l. Exploration of the contralateral side revealed a large right-sided parathyroid lesion densely adherent to the right thyroid lobe and an *en bloc* completion thyroidectomy was performed. The left superior parathyroid gland was preserved. After excision of the right parathyroid lesion, the PTH levels dropped to 0.2pmol/l with normalisation of calcium levels on postoperative day 1. The patient was discharged on day 4. She developed temporary neuropraxia and hypocalcaemia, which resolved after two weeks.

Microscopic examination revealed three synchronous tumours: two malignant and one benign. In the left hemithyroid specimen, a 3.9cm encapsulated FTC with capsular and lymphovascular invasion was seen (Fig 2A) with no extrathyroidal extension. Immunohistochemistry performed on this tumour exhibited positive staining for

thyroid transcription factor 1 (TTF-1) and thyroglobulin but PTH was negative (Fig 2B). The left inferior parathyroid gland demonstrated histological features of a parathyroid adenoma. The right hemithyroid specimen showed a 1.7cm parathyroid carcinoma, with lymphovascular invasion and local invasion into the adjacent thyroid gland and the perithyroidal soft tissue (Fig 2C). Immunohistochemistry of this tumour revealed positive staining for PTH but TTF-1 and thyroglobulin were negative (Fig 2D). In view of the patient's age, no further treatment was recommended by the multidisciplinary team, apart from surveillance.

Discussion

Concomitant thyroid disease is not an uncommon phenomenon in patients with pHPT, occurring in 15–70% of cases.² Of these, 2–6% may demonstrate thyroid carcinomas.³ However, synchronous thyroid and parathyroid carcinomas are extremely rare.² In this subgroup, PCs are

Figure 1 Prominent uptake in a 4.1cm x 2.9cm x 3.0cm lesion in the early phase of sestamibi scintigraphy, localised in the upper to middle poles of the left thyroid lobe, in keeping with a large adenoma (A); and ultrasonography of the neck demonstrating a hypoechoic solid-cystic nodule with internal vascularity and peripheral coarse calcification in the left thyroid lobe (B), and a dominant right-sided thyroid nodule posteriorly, measuring 1.5cm x 1.4cm x 1.6cm, with no Doppler hypervascularity (C and D)

most commonly detected with papillary thyroid carcinomas or their follicular variant. To our knowledge, this is the first reported case of a parathyroid adenoma, a parathyroid carcinoma and a synchronous follicular carcinoma.

Preoperative investigation for pHPT typically involves biochemistry and imaging in the form of dual phase sestamibi scintigraphy and ultrasonography.⁴ Patients with parathyroid adenoma usually show elevated adjusted serum calcium and PTH levels but in parathyroid cancer, these biochemical markers may be inappropriately elevated. The '>3 + >3' rule (parathyroid lesion >3cm, calcium >3mmol/l) helps to stratify the risk of malignancy in patients with pHPT who should undergo further preoperative investigations. Furthermore, patients with PC may present with symptoms consistent with severe hyperparathyroidism, specifically renal and neurological complications of pHPT. In our patient, the PTH levels were more in keeping with an adenoma despite fulfilling other clinical indicators of parathyroid malignancy.

The combination of both imaging modalities is crucial for parathyroid lesions.⁴ Sestamibi scintigraphy assists in the localisation and the diagnosis of the parathyroid lesion.⁵ Nevertheless, synchronous thyroid lesions, which may be sestamibi avid, may be difficult to distinguish from parathyroid lesions on this imaging modality. Ultrasonography is important to detect any other thyroid nodules that may result in concurrent thyroid resection. In a prospective study performed by Guo *et al*, in 741 patients who had undergone neck exploration for pHPT, 222 had undergone both thyroidectomy and parathyroidectomy after evaluation with sestamibi scintigraphy and ultrasonography for

suspected parathyroid adenoma; 13% of these patients had a concomitant thyroid malignancy.⁵ The authors described a sensitivity and specificity of 35.7% and 88.6% respectively in detecting thyroid carcinoma on sestamibi scintigraphy, compared with 73.8% and 95.1% on ultrasonography.

In our patient, the parathyroid imaging had failed to pick up the right-sided parathyroid carcinoma, which was possibly non-functional, in keeping with mildly elevated PTH seen in adenomas. Instead, a sestamibi avid, left-sided lesion was noted, conferring a false positive result; it is uncertain whether this left-sided lesion was a FTC or parathyroid adenoma.

This case report demonstrates some salient points. First, PCs may not be sestamibi avid, resulting in a false negative on sestamibi scintigraphy. As such, ultrasonography is crucial to identify any concomitant thyroid/parathyroid carcinomas, which may influence management. Second, thyroidal carcinomas may be sestamibi avid, leading to false positive results on sestamibi scintigraphy.⁶ Ultrasonography is again indicated in such instances. In conclusion, patients with pHPT can have concomitant thyroid disease; dual phase sestamibi scintigraphy and ultrasonography are required before resection.⁵

The surgical treatment of choice in concomitant PC and thyroid carcinoma is complete PC resection with *en bloc* ipsilateral thyroid lobectomy or *en bloc* total thyroidectomy if the lesions are contralateral.¹ Persistence or recurrence of disease may occur in more than 50% of patients with PC.¹ FNA may be useful in establishing a diagnosis of recurrent or metastatic disease of PC. Where there is a suspicion of parathyroid cancer, open exploration should

Figure 2 Haematoxylin and eosin stain of the left thyroid showing edge of tumour nodule with capsule (main part of nodule is in lower part of image), with capsular invasion and vascular invasion (arrow) (40x magnification) (A); immunohistochemistry for left thyroid tumour with PTH negative and thyroglobulin positive (100x magnification) (B); haematoxylin and eosin stain of the right thyroid showing infiltrative tumour composed of large eosinophilic cells surrounding normal parathyroid tissue (arrow) (40x magnification) (C); and immunohistochemistry for right thyroid tumour with PTH positive and thyroglobulin negative (100x magnification) (D)
PTH = parathyroid hormone

be performed. In adenomas that are localised on imaging, minimally invasive parathyroidectomy should be carried out. The role of intraoperative PTH assists with operative success in surgical resection of all hyperfunctioning parathyroid tissue, particularly in minimally invasive parathyroidectomy, thereby avoiding bilateral neck exploration and its complications.^{7,8}

References

1. Wei CH, Harari A. Parathyroid carcinoma: update and guidelines for management. *Curr Treat Options Oncol* 2012; **13**: 11–23.
2. Baek CO, Kim KH, Song SK. Synchronous parathyroid carcinoma and papillary thyroid carcinoma in a patient with long-standing schizophrenia. *Korean J Intern Med* 2017; **32**: 1104–1107.
3. Lee KA, Jin HY, Baek HS, Park TS. Importance of careful Tc-MIBI interpretation in patients with thyroid cancer and primary hyperparathyroidism. *Korean J Intern Med* 2015; **30**: 556–557.
4. Schulte KM, Talat N. Diagnosis and management of parathyroid cancer. *Nature Rev Endocrinol* 2012; **8**: 612–622.
5. Guo R, Wang J, Zhang M *et al*. Value of 99mTc-MIBI SPECT/CT parathyroid imaging and ultrasonography for concomitant thyroid carcinoma. *Nucl Med Commun* 2017; **38**: 676–682.
6. Koss WG, Brown MR, Balfour JF. A false-positive localization of a parathyroid adenoma with technetium Tc 99m sestamibi scan secondary to a thyroid follicular carcinoma. *Arch Surg* 1996; **131**: 216–217.
7. Dobrinja C, Santandrea G, Giacca M *et al*. Effectiveness of intraoperative parathyroid monitoring (ioPTH) in predicting a multiglandular or malignant parathyroid disease. *Int J Surg* 2017; **41**: S26–S33.
8. Laird AM, Libutti SK. Minimally invasive parathyroidectomy versus bilateral neck exploration for primary hyperparathyroidism. *Surg Oncol Clin N Am* 2016; **25**: 103–118.