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Coexistence of a large functioning parathyroid cyst with papillary thyroid carcinoma: A case report and review of the literature

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ABSTRACT

Parathyroid cysts constitute a rare cause of primary hyperparathyroidism (PHPT). PHPT may also rarely coexist with non-medullary thyroid carcinoma (NMTC). We describe a case of a 70-year-old woman who was diagnosed with PHPT, on the occasion of nephrolithiasis (corrected calcium and PTH levels: 10.8 mg/dl and 187 pg/ml, respectively). Ultrasonographic and scintigraphic investigation confirmed the diagnosis of a large parathyroid cyst attached to the lower pole of the right thyroid lobe and, consequently, the patient underwent parathyroidectomy. Due to the coexistence of multinodular goitre, with some nodules characterized as suspicious of malignancy, a total thyroidectomy was also performed. A histological diagnosis of cystic parathyroid adenoma was made. A unifocal papillary thyroid carcinoma of follicular subtype, 6 mm in diameter, was also detected. The patient's post-surgical course was uneventful and she remained normocalcaemic two years later. PHPT may rarely coexist with papillary thyroid carcinoma (PTC). The pathogenetic mechanisms linking these two endocrine entities are currently unknown.

1. Introduction

Parathyroid cysts constitute a rare cause of primary hyperparathyroidism (PHPT) [1–3]. PHPT may also rarely coexist with non-medullary thyroid carcinoma (NMTC) [4,5]. Whether NMTC has a different clinical course in cases of PHPT is unknown. It is also not known whether their coexistence is merely coincidental or whether common pathogenetic mechanisms link PHPT and NMTC. We describe a rare case of a functioning parathyroid cyst, coexisting with papillary thyroid carcinoma, successfully managed with parathyroidectomy and total thyroidectomy.

2. Case Presentation

A 70-year-old woman was admitted to our department for management of type 2 diabetes mellitus (T2DM). She also reported nephritic colics due to kidney stone disease. There were no reports of fractures, symptoms of hypercalcemia or obstructive neck symptomatology. Thorough laboratory investigation for nephrolithiasis was decided. Her T2DM was well-controlled (HbA1c: 6.9%) with gliclazide and metformin. Her medical history was also positive for arterial hypertension (treated with ramipril) and dyslipidaemia (treated with atorvastatin).

A thorough serologic investigation for nephrolithiasis was conducted, which showed elevated serum total calcium and parathyroid hormone (PTH) concentrations: 10.8 mg/dl [2.7 mmol/l; corrected calcium, normal range: 8.4–10.4 mg/dl (2.1–2.6 mmol/l)] and 187 pg/ml [19.8 pmol/l; normal range: 10–53 pg/ml (1.1–5.6 pmol/l)]. Serum phosphorus, magnesium and 25-hydroxy-vitamin D levels were low: 2.3 mg/dl [0.7 mmol/l; normal range: 2.5–4.5 mg/dl (0.8–1.4 mmol/l)], 1.7 mg/dl [0.7 mmol/l; normal range 1.9–2.5 mg/dl (0.8–1 mmol/l)] and 9 ng/ml [22.4 nmol/l; sufficiency levels >30 ng/ml (>75 nmol/l)], respectively. Renal function was normal [estimated glomerular filtration rate (eGFR): 144.3 ml/min/1.73 m^2], as was the 24-h urinary calcium concentration, at 189 mg/24-h (normal range: 50–300). Dual-energy X-ray absorptiometry (DXA) at the lumbar spine was indicative of osteopenia (T-score: −2.3). Renal ultrasound was negative for the presence of kidney stones.

Therefore, a provisional diagnosis of primary (PHPT) combined with secondary hyperparathyroidism was made and the patient underwent a neck ultrasound and parathyroid scintigraphy (Sestamibi) scan in order to localize potential parathyroid pathology. Radiological investigation was indicative of a cystic mass attached to the lower pole of the right thyroid lobe with an estimated maximum diameter of 6.5 cm. A large goitre was also diagnosed (the volumes of the right and left thyroid lobe were 25.6 and 19.3 cc, respectively) with a plethora of thyroid nodules, some of which had sonographic features suggestive of malignancy (Fig. 1). Other causes of high calcium and PTH levels, such as familial hypocalciuric hypercalcemia, as well as lithium, vitamin A and thiazide

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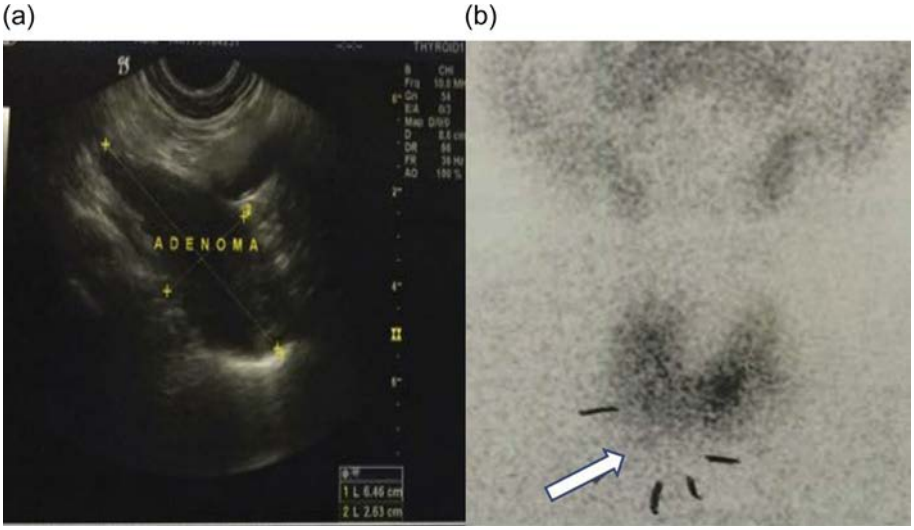

Fig. 1. Neck ultrasound (A) and sestamibi scan (the location of parathyroid cyst shown with white arrow) (B).

diuretic use were excluded. Of course, the contributory role of the patient's hypomagnesaemia was also taken into account.

The patient underwent an uneventful right parathyroidectomy and total thyroidectomy, after receiving four weekly doses of cholecalciferol (25.000 IU) and 2.8 g/10 ml of magnesium pidolate per day. Post-operative corrected calcium and PTH levels were 9.3 mg/dl and 17 pg/ml. A histopathological diagnosis was made of a unifocal papillary thyroid carcinoma (PTC) of follicular variant, 6 mm in diameter, without extrathyroidal extension. Due to the patient's low risk of PTC recurrence, no radioiodine was administered (Fig. 2). Two years later (at the time of writing), the patient remained normocalcaemic (with normal PTH levels and vitamin D sufficiency), with no signs of PTC recurrence.

3. Discussion

We have described a rare case of a functional parathyroid cyst as a cause of PHPT, co-existing with PTC. Parathyroid cysts are a rare cause of neck masses and they are usually non-functioning (in >90% of cases) [2,3], although one surgical study reported a higher prevalence of functional parathyroid cysts (85%) [1]. Functioning cysts usually derive from parathyroid adenomas and constitute 1–2% of cases of PHPT [2,3]. They usually present as a palpable asymptomatic neck mass, often misdiagnosed as thyroid nodules. Sometimes they may cause compressive symptoms (such as dyspnoea, dysphagia or paralysis of the recurrent laryngeal nerve) or may rarely be discovered as a mediastinal mass on chest radiography in patients undergoing investigation for respiratory discomfort [6], as in cases of ectopic parathyroids [7,8]. Their size is quite variable, ranging from 2 to 10 cm in maximum diameter (8). In cases of PHPT, symptoms related to hypercalcaemia may also develop [2]. Parathyroid adenomas detected inside a parathyroid cyst [9] or multiple functioning cysts comprise extremely rare manifestations [10].

Non-functioning parathyroid cysts may be found in 40–50% of cadaveric autopsies and are usually located in the inferior parathyroid glands, whereas functioning cysts have no typical location (from the angle of the mandible to the mediastinum), are found predominantly in men and in the 4th and 5th decade of life [11–13]. From a pathogenetic point of view, parathyroid cysts may either arise from vestigial remnants of the 3rd or 4th brachial cleft or from degeneration of a parathyroid adenoma or coalescence of cysts developing in normal parathyroid glands [11,12].

Parathyroid cysts are usually invisible on scintigraphy. Indeed, a thyroid scan may reveal a cold nodule, as in our patient [11]. The diagnosis

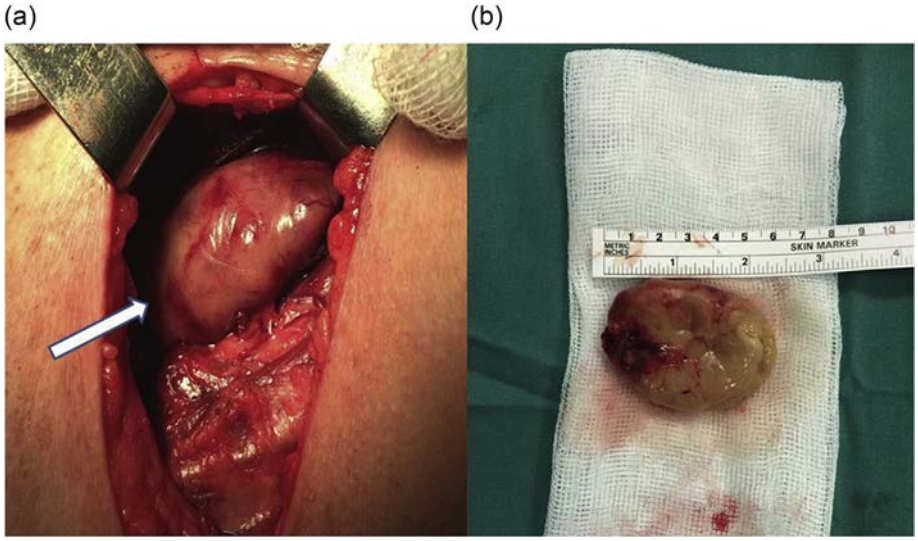

Fig. 2. Intra-operative view (A) and size (B) of parathyroid cyst.

is usually made by PTH assessment in the crystal clear fluid aspired from the cyst, a levels are extremely high (from 1198 to >5000 pg/ml), and is confirmed by histopathology (presence of parathyroid tissue within the cyst wall) [10]. Preoperative sestamibi single-photon emission computed tomography (SPECT) is useful in localizing the parathyroid cyst in one-third of patients, with its accuracy improving to 79% if it is interpreted in combination with cervical ultrasound images [14].

Fine-needle aspiration biopsy may also lead to complete remission of non-functioning parathyroid cysts, although it may relapse in many cases. In the latter situation, sclerotherapy with tetracycline and alcohol can be efficacious, although these procedures may result in fibrosis and recurrent laryngeal nerve palsy. In cases of small and asymptomatic parathyroid cysts, simple surveillance is suggested, whereas parathyroidectomy is reserved for cases of symptomatic or functioning parathyroid cysts, as in our case. Rare complications following a parathyroid cyst resection include hypocalcaemia or hypercalcaemic crisis, haemorrage and recurrent laryngeal nerve paralysis [8,11–13].

NMTC may be rarely incidentally discovered after synchronous parathyroidectomy and thyroidectomy or after FNAB of a suspicious thyroid nodule in a patient with PHPT (with a reported incidence of 2–13%) [4,5,15]. The most common type is PTC, manifesting usually as a unifocal microcarcinoma, located in the right thyroid lobe, being more common in women [4,5,15]. By contrast, patients with follicular NMTC present with larger tumors, with frequent extrathyroidal growth and lower pre-operative PTH levels than in those with PTC [5]. Whether these two entities share common pathogenetic pathways is currently unknown. Some contributory factors that may be suggested for such a link between these two entities are the shared embryological origin of the thyroid and parathyroid glands, common genes and transcription factors involved in thyroid and parathyroid organogenesis (such as *Hoxa3, Pax1* and *Pax9*), the increased expression of angiogenic growth factors (such as basic Fibroblast and Vascular Endothelial Growth Factor), the tumor-promoting effect of high PTH and calcium levels, as well as, low 1,25-dihydroxy-vitamin D concentrations, which result in high levels of angiogenic growth factors [15]. Interestingly, the coexistence of a functioning parathyroid cyst with NMTC is extremely rare (we found just one other case report in the literature) [16].

4. Conclusion

In conclusion, we have described a rare case of a 70-year-old woman with PHPT and nephrolithiasis, due to a cystic parathyroid adenoma. A unifocal PTC of follicular subtype, 6 mm in diameter, was also detected. The patient's post-surgical course was uneventful and she remained normocalcaemic two years later. PHPT may rarely coexist with PTC. The pathogenetic mechanisms linking these two endocrine entities are currently unknown.

Contributors

Panagiotis Anagnostis wrote the paper, and conceived and designed the case report.

Athanasios Panagiotou analyzed and interpreted the data.

Savvas Rafailidis contributed to the analysis.

Marina Kita provided scientific input and approved the final version of the paper.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

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