Intrathyroidal parathyroid adenoma mimicking thyroid cancer

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Abstract. Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia; patients are usually asymptomatic and the cause in 80–85% of cases is a single parathyroid adenoma (PA). Parathyroid adenomas arise from clonal expansion of tumor cells and may be located either posteriorly to the thyroid lobes or in ectopic sites. The incidence of intrathyroidal PAs varies from 1% to 6% and although uncommon, they pose certain diagnostic difficulties which may complicate treatment. The identification of the adenoma requires a combination of clinical evidence, imaging information and cytological findings due to the challenging distinction between thyroid and parathyroid lesions. We present the case of a patient with a large, partially cystic intrathyroidal parathyroid adenoma which was initially identified as a malignant thyroid nodule. We discuss the caveats that present in these rare cases and the important clinical and histological features that aid in the final diagnosis. In the case of our patient the cytological similarities between thyroid malignant cells and parathyroid cells, in combination with the negative sestamibi scan, resulted in a more invasive surgery than that a single parathyroid adenoma would require. Clinicians need to be vigilant in terms of the similarities between parathyroid and thyroid cytology in order to provide optimal patient care in these rare cases.

Key words: Parathyroid adenoma, Thyroid cancer, Primary hyperparathyroidism, Intrathyroidal, Ectopic

PRIMARY HYPERPARATHYROIDISM (PHPT) is the most common cause of hypercalcemia. Patients do not usually present with symptoms and the diagnosis is suspected when there is biochemical evidence of high serum calcium and inappropriately high levels of serum parathyroid hormone (PTH). Primary hyperparathyroidism is commonly caused by a single parathyroid adenoma (PA), which is found in 80–85% of cases, or parathyroid hyperplasia in 10–15% of cases, whereas parathyroid carcinomas are very rare [1].

Parathyroid adenomas arise from clonal expansion of tumor cells and may be located either posteriorly to the thyroid lobes or in ectopic sites such as the thymus gland, the tracheoesophageal and pharyngeal spaces, the mediastinum or within the thyroid gland. The incidence of intrathyroidal PAs varies from 1% to 6% and although uncommon, they pose certain diagnostic difficulties which may complicate treatment [2, 3]. The diagnosis of PHPT is primarily suspected based on clinical and laboratory findings. However, the localization of the affected gland is important for the subsequent surgical management, especially when PAs are found in ectopic locations [4].

The first imaging modality implemented during the investigation of a parathyroid adenoma is neck ultrasonography. If the adenoma is not identified, a technetium-99m-labeled sestamibi (99mTc sestamibi) scan is the preferred diagnostic tool but complementary magnetic resonance imaging or high resolution computed tomography may also be indicated. Fine needle aspiration (FNA) is of diagnostic importance, albeit problematic, due to the overlapping cytomorphologic features of parathyroid and thyroid lesions.

Case Presentation

A 43-year-old female patient was referred to the endocrinology outpatient clinic for evaluation of a palpable cervical mass at the level of the right thyroid lobe. Her personal history was not significant except for rare episodes of nephrolithiasis. Her family history was unremarkable. Physical examination revealed a painless
palpable hard mass in the lower pole of the right thyroid lobe without cervical lymphadenopathy and tachycardia at rest. The patient was biochemically euthyroid and the thyroid anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies were negative. Ultrasonography of the neck confirmed the presence of a 3.7 × 2.5 × 4 cm predominantly cystic nodule with a solid component and increased peripheral vascularity (Fig. 1).

The patient consented to a diagnostic FNA and simultaneous evacuation of the cystic component. The fluid that was aspirated was macroscopically hemorrhagic and the cytology report categorized the solid component of the nodule as suspicious for malignancy (Bethesda Category V). The smear revealed hypercellularity, with cellular discohesion, many naked nuclei and syncytial tissue fragments. The cells demonstrated anisokaryosis, with occasional very large nuclei, frequent coarsely granular chromatin and macronucleoli (Fig. 2). The patient was referred for surgical treatment due to the high suspicion for malignancy. However, routine preoperative biochemistry revealed hypercalcemia with high levels of PTH and normal kidney function (Table 1). The plasma and urinary calcium excretion were assessed using the Cobas c 501 analyzer (Roche Diagnostics) and the plasma PTH concentration was measured by electrochemiluminescence (Elecsys PTH kit; Roche Diagnostics). Consequently, the patient was diagnosed with PHPT and in order to avoid potential complications of hypercalcemia, treatment with intravenous fluids, cinacalcet with titrated dosage up to 120 mg/d and vitamin D supplementation was initiated. The patient underwent a neck sonography, a 99mTc sestamibi scan (Fig. 3) and an MRI scan to identify the location of the parathyroid lesion preoperatively, however all three imaging modalities were negative for parathyroid pathology.

The patient was then admitted to the surgical department to undergo thyroidectomy, central neck lymph node dissection and neck exploration for the identification of the parathyroid adenoma. Despite thorough neck explo-
Discussion

This is a case of a patient with a cystic intrathyroidal PA, whose FNA erroneously indicated the presence of thyroid cancer. The difficulties that arise in the cytological differential diagnosis between intrathyroidal PAs and thyroid malignancies are known. However, this particular case was further complicated by the presence of a cystic component and the repeatedly negative parathyroid imaging studies. Eventually, the correct diagnosis was suspected during surgery due to the rapid decline in PTH levels after thyroidectomy and confirmed by the histologic examination.

According to a previous large series, intrathyroidal PAs account for 1% of all PAs [5]. Cystic intrathyroidal PAs are even rarer, with a few cases described in the literature so far [6-8]. The rarity of this entity makes the pre-operative diagnosis elusive. Intrathyroidal PAs have no specific sonographic features, apart from the hypoechoic appearance and the abundant blood supply. Even so, they are difficult to be distinguished from thyroid nodules, which may exhibit similar morphology [3, 9]. On functional imaging with 99mTc sestamibi scan, both thyroid nodules and PAs may be visualized and therefore, the presence of tracer accumulation is not always indicative of a PA. Cystic PAs however are further complicated by the lack of tracer accumulation as seen in our case and other reports [7, 10].

Table 1  Patient laboratory findings prior and after surgery

|                        | Preoperative | Postoperative | Normal range |
|------------------------|--------------|---------------|--------------|
| Calcium (mg/dL)        | 12.97        | 8.9           | 8.4–10.2     |
| Phosphorus (mg/dL)     | 2.08         | 4.6           | 2.7–4.5      |
| PTH (pg/mL)            | 457.2        | 19.61         | 15–65        |
| Alkaline Phosphatase (IU/L) | 116         | 90             | 33–122       |
| Albumin (g/dL)         | 4.5          | 4.3           | 3.5–5        |
| Urea (mg/dL)           | 23           | 33            | 10–50        |
| Creatinine (mg/dL)     | 0.88         | 0.49          | 0.7–1.1      |
| TSH (mIU/L)            | 2.41         | 0.316         | 0.3–4        |
| FT4 (ng/dL)            | 1.05         | 1.32          | 0.932–1.71   |
| Anti-thyroglobulin Antibodies (IU/mL) | 6.1    | —             | <50          |
| Anti-thyroid peroxidase Antibodies (IU/mL) | 8.8   | —             | <50          |
| 25-hydroxy-vitamin D (mg/dL) | 24.6 | 26             | >30          |

The bold represents abnormal values.

Fig. 3  The 99mTc sestamibi scan showed no tracer uptake in the delayed phases.
In respect to FNA cytology, parathyroid and thyroid aspirates are also difficult to be distinguished from each other, due to overlapping architectural features. Parathyroid cytology includes the presence of papillary fragments, microfollicles, naked nuclei and anisokaryosis, all of which may be indicative of neoplastic thyroid lesions. As a result, parathyroid lesions are commonly misdiagnosed as follicular neoplasms (Bethesda system category IV) [11, 12]. Smears from parathyroid lesions can also resemble thyroid papillary carcinoma especially when scattered naked nuclei and nuclei with stippled chromatin are present [13] which can be misinterpreted as a Bethesda category V lesion, as in our case.

Conclusion

Thyroid nodules are part of the everyday practice in endocrinology. The diagnostic steps include clinical examination, thyroid imaging, thyroid function tests and FNA when possible. Ultrasonography is almost universally recommended in thyroid disorders and FNA is a key component in the determination of the final therapeutic approach. However, the two most valuable diagnostic tools of everyday endocrine practice fall short when it comes to parathyroid pathology. In our case the 99mTc sestamibi scan did not assist in the diagnosis probably due to its cystic morphology. The 18F-fluorocholine PET/CT and the 11C-methionine PET/CT have shown excellent sensitivity for parathyroid lesions and could be of diagnostic assistance when available [14, 15].

In the case of our patient the cytological similarities between thyroid malignant cells and parathyroid cells, in combination with the negative sestamibi scan, resulted in a more invasive surgery than that a single parathyroid adenoma would require. In cases when primary hyperparathyroidism without localization is diagnosed in patients with thyroid nodules, measuring PTH in thyroid FNA aspirates is probably the most effective way to diagnose intrathyroidal parathyroid pathology.

Disclosure

The patient’s informed consent was obtained prior to submission.
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