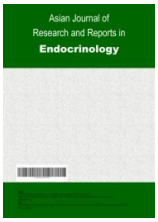

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A Case Report of Intrathyroid Parathyroid Adenoma

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FHK and MM designed the case. Authors HB and KB wrote the first draft of the manuscript. Authors FHK and MAM managed the analyses of the case. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Intrathyroid parathyroid adenoma as a cause of hypercalcemic crisis presents a diagnostic and therapeutic challenge, since it is uncommon and should be thoroughly differentiated from a thyroid nodule.

Herein, we report a case of a 71-year-old woman, with a history of nephrolithiasis, who presented with asthenia, vomiting and a right flank pain radiating to the right lower quadrant. Laboratory evaluation revealed severe hypercalcemia, hypophosphatemia and an elevated parathyroid hormone (PTH) level.

An ultrasonography of the neck did not detect any parathyroid adenoma, but revealed a hypoechoic nodule located within the left lobe of the thyroid. Although the intrathyroid location is difficult to appreciate,99m Technetium (Tc)-sestamibi scan revealed a partial radiotracer uptake located within the thyroid nodule.

Then,radiological features were consistent with an intrathyroid parathyroid adenoma. The patient's parathyroid crisis was managed by intravenous hydration, furosemide and biphosphonate treatment.

After improvement of calcium level, hemithyroidectomy was performed. Pathological analysis was consistent with the diagnosis of intrathyroid parathyroid adenoma. The patient was asymptomatic

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and serum calcium and PTH levels remained within normal limits.
Even rare, intrathyroid parathyroid adenomas should be suspected in patients with parathyroid crisis. Multidisplinary management is recommended for accurate diagnosis and appropriate treatment.

Keywords: Parathyroid crisis; primary hyperparathyroidism; ectopic; intrathyroid parathyroid adenoma; thyroid nodule.

1. INTRODUCTION

Parathyroid crisis, also known as parathyrotoxicosis or parathyroid storm, is an unusual and potentially life-threatening complication of PHPT. It can lead, if not diagnosed and treated early, to multiple organ dysfunction affecting mainly cardiovascular and neurological systems [1].

Hypercalcemic crisis requires immediate multidisciplinary management consisting of rapid medical therapy and definitive surgical treatment [2].

Ectopic parathyroid adenomas still pose specific diagnostic difficulties and present the most common cause of parathyroid surgical failure, leading to persistent and recurrent hyperparathyroidism.

Parathyroid crisis secondary to ectopic parathyroid adenoma is an infrequent clinical presentation whose diagnosis and management are challenging.

Herein, we report an uncommon case of hyperparathyroidism crisis due to an intrathyroid parathyroid adenoma, successfully managed in our department.

2. CASE PRESENTATION

A 71-year-old female was referred to the department of urology with asthenia, vomiting and a right flank pain radiating to the right lower quadrant. She was initially thought to have a renal colic.

She had a family history of diabetes, hypertension and breast cancer. There was no family history of multiple endocrine neoplasia syndromes or parathyroid disorders.

Her medical history included hypertension, type 2 diabetes with a 5-year history of recurrent kidney stones requiring surgery or lithotripsy.

On physical examination, she was tachycardic (125 bpm) and her blood pressure was of 154/85 mmHg. There was no palpable neck mass. Electrocardiogram demonstrated a shortened QT interval.

Laboratory investigations revealed that serum calcium level was significantly elevated of 3,6 mmol/l (normal range 2,2-2,6 mmol/l), hypophoshatemia of 0,73 mmol/l (normal range 0,81-1,62 mmol/l) and serum creatinine of 135µmol/l (normal range 45-105 µmol/l).

Serum parathyroid hormone (PTH) level was markedly increased to 392,5 pg/ml (normal range 15-65 pg/ml) with associated 25 (OH) vitamin D deficiency of 9,2 ng/ml (normal range 30-100 ng/ml). Her thyroid function test was within normal ranges.

The diagnosis of hypercalcemic crisis resulting from PHPT was retained and intravenous hydration was initiated with furosemide and biphosphonate therapy.

Computed tomography (CT) urogram showed two lower pole caliceal stones measuring 1 cm each, located in the right kidney. The left kidney was the site of two lower pole calcifications of 6 and 7 mm, respectively (Fig. 1).

She was then referred to the endocrinology department for PHPT.

Ultrasound of the neck revealed a hypoechoic nodule measuring 34*13 mm located within the left lobe of the thyroid. No parathyroid lesion was detected.

99m Technetium (Tc) -sestamibi scan demonstrated a well defined cold area that is located in the left thyroid lobe and co-localizing with the ultrasonography nodule. This thyroid lesion showed abnormal partial enhanced activity retention. No radiotracer uptake was seen in parathyroid glands (Fig. 2 and 3).

Cervical CT scan detected a 1,5 * 1,2 * 0,9 cm rounded low density mass within the thyroid nodule of 3.3 * 2.2 * 3 cm.

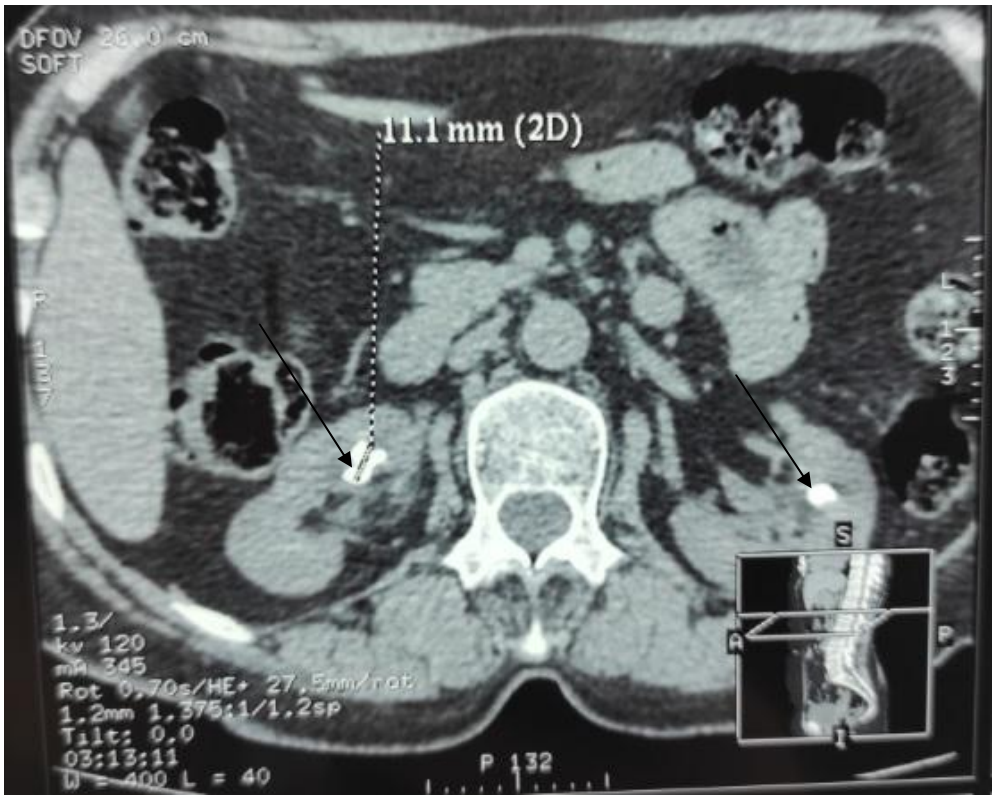

Fig. 1. Axial CT scans showing bilateral renal lithiasis

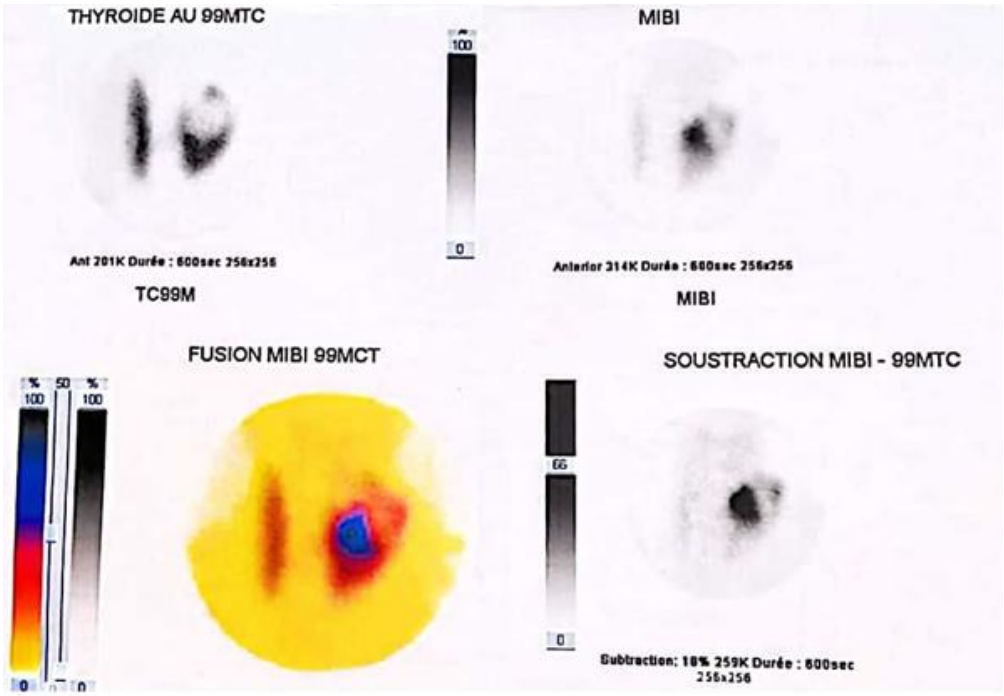

Fig. 2. Parathyroid subtraction 99m Tc-sestamibi scintigraphy revealing an increased radiotracer uptake in the the left thyroid nodule

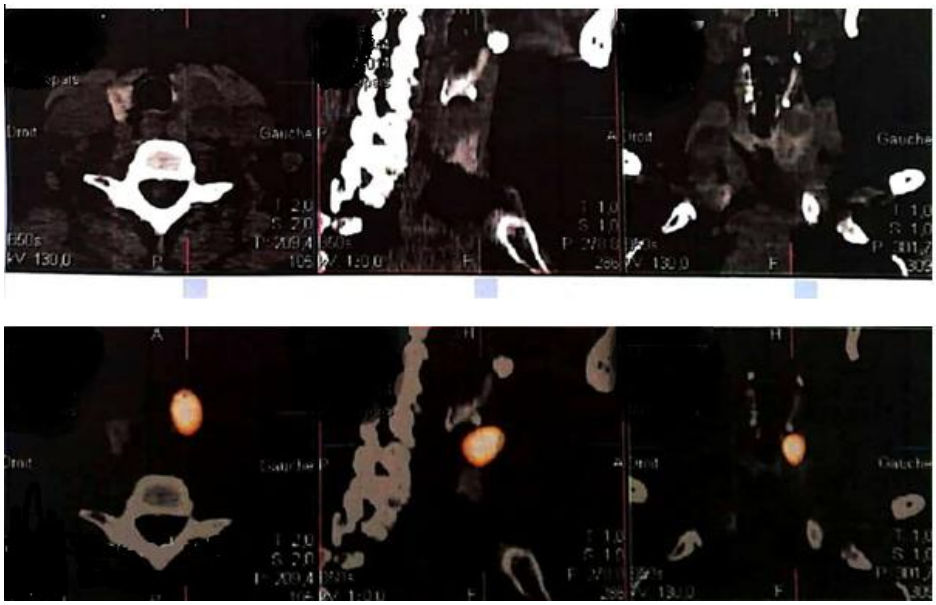

Fig. 3.The accurate localization of intrathyroid parathyroid adenoma with SPECT/CT

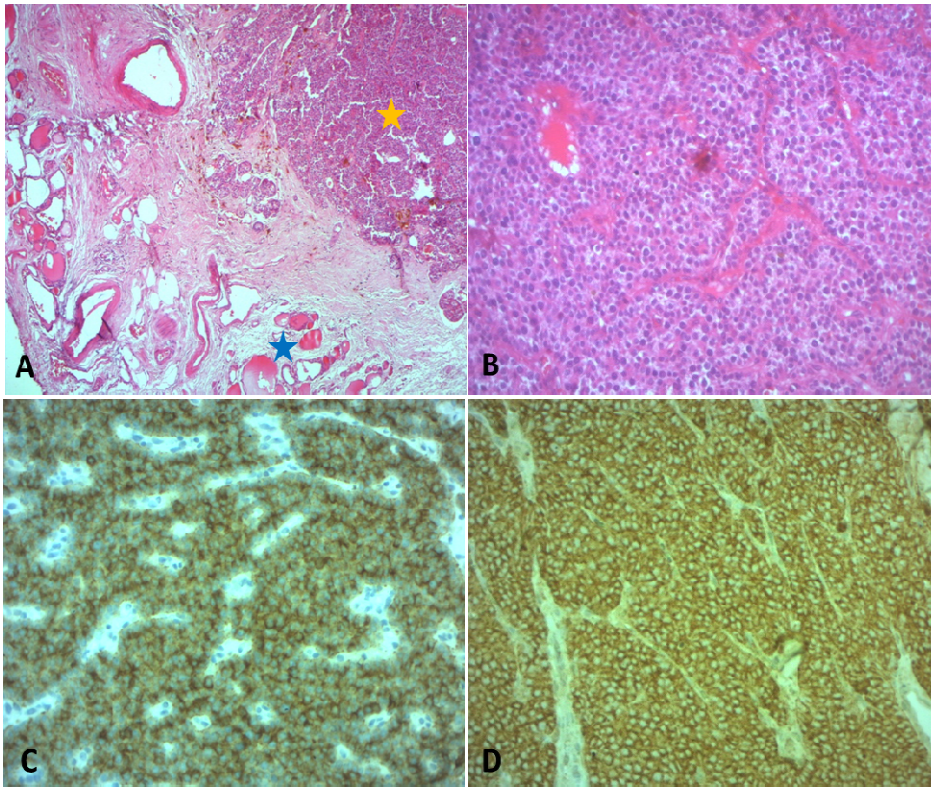

Fig. 4. Intrathyroid parathyroid adenoma: *(A)* Histological section demonstrates a thin fibrous capsule separates the adenoma (Yellow asterisk) from the surrounding normal thyroid tissue (blue asterisk) (HEX 50). *B:* The adenoma is composed of a proliferation of chief cells arranged in a solid and acinarglandular distribution (HEX 50). The tumor cells showed diffuse strong positivity for parathyroid hormone *(C)* (X100) and chromogranin (D)(X100).

Subsequently, radiological features were consistent with an ectopic parathyroid adenoma located in a thyroid nodule.

After normalization of her calcium level, the patient underwent a left thyroid lobectomy. Pathological examination of the removed thyroid lobe confirmed the diagnosis of an intrathyoid parathyroid adenoma (Fig. 4).

Post operative period was marked by hypocalcemia and hungry bone syndrome occurring two days after surgery. The patient was prescribed calcium gluconate administered intravenously. On postoperative day 5, Hungry bone syndrome's symptoms had totally improved. Calcium level recovered to normal ranges and the patient was discharged.

During the 4-year follow-up, PTH and serum calcium level remained normal.

3. DISCUSSION

PHPT is an endocrine disorder affecting approximately 0,1 to 0,3% of the population , being caused in 85% of cases by a benign and single parathyroid adenoma [3].

Most of patients suffering from PHPT present with a moderate increase in serum calcium and PTH level, expressing mild signs or even being asymptomatic [4].

However, parathyroid crisis, also known as parathyroid storm, is an unusual presentation of PHPT occurring in less than 7% of cases [1].

Currently, there is no consensus on the definition of hyperparathyroid crisis. But, the diagnostic criteria typically include a markedly increased serum calcium level of >3,5 mmol/l, associated with clinical manifestations of hypercalcemia leading, if is not diagnosed and managed swiftly, to dramatic consequences and multiorgan dysfunction.

Initial management of parathyroid crisis consists of aggressive intravenous hydration with furosemide-induced dieresis, administered with 3-4 l/day of isotonic saline solution depending on calcium level and patient's renal and cardiac function [5]. Indeed, biphosphonate therapy and calcitonin may be prescribed to treat hypercalcemic crisis, to further reduce calcium bone resorption [6].

Surgical treatment, consisting of the removal of the hyperfunctioning parathyroid gland, remains the definitive treatment of parathyroid crisis [7]. Hypercalcemic crisis is most often due to parathyroid carcinoma [1]. By contrast, parathyroid crisis resulting from an ectopic parathyroid adenoma is unusual.

An intrathyroid parathyroid adenoma is a rare ectopic location, representing 1% to 3,4% of all cases of PHPT [8,9] and 2,2 to 4 % of all intrathyroid adenomas [10].

Ectopic intrathyroid parathyroid adenoma, as seen in our patient, is infrequent and preoperative localization is still the main target of research into this rare disease.

Parathyroid glands are endodermal in origin and arise from the third and fourth pharyngeal pouches [11]. Furthermore, parathyroid glands are encapsulated within the thyroid gland during embryogenesis, which can lead to intrathyroid parathyroid glands [12].

Most of intrathyroid parathyroid lesions are located in the right lobe [13] and are classified into complete and partial lesions according to their location in relation to the thyroid parenchyma [9,13].

Successful management of ectopic parathyroid adenoma requires an accurate preoperative localization to reach the appropriate surgical area.

Neck ultrasound can be performed as a first-line imaging modality since it is affordable, economical and noninvasive. Nevertheless, intrathyroid parathyroid adenomas are difficult to be differentiated from common thyroid nodules [14]. According to the applied ultrasonography criteria, intrathyroid parathyroid adenoma appears as a solid mass, profoundly hypoechoic, and commonly involves a polar feeding vessel [15].

In Heller's series of 53 patients with intrathyroid parathyroid adenoma, an ultrasound diagnosis was made in 75% of cases [16].

Tc-99m sestamibi-scintigraphy with single photon emission CT (Sestamibi SPECT/CT) has a high diagnostic sensitivity ranging from 78% to 97% and allows for a better understanding of the localization of hyperfonctioning parathyroid lesions [17]. However, it does not have sufficient specificity and its efficiency in identifying anatomical structures is not excellent.

Combination of ultrasound and sestamibi-SPECT/CT findings provides an accurate location of intrathyroid parathyroid adenomas, as demonstrated in our case.

In a meta-analysis reported by Roy et al, the diagnostic accuracy of ultrasound compared to sestamibi-scan was 53% versus 76% for ectopic parathyroid adenomas, and the correlation between the 2 methods furnishes a better accuracy (92,3%) [18].

Indeed, the 18F-Fluorocholoine PET/CT has shown excellent sensitivity for parathyroid lesions and could be helpful in the preoperative diagnostic assistance when available [19].

Definitive treatment of intrathyroid parathyroid adenomas remains as surgical excision of the abnormal gland. There is no evident procedure or surgical approach for patients with intrathyroid parathyroid adenomas, as long as preoperative localization investigations do not usually reliably determine the intrathyroid situations of these adenomas.

According to the literature, when meticulous bilateral cervical examination fails to target the hyperfonctioning gland, an hemithyroidectomy, based on preoperative radiological findings, should be considered [10]. In our case, an ipsilateral lobectomy was performed.

Moreover, recent studies have described radioguided enucleation as a potential advantage in avoiding thyroid lobectomy and preserving normal thyroid parenchyma [20].

In the cytological study, intrathyroid parathyroid adenomas are similar to those eutopic.

The component cells may be organized in cords, nests and follicles.

The nuclei are commonly larger than adjacent normal parenchyma cells and are typically rounded with a regular nuclear membrane [21].

The pathological differential diagnosis of intrathyroid parathyroid adenoma is thyroid carcinoma, due to its papillary or pseudopapillary features.

As for immunohistochemical markers, parathyroid adenomas express parathormone and chromogranin A [22].

4. CONCLUSION

Any parathyroid crisis without parathyroid adenoma in the neck should alert clinicians to search for ectopic sites. Although they are a rare entity, intrathyroid parathyroid adenomas should be considered and may lead to failed parathyroid surgery if they are not recognized in the preoperative period.

Their preoperative identification needs high clinical suspicion and an accurate localization through combination of imaging techniques.

Since hypercalcemic crisis is a potential endocrine emergency, it requires early medical treatment and surgical removal of the hyperfunctioning gland.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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