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Case report

Supernumerary ectopic parathyroid adenoma in the aortopulmonary window: Navigating diagnostic and surgical challenges

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ABSTRACT

Introduction: Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia and has shifted from a rare condition to a common endocrine disorder. Advances in diagnostic methods have led to more incidental diagnoses, particularly in asymptomatic patients. Ectopic parathyroid adenomas are a rare cause of PHPT, with the vast majority of cases involving parathyroid glands in typical anatomical locations. However, the occurrence of a fifth parathyroid adenoma is exceptionally uncommon, especially when located in an ectopic position.

Case presentation: We report an uncommon case of primary hyperparathyroidism in a 60-year-old male with longstanding hypercalcemia attributed to a fifth ectopic parathyroid adenoma localized in the aortopulmonary window. Initial imaging modalities failed to localize the adenoma, which was detected by 4D-CT but not on SPECT/CT, and remission was achieved through surgical resection, with intraoperative PTH monitoring confirming total resection.

Discussion: Delayed diagnosis of ectopic parathyroid adenomas can lead to complications, as in our patient with nephrolithiasis and hypercalcemia. Advanced imaging techniques like 4D-CT are crucial when conventional methods fail. Embryological anomalies can result in ectopic or supernumerary parathyroid glands, complicating localization. Intraoperative PTH monitoring ensures complete resection and lowers reoperation rates.

Conclusion: This case highlights the challenges of diagnosing ectopic parathyroid adenomas and the importance of considering rare ectopic adenomas in patients with PHPT, particularly when standard imaging doesn't yield conclusive results. We also discuss the role of advanced imaging modalities and intraoperative PTH monitoring in guiding surgical decisions and determining the appropriate point to conclude the procedure, ensuring successful outcomes.

1. Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia, and has evolved from being a rare condition to a common endocrine disorder. The estimated incidence of PHPT is about 1 % in the general population, with a female-to-male ratio of 3:1 [1]. A study conducted in Denmark reported a steady increase in the incidence of PHPT from 1997 to 2010, reaching an annual rate of 16 cases per 100,000 individuals in 2010, with a higher incidence among women [2]. Similarly, a study from Spain found that women accounted for 90 % of all hospital admissions for PHPT with a consistent rise in the incidence of hyperparathyroidism reaching 40.3 per 100,000 woman-years and 13.7 per 100,000 man-years [3]. Advances in diagnostic approaches and imaging modalities with improved sensitivity and specificity has shifted the clinical presentation of PHPT. Many cases are being diagnosed incidentally during routine blood test, with the majority of patients being asymptomatic at presentation rather than with complications [4]. Single parathyroid adenomas account for roughly 85 % of cases, whereas multiple adenomas or hyperplasia occur in about 15 %. Parathyroid carcinoma is rare, representing <1 % of cases. PTHP due to ectopic parathyroid adenoma is reported in an estimated 2 % of patients [5], which poses a significant challenge in the preoperative localization of the adenoma. We herein, describe a case of PHPT in a patient with a longstanding complication of hypercalcemia caused by a fifth ectopic

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parathyroid adenoma located in the aortopulmonary window. Initial imaging modalities failed to identify the adenoma's location and remission was achieved following surgical resection with intra-operative parathyroid hormone monitoring confirming the adequacy of the resection.

2. Case presentation

A 60-year-old male patient presented to our institution for a four-day history of dysuria, frequency, and fever. Vital signs at the presentation were normal. His urinalysis was positive for white blood cells and nitrite, and C-reactive protein was elevated at 67 mg/dl (Reference rang <5 mg/L) with a negative costovertebral angle tenderness. The patient was diagnosed with prostatitis and was started on ceftriaxone. Blood chemistry revealed an elevated serum calcium level at 12.8 mg/dl and further evaluation for his hypercalcemia revealed an elevated parathyroid hormone (PTH) level at 240 pg/ml (reference range 15–65 pg/ml). The patient has no family history of primary hyperparathyroidism and/or multiple endocrine neoplasia. Further inquiry from the patient showed a history of urolithiasis five years ago that required double J insertion and lithotripsy, two episodes of pancreatitis attributed to his alcohol consumption, and a new onset of abdominal pain and constipation three years ago for which investigation revealed a serum calcium level of 15.4 mg/dl and PTH level at 265 pg/ml. Ultrasonography of the neck back then revealed that the appearance of the four parathyroid glands was normal. A ^{99m}Tc-sestamibi scintigraphy did not reveal any abnormality. The patient was lost to follow-up and presented one year later for his second episode of urolithiasis. A ^{99m}Tc-sestamibi scintigraphy with single-photon emission computerized tomography (SPECT) of the neck and chest failed to identify any ectopic thoracic adenoma and the decision was made to proceed with a neck exploration at another institution that revealed four eutopic glands that failed to identify any abnormal or ectopic parathyroid gland. The patient was admitted a few months later for a new episode of pancreatitis and a thoracic CT scan revealed a 1.3 cm lesion in the aortopulmonary window showing enhancement in the arterial phase and a washout in the portal phase that was highly suspicious of a parathyroid adenoma. The patient underwent a thoracoscopy for excision of the fifth nodule however, the pathology result yielded a negative result for a parathyroid adenoma. During this admission, the patient underwent a 4D-CT (Fig. 1) that revealed the same lesion in the location described two years ago. The decision was made this time to proceed again with a thoracotomy to allow for a more extensive surgical approach, with serial measurement of intraoperative PTH levels. Ten minutes after the excision of the suspected nodule, PTH dropped to 17 pg/ml and pathology confirmed the presence of a parathyroid adenoma (Fig. 2). The serum calcium level returned to normal after the operation and remained so over the subsequent days. The patient remained normocalcemic during a six-month follow-up.

3. Discussion

Delayed diagnosis and localization of an ectopic parathyroid adenoma can result in increased complications. Our patient presented with long-standing severe hypercalcemia. Over the five years preceding his presentation, he developed two episodes of nephrolithiasis. Although the exact composition of the stone (calcium phosphate or calcium oxalate) was not investigated, hypercalciuria remains the major risk factor for kidney stones in patients with hyperparathyroidism. Furthermore, the initial diagnostic workup may have been delayed as serum calcium levels could have been within the normal range following the patient's episodes of pancreatitis which were attributed to alcohol consumption. While PHPT is reported in <1 % of patients presenting with acute pancreatitis [6], a review of large cohorts, suggests that patients with PHPT have a higher rate of pancreatitis compared to those without PHPT [7]. A notable feature in our patient's case was the failure of

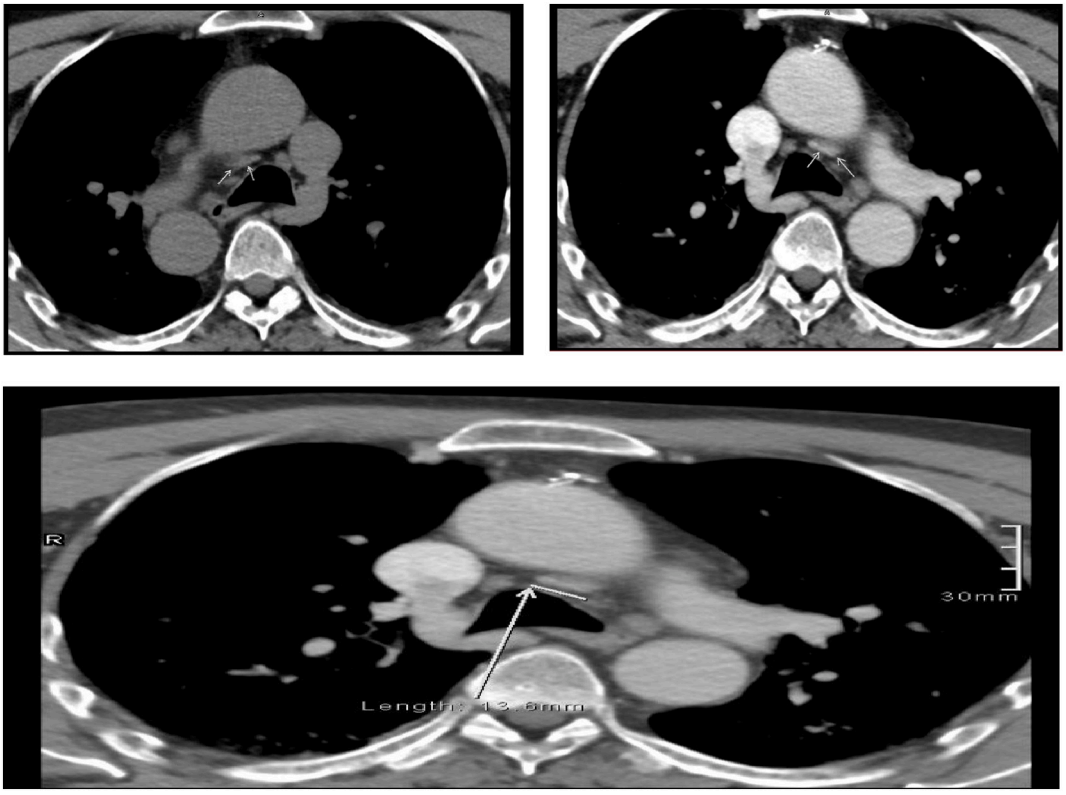

Fig. 1. 13 × 7 × 7 mm nodule in the aortopulmonary window, showing enhancement in the arterial phase and a washout in the portal phase. This nodule shows a different pattern of enhancement than the surrounding lymph nodes. Findings suggestive of a parathyroid adenoma.

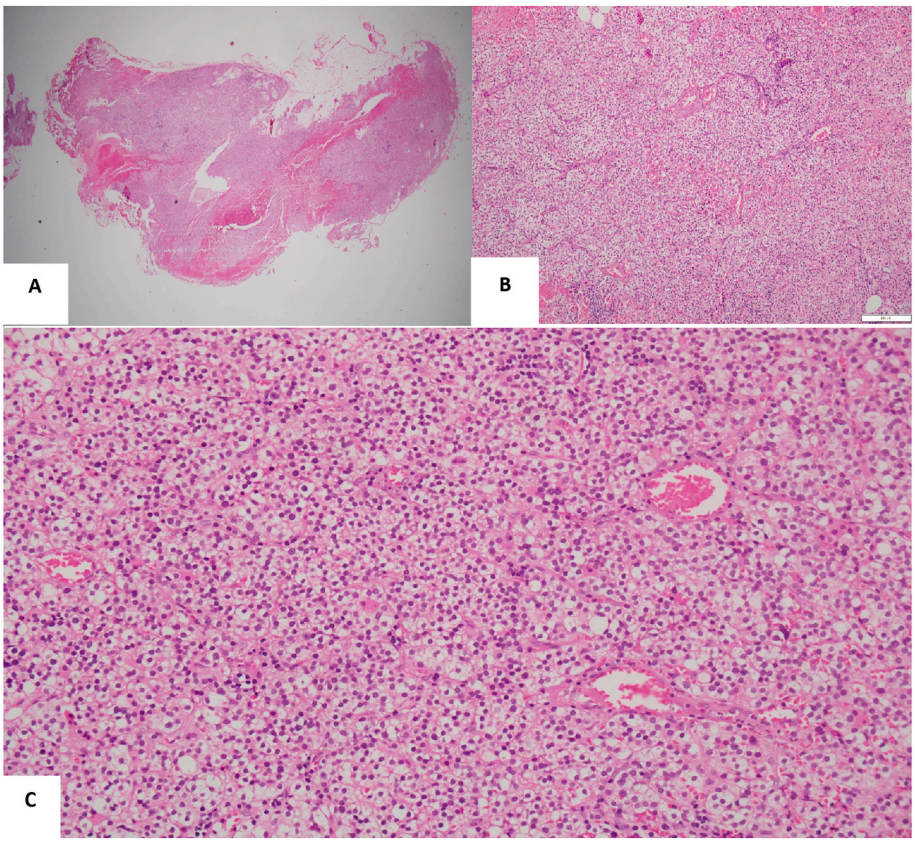

Fig. 2. Microscopic features showing glandular elements intermixed with adipose tissue (A), small round chief cells with central nuclei and clear cytoplasm (B, C).

scintigraphy and SPECT/CT to localize the lesion, which was eventually detected using 4D-CT. Multiple imaging modalities are available for the diagnosis of parathyroid gland abnormalities. While ultrasound (US) is cost-effective and doesn't involve ionizing radiation, it has a limited role in identifying mediastinal parathyroid adenomas. In a retrospective study by Zerizer et al. [8], among 656 patients with primary hyperparathyroidism (PHPT), 11 were suspected of having ectopic parathyroid adenoma. US failed to identify the location of the parathyroid adenoma in all but one patient yielding a sensitivity of 11 %. In addition, the sensitivity is further reduced in the presence of concomitant thyroid pathology [9]. Combining the anatomical and functional data, single-photon emission computed tomography combined with computed tomography (SPECT/CT) has emerged as an essential tool in accurately diagnosing and managing patients with hyperparathyroidism. A meta-analysis by Wong et al. [10], including 1276 patients across 24 studies, concluded that SPECT/CT is more sensitive than planar imaging, with a pooled sensitivity of 86 %. SPECT/CT has been of major benefit in patients with concurrent multinodular thyroid, distinguishing false positive uptake and late retention of Sestamibi in thyroid nodules from true eutopic adenomas. Furthermore, in the context of minimally invasive surgeries, accurate localization of the parathyroid adenoma has reduced the extent and duration of the surgical exploration. SPECT/CT changed the surgical approach in 42 % of patients with ectopic parathyroid adenoma, avoiding sternotomy in cases where adenomas were localized to the superior mediastinum [8]. Additionally, integrating a late contrast washout phase into traditional CT has resulted in a 4D-CT which has yielded better results in clinical discordance or failed detection with SPECT/CT [11].

A retrospective study investigating factors leading to missed lesions in scintigraphy and 4D-CT [12], concluded that the mean weight of the lesion detected and missed in scintigraphy was 0.8 g and 0.4 g, respectively. This might explain why the 0.37 g lesion was not detected by scintigraphy. However, the smallest lesions correctly identified by scintigraphy in this study were 10 mm in diameter. Furthermore, the content of the oxyphilic cells, which consist of numerous mitochondria, could have impacted the Sestamibi uptake in the parathyroid adenoma resulting in the false negative findings in our patient.

The superior parathyroid glands originate from the fourth pharyngeal pouch, while the inferior parathyroid glands develop from the third pouch, along with the thymus. Ectopic parathyroid glands arise from the aberrant migration during embryogenesis. However, ectopia can also occur when a eutopic gland enlarges during development and becomes displaced to an ectopic location, as the parathyroid glands lack capsular fixation. Due to the more extensive migration of the inferior parathyroid glands, they are more commonly found in ectopic locations. Superior glands are most commonly located in the tracheoesophageal groove, retroesophageal, or posterosuperior mediastinum. In contrast, inferior glands are often found in the thymus, anterosuperior mediastinum, or intrathyroidal. Other uncommon ectopic sites reported in the literature include the aortopulmonary window, similar to our patient's case, the pleura, the lungs [13].

The occurrence of supernumerary parathyroid glands is similarly rare, with a reported prevalence of 2.5 % to 13 % in the general population [14]. A study by Chiu et al. [15], involving 160 dissected cadavers, identified an incidence of 1.8 % for individuals with five glands and 0.6 % for those with up to six glands. In the context of PHPT, supernumerary parathyroid adenomas are even rarer, with an incidence of approximately 0.7 %. About 60 % of these adenomas are located in the mediastinum, most commonly within the thymus. While most of these adenomas can be excised through a cervical incision, around 18 % necessitate a mediastinal surgical approach [16].

Parathyroid hormone (PTH) is an 84-amino-acid peptide hormone with a half-life of less than five minutes, with most of its metabolism occurring in the liver and the remainder in the kidneys. Intraoperative PTH (ioPTH) monitoring is a technique used to assess the adequacy of parathyroid tissue resection; a critically important resource in patients

suspected of having multiple gland disease. A reduction in pre-excision PTH levels by 50 % from the baseline—or the higher value between baseline and pre-excision levels—within 5 to 10 min after removing the pathological parathyroid gland reliably predicts the cure of PHPT. This criterion provides a critical guide for surgeons during parathyroidectomy, even if PTH levels do not fully normalize [17]. Furthermore, another study emphasized the importance of measuring PTH levels 20 min post-excision when values don't significantly drop 10 min after resection. This additional step can confirm adequate resection and help avoid unnecessary bilateral neck exploration [18]. A 2021 systematic review and meta-analysis demonstrated that the use of ioPTH monitoring is associated with higher cure rates for patients with PHPT undergoing minimally invasive parathyroidectomy (MIP). However, the review also highlighted that while performing MIP without ioPTH monitoring results in fewer conversions to bilateral neck exploration during the initial surgery, it is associated with lower cure rates and a higher risk of reoperation [19]. If serial intraoperative PTH level measurements had been performed to our patient during the initial surgery, further exploration and dissection could have enabled a successful identification of the parathyroid adenoma. This approach could have spared the patient the need for the subsequent surgery to resect the ectopic parathyroid adenoma identified on the 4D-CT scan, which had been described two years earlier. Moreover, it could have reduced the burden of the patient's longstanding hypercalcemia. A case series highlighted that accurately identifying the location of ectopic parathyroid adenomas preoperatively remains a significant challenge, despite advances in imaging techniques. In such cases, the intraoperative parathyroid hormone assay serves as a critical tool for ensuring effective surgical management [20].

4. Conclusion

This case adds to the growing body of literature documenting supernumerary ectopic parathyroid adenoma in unconventional locations. We report a case of PHPT caused by an ectopic parathyroid adenoma in the aortopulmonary window, emphasizing the importance of accurate preoperative localization. The combination of imaging modalities has incremental value in localizing ectopic parathyroid adenoma compared to individual techniques. In fact, the lesion in our patient was accurately described on 4D-CT scan but not detected on SPECT/CT. This case highlights the critical role of intraoperative PTH level measurement in guiding surgical decisions and determining when to conclude the procedure.

Author contribution

Nicolas Sandakly: Conceptualization, Methodology, Software **Nicolas Sandakly, Bachir Zreika**: Data curation, Writing - Original draft preparation. **Fadi Haddad, Claude Ghorra**: Visualization, Investigation. ***Bassam Abboud***: Supervision. **Claude Ghorra**: Software, Validation. **Fadi Haddad, Bassam Abboud**: Writing- Reviewing and Editing.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

Ethical approval for this study (Ethical Committee NO 103/2025) was provided by the Ethical Committee of Lebanese Hospital Geitaoui-University Medical Center, Achrafieh Lebanon on 6 January 2025.

Guarantor

Bassam Abboud

Research registration number

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Method

The work has been reported in line with the SCARE criteria [21].

Conflict of interest statement

Authors declare no conflict of interest.

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