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Case Report

Navigating diagnostic dilemmas: Localizing parathyroid adenoma in the presence of MIBI-avid thyroid nodules: A case report and literature review ☆,☆☆

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ABSTRACT

Surgery is the preferred treatment for primary hyperparathyroidism (PHPT), but the presence of MIBI-avid thyroid nodules can complicate the localization of parathyroid adenoma (PA). In this case report, we discuss the role of imaging in localizing PA in a patient with concurrent thyroid nodules. A 49-year-old female presented with hypercalcemia and elevated parathyroid hormone levels. Technetium-99m-sestamibi single-photon emission computed tomography/computed tomography (SPECT/CT) showed MIBI-avid enhancement in the left thyroid lobe. Neck ultrasonography revealed 3 thyroid nodules in the left lobe, categorized as Thyroid Imaging Reporting and Data System (TI-RADS) 4. Fine-needle aspiration cytology yielded indeterminate results, and iPTH washout concentration was not elevated. Parathyroid 4-dimensional computed tomography (4D CT) was performed, which revealed an extra thyroid lesion on the left side, favoring PA. Left thyroid lobectomy and parathyroidectomy were performed, and the pathology report confirmed PA and follicular thyroid carcinoma. In cases where MIBI-avid thyroid nodules mimic PA, a combination of imaging modalities including technetium-99m-sestamibi SPECT/CT, neck ultrasonography, and parathyroid 4D

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CT can aid in differentiating between intrathyroid PA and extrathyroidal locations. Accurate preoperative localization is crucial for successful surgical management of PHPT. These imaging techniques play a pivotal role in guiding surgical decisions and ensuring optimal patient outcomes.

Introduction

Primary hyperparathyroidism (PHPT) is characterized by elevated or inappropriately normal levels of parathyroid hormone (PTH) in the presence of hypercalcemia. It is a relatively common endocrine disorder, with an age-adjusted estimated prevalence of 233 and 85 per 100,000 women and men, respectively [1]. Since Parathyroidectomy (PTX) is the main curative treatment in patients with symptomatic PHPT, preoperative localization allows the removal of the aberrant gland [2,3].

PHPT usually originates from a single parathyroid adenoma (PA) (85%-90%) [4]. Moreover, the incidence of ectopic adenomas varies from 6% to 16% [5,6]. Intrathyroidal parathyroid adenoma (IPA) is a rare ectopic location for parathyroid adenoma. It occurs between 0.7% and 6% [7]. On the other hand, the presence of concurrent thyroid nodules is reported in 20 to 60 percent of the patients with PHPT. Therefore, an in-time workup prevents presumable reoperation [8].

Considering the variety of well-known modalities to localize PA, it is essential to consider the strengths and limitations of different methods in the presence of thyroid nodules. One challenging issue is the differentiation between IPA and thyroid nodule-mimicking IPA during the primary investigation. This case presentation demonstrates how the current localization approach can help appropriately identify the PA location when the initial investigation suggests the presence of thyroid nodules. Interestingly, these modalities ultimately revealed follicular thyroid cancer (FTC) with concomitant extra thyroid PA.

Case presentation

A 49-year-old female was referred to the endocrinology service for evaluation of hypercalcemia with high serum PTH level. She suffered from fatigue and generalized bone pain for the past 2 years.

Blood tests revealed the followings: albumin-corrected calcium = 11.6 mg/dL, Phosphor = 1.6 mg/dL, PTH = 306 pg/mL, 25-hydroxyvitamin D = 43 ng/mL, and 24-hour urine Calcium/creatinine ratio = 3%. The estimated glomerular filtration rate was 86.57 mL/min/1.73. A dual-energy X-ray absorptiometry (DXA) scan revealed bone mineral density (BMD) below the expected age range.

A preoperative localization survey was done. Technetium-sestamibi (^{99m}Tc-MIBI) parathyroid planar scan suggested IPA in the left thyroid lobe (Figs. 1A and B). A Parathyroid ^{99m}Tc-MIBI single-photon emission computed tomography/computed tomography (SPECT/CT) revealed a MIBI-avid lesion in the mid-pole of the left thyroid lobe, suggesting a thyroid MIBI-Avid nodule or functioning IPA (Fig. 1C).

Neck ultrasound (US) showed three thyroid nodules measuring about 16 × 12 mm, 13 × 14 mm, and 8 × 8 mm, with ultrasound features suspicious of malignancy (Fig. 2) and with no evidence of extrathyroidal parathyroid adenoma on the left-hand side.

Due to the rarity of IPA and the highly suspicious malignancy, Fine-needle aspiration (FNA) of the nodules was performed, and a PTH washout assay was requested. The cytology report indicated Hurthle cell neoplasm in one of the nodules and atypia of undetermined significance (AUS) in the remaining nodules. PTH washout assay revealed PTH level of 10 pg/mL, not indicative of IPA.

Finally, parathyroid 4-dimensional computed tomography (4DCT) was done to localize the PA There was an 8 × 6 × 12 mm avid enhancing mass lesion located in the posterior lower pole of the left thyroid lobe, posterolateral to the esophagus, suggesting PA (Fig. 2).

Left thyroid lobectomy and removal of the lesion detected by 4DCT scan were performed. Histopathological results confirmed the coexistence of PA and minimally invasive FTC (18 mm) (Fig. 3). Twenty-four hours after surgery, serum iPTH and calcium levels were 17.2 pg/mL and 8.7 mg/dL, respectively. One month after surgery, serum iPTH and calcium were reported within the normal ranges: 23 pg/dL and 9.1 mg/dL, respectively. Serum calcium level remained within the normal range after that, and there was no evidence of FTC recurrence.

After 1 year, the neck sonographic follow-up revealed a well-defined isoechoic nodule without calcification, measuring 12 × 9 × 6 mm. The cytology result of the thyroid nodule aspiration was AUS. Regarding the history of FTC, the right thyroid lobectomy was performed. Finally, micropapillary thyroid carcinoma (9mm) was reported by the pathologist (Fig. 4). She received a Radioactive iodine dose of 30 mci for remnant ablation after surgery.

Discussion

Considering the rarity of IPA, several diagnostic modalities are needed preoperatively for patients with clinical PHPT in the presence of a MIBI-avid thyroid lesion.

IPA is a rare presentation of PHPT located in the lower lateral part of the thyroid gland; it is also considered 1 reason for PA surgery failure and persistent hyperparathyroidism [9]. The most common imaging modalities that could lead to the IPA diagnosis are the combination of US and ^{99m}Tc-sestamibi parathyroid scan [9,10]. The sensitivity and specificity of the ultrasound and ^{99m}Tc-sestamibi parathyroid scans highly depend on the operator's expertise [11].

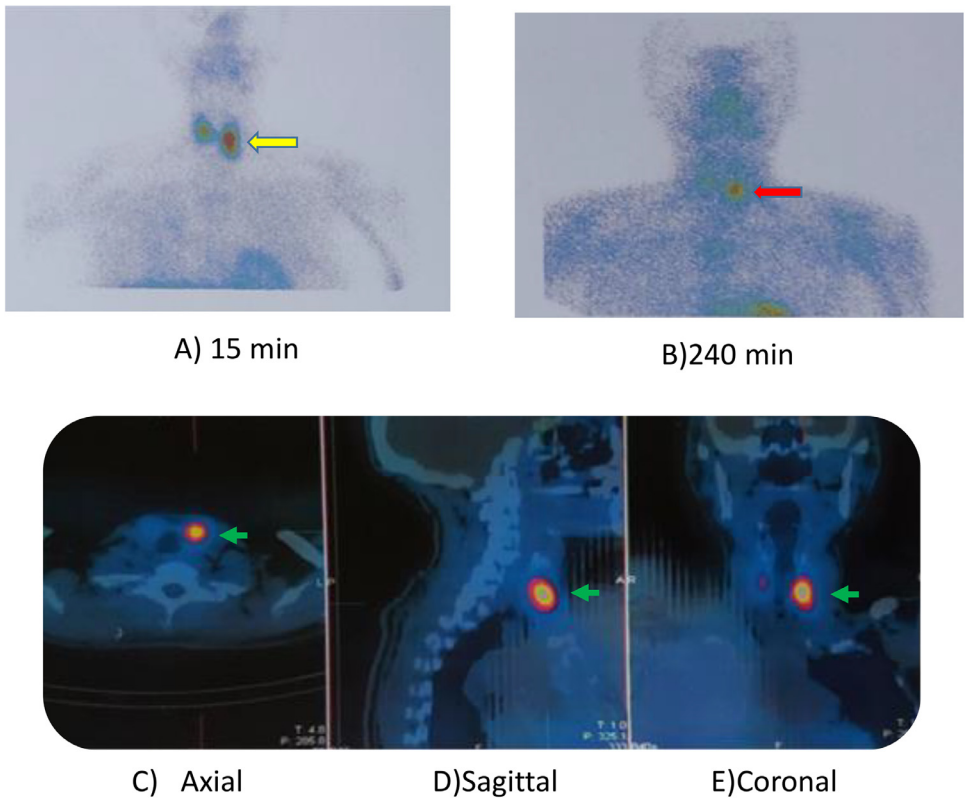

Fig. 1 – ^{99m}Tc-sestamibi parathyroid imaging. Anteroposterior images were obtained 15, 120, and 240 minutes after ^{99m}Tc-sestamibi for localizing parathyroid adenoma. (A) Early images of the PTH scan show homogeneous uptake in a normal-appearing thyroid gland (yellow arrow). (B) Late images of the PTH scan show persistent focal area of increased activity in the mid-left thyroid lobe area (red arrow). No other abnormal retention of TC-MIBI is seen from the mandible to the base of the heart until 4 hours after injection. (C) ^{99m}Tc-sestamibi SPECT/CT imaging can aid in anatomical localization. Intrathyroidal MIBI-Avid uptake lesion has been shown in axial sagittal and coronal views (green arrow).

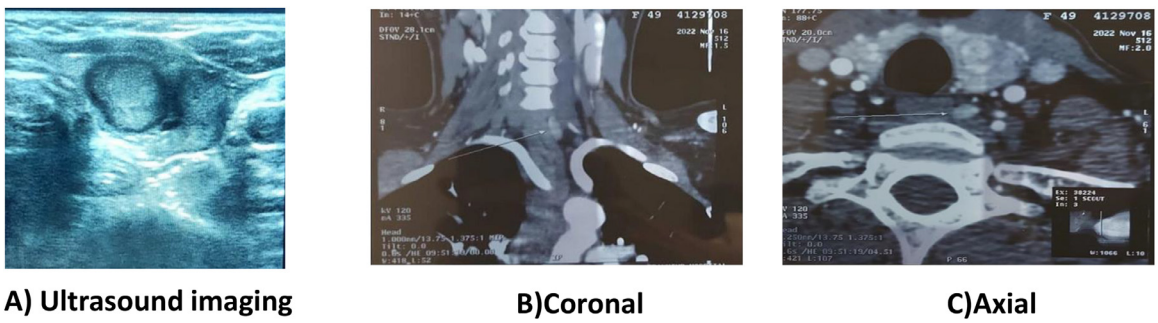

Fig. 2. – (A) Ultrasound imaging of the largest thyroid nodule presented as isoecho nodule, with an irregular border, thin hypoechoic hallo, and fine microcalcification without extra thyroid extension. Color Doppler's image demonstrates a slightly hypervascular and disorganized vascular appearance (not shown). (B-D) 4DCT imaging of Left parathyroid adenomas [white arrows] are visualized as arterially enhancing soft tissue structures (size: 8 x 6 x 12 mm).

After PAs are localized, minimally invasive parathyroidectomy (MIP) is preferred over bilateral neck exploration [12]. As the incidence rate of nonmedullary thyroid cancer (NMTC) among patients with PHPT undergoing PTX is about 3.5% [13] to 8.2% [14], concomitant thyroid cancer could be missed. Hence, further preoperative diagnostic modalities may be needed to localize PHP. Current guidelines provide no clear recommendation regarding the management of patients with PA in the presence of concurrent thyroid nodules [13,15]. In most centers, combining Neck US and emission CT is the preferred approach to localize PA [16]. On the other hand, thyroid nodules could lead to false positive results [17]. Thus,

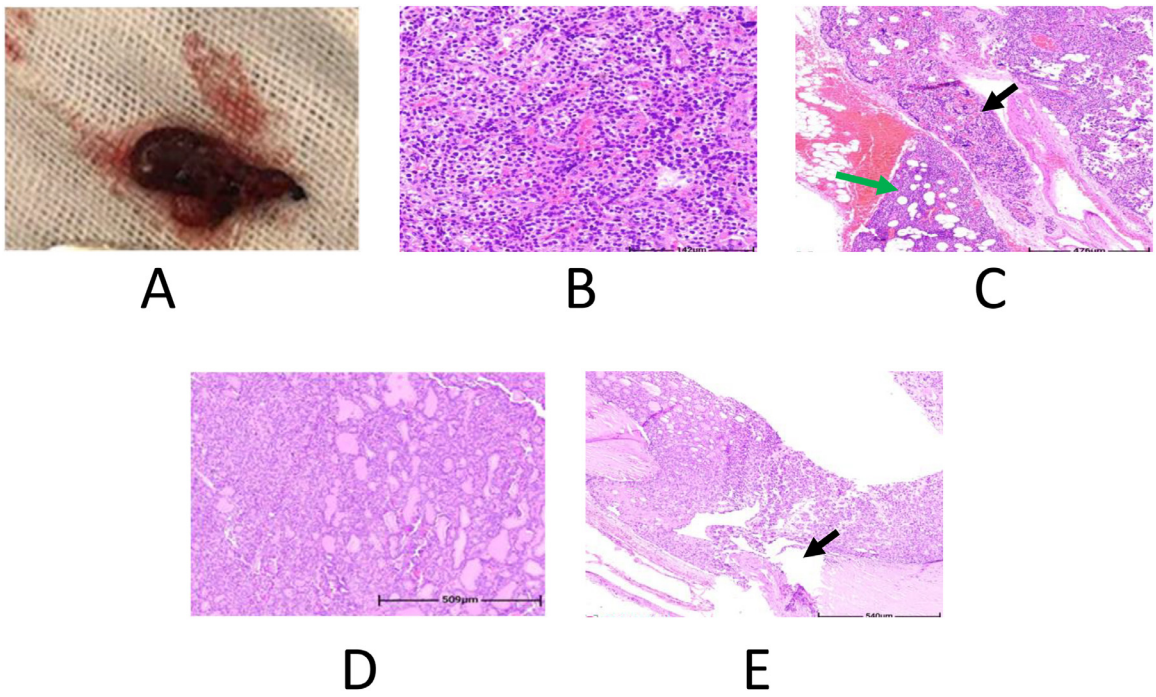

Fig. 3 – Gross and histopathological sections of parathyroid adenoma and follicular thyroid carcinoma (A) Gross image of parathyroid adenoma. (B, C) H&E staining of parathyroid adenoma (B). Well-circumscribed parathyroid tissue is mostly composed of oxyphilic cells (black arrow) surrounded by the rim of normal parathyroid tissue (green arrow) (D, E). H&E staining of follicular thyroid carcinoma: (D). A solid and trabecular pattern of follicles without nuclear features of papillary thyroid carcinoma, (C). The black arrow indicates the full-thickness capsular invasion of follicular thyroid carcinoma.

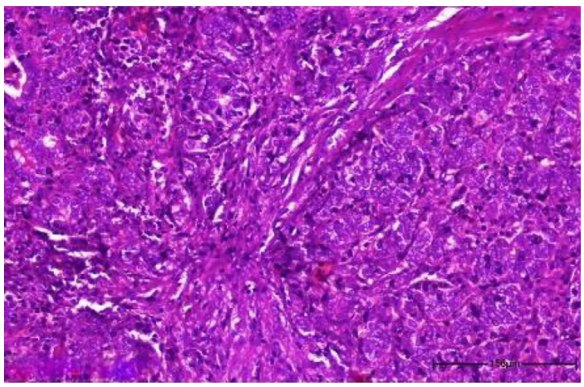

Fig. 4 – H&E staining of PTC. Characterized by nuclear features: The nuclear enlargement, overlapping, and glassy nuclei.

clinicians should be cautious about the limitations of various combination imaging studies, including US, MIBI, and CT imaging scans [7].

Considering cost and accessibility, the cervical US is most frequently utilized to localize PA [18]. However, It is notably low sensitive with ectopic PA, normocalcemic PHPT [16], or a PA length ≤13 mm [19]. Low sensitivity and positive predictive value (PPV) of US in patients with concurrent thyroid nodules are also reported: 57.0% and 43.6%, respectively [20]. In this case presentation, the most limiting factors of the US to localize PA were the presence of concomitant thyroid nodules and, of course, the size of the lesion.

Parathyroid scintigraphy with ^{99m}Tc-sestamibi SPECT/CT is proposed to identify both anatomical structures and functional activity of parathyroid tissue [16]. Interestingly, the sensitivity of ^{99m}Tc- sestamibi SPECT/CT dwindled in patients with PA length ≤1.3 cm or serum PTH levels ≤252 pg/mL [19]. Moreover, MIBI may be trapped by mitochondria-rich cells other than PA, leading to false-positive results. The expected false positive results have been seen in thyroid adenomas and malignancies [21]. Therefore, the presence of concomitant thyroid nodules with PA can be misreported as positive results [20,22]. Guo et al. reported that thyroid malignancies could be easily missed with SPECT/CT scan when the patient has simultaneous thyroid cancer and PA. This study demonstrated that in the presence of PA, thyroid cancer could be detected by SPECT/CT with a sensitivity and specificity of 35.7% and 88.6%, respectively [23]. In this case presentation, the coexistence of a highly suspicious thyroid nodule in the left thyroid lobe leads to false positive results of ^{99m}Tc-sestamibi SPECT/CT, which remains to delay phase and hide the extrathyroid PA Since IPA is rare [11], the coexistence of thyroid MIBI avid nodules must be considered, and further evaluation is needed to differentiate IPA and thyroid nodules [21].

PTH washout, a safe and reliable procedure for patients with biochemically confirmed PHPT and discordant imaging, could be utilized as a rule-in test for MIP. The sample was con-

sidered positive for parathyroid tissue if the PTH washout level was higher than the serum. The sensitivity and positive predictive value (PPV) for PHPT localization are 95% and 97%, respectively. In addition to assessing PTH levels, FNA is one of the valuable diagnostic tools for diagnosing thyroid cytology [24]. The PTH washout results in this case, with indeterminate cytology and low PTH, were suggestive of MIBI avid thyroid nodule and excluded IPA.

4D-CT is a revolutionary multiphase CT imaging approach providing high-resolution images of neck structure details to detect small and ectopic parathyroid glands [25]. It has proven power in the localization of the lesion in patients with a history of prior neck surgery, mild hyperparathyroidism, multigland disease, and patients with negative sestamibi and US imaging scans [26].

This case scenario showed that the presence of concurrent malignant thyroid nodules interferes with the proper localization of PA. The main points to be considered include: in the presence of MIBI-avid thyroid nodules, PAs may not be falsely sestamibi avid, FTC can be presented with MIBI-avid thyroid nodules, and the US as one of the first modalities used for PA localization could miss smaller-size PA Therefore, other modalities, such as 4DCT, should be considered to localize PA when Sestamibi scan and the US suggest IPA.

Another interesting presentation of this case was the development of PTC in the contralateral lobe of the thyroid, which was previously involved with FTC. While there are a few case reports that describe thyroid carcinomas as collision tumors [27]. To the best of our knowledge, PTC development as the second primary malignancy (SPM) after FTC is extremely rare. The SPM is a primary pathological tumor that may involve the same or different organs from the primary malignancy [28]. Increasing trends in conservative surgery [29] may increase reports of thyroid malignancy as SPM following thyroid tumors.This case illustrates that the patients who underwent surgery need to be followed up by sonography.

Conclusion

IPA is a rare location for PHPT. Therefore, in the presence of highly suspicious thyroid nodules in patients with clinical PHPT, multimodal imaging needs to localize extra thyroid PA.

Author contributions

All authors have contributed to this work and have read and approved the final version.

Ethical approval

The study is approved by institutional ethics committee (Ethical Approval ID: I.R.IUMS.REC.1401.967).

Patient consent

We confirm that we have obtained consent from the patient, for the use of their medical information and images in the case report. The patient has given their explicit consent for the publication and dissemination of this case report, understanding that their personal information will be kept confidential and their identity will be protected through anonymity measures.

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