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CASE REPORT

Contribution of hybrid SPECT/CT dual-tracer imaging with Na[^{99m}Tc]TcO_4 / [^{99m}Tc] Tc-MIBI in the diagnosis of a mediastinal ectopic parathyroid adenoma

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ABSTRACT

Introduction: Primary hyperparathyroidism is the third most common endocrine disorder, affecting women 2 to 3 times more frequently than men. In 80% of cases, it is caused by a parathyroid adenoma. In 15%–20% of cases, the parathyroid adenoma is ectopic, resulting from aberrant embryological migration. Mediastinal localization is less common, representing 10%–15% of ectopic parathyroid adenomas. Dual-tracer scintigraphy using technetium-sestamibi and technetium pertechnetate improves the sensitivity for detecting parathyroid adenomas. The aim of this study was to demonstrate the contribution of dual-tracer hybrid imaging in the diagnosis of an ectopic parathyroid adenoma.
Case Report: We report a patient whose biological assessment revealed hypercalcemia (11.1 mg/dl) associated with elevated serum parathyroid hormone levels (258 pg/ml), suggesting a parathyroid adenoma. Initial cervical ultrasonography failed to identify a suspicious parathyroid lesion. Hybrid single photon emission computed tomography / computed tomography imaging revealed a 12 × 10 mm hypodense nodule located in the right retrosternal region, compatible with a parathyroid adenoma.
Conclusion: The high sensitivity of hybrid imaging allowed the detection of an ectopic parathyroid adenoma and facilitated precise preoperative localization. However, in cases of diagnostic uncertainty, fluorocholine PET/CT has been shown to be more sensitive and more specific.

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Introduction

Primary hyperparathyroidism (PHPT) is an endocrine disorder caused by autonomous, inappropriate, and prolonged overproduction of parathyroid hormone (PTH) by one or more hyperfunctioning parathyroid glands, with hypercalcemia as the primary metabolic consequence [1]. It is the third most common endocrine disorder, affecting women 2 to 3 times more frequently than men [2].

PHPT is associated with parathyroid hyperplasia in 15%–20% of cases, parathyroid carcinoma in 1%, and parathyroid adenoma in 80% of cases. Among these adenomas, 15%–20% are ectopic, resulting from aberrant embryological migration [3]. The most frequent location of ectopic superior parathyroid glands is along the esophagus, whereas ectopic inferior parathyroid glands are most commonly found in the intrathymic region [4-7]. Mediastinal localization is less frequent, representing 10%–15% of ectopic parathyroid adenomas [5].

Histologically, parathyroid glands consist of oxyphil and chief cells. Oxyphil cells are more abundant and rich in mitochondria [6]. They have a secretory function, responsible for the synthesis and secretion of PTH. Due to the high mitochondrial content of oxyphil cells, there is strong uptake of technetium-sestamibi ([^{99m}Tc]Tc-MIBI) in hyperfunctioning parathyroid glands. Planar scintigraphy demonstrates high sensitivity in revealing hyperfunctioning glands at typical as well as ectopic locations. The use of hybrid imaging further increases specificity and provides precise anatomical detail [3].

Scintigraphy with [^{99m}Tc]Tc-MIBI is the current standard method for detecting hyperfunctioning

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parathyroid glands. However, its sensitivity is significantly lower in multiglandular disease compared to single-gland involvement [7]. Nichols et al. [7] reported, in a study evaluating dual-tracer scintigraphy using technetium-sestamibi and technetium pertechnetate ([^{99m}Tc]Tc-MIBI / Na[^{99m}Tc]TcO_4), a significant improvement in diagnostic sensitivity compared to [^{99m}Tc]Tc-MIBI scintigraphy alone (61% for multiglandular disease *vs.* 97% for single-gland disease).

The aim of this study was to demonstrate the contribution of dual-tracer hybrid imaging in the diagnosis of an ectopic parathyroid adenoma.

Case Report

We report a 68-year-old female patient with a history of type 2 diabetes mellitus and well-controlled hypertension under medical treatment. During a biological work-up following gastrointestinal complaints reported by the patient, hypercalcemia (11.1 mg/dl) was identified, associated with elevated serum PTH (258 pg/ml), suggestive of a parathyroid adenoma.

Initial cervical ultrasonography failed to identify a suspicious parathyroid lesion, rendering preoperative localization challenging. To further clarify the diagnosis and locate the pathological gland, a parathyroid scintigraphy was performed.

Examination protocol

The study was performed using a dual-head gamma camera equipped with low-energy high-resolution collimators (Siemens SYMBIA-Intervo), coupled with a low-dose CT scanner [single photon emission computed tomography / computed tomography (SPECT/CT)]. The matrix used was 128 × 128 with a zoom factor of 1.0.

The dual-tracer parathyroid scintigraphy protocol ([^{99m}Tc]Tc-MIBI / Na[^{99m}Tc]TcO_4), in accordance with European Association of Nuclear Medicine recommendations, began with a thyroid acquisition covering the cervical region and upper mediastinum, using an anterior planar view, performed 15 minutes after injection of 1.5 mCi of technetium pertechnetate (Na[^{99m}Tc]TcO_4).

The patient subsequently underwent an early acquisition 10 minutes after injection of 18 mCi of [^{99m}Tc]Tc-MIBI, followed by a delayed acquisition 90 minutes post-injection, using an anterior planar view, complemented by SPECT/CT for precise anatomical localization.

Images were processed using digital subtraction (MIBI image minus pertechnetate image), allowing visualization of persistent focal uptake specific to parathyroid glands, compatible with a parathyroid adenoma.

Imaging results

The initial Na[^{99m}Tc]TcO_4 acquisition demonstrated a thyroid gland of normal morphology and volume, with homogeneous uptake and no detectable nodules or focal abnormalities (Fig. 1), excluding any thyroidal interference that could affect the interpretation of parathyroid scintigraphy.

During the second [^{99m}Tc]Tc-MIBI acquisition, an intense focal uptake was identified in the right upper mediastinal region (Fig. 2), suggesting the presence of ectopic parathyroid tissue.

The digital subtraction images, obtained by subtracting the Na[^{99m}Tc]TcO_4 image from the MIBI image, confirmed the persistence of this focus, indicating specific parathyroid activity and allowing differentiation from physiological thyroid uptake (Fig. 3).

The SPECT/CT acquisition provided precise anatomical localization, revealing a 12 × 10 mm hypodense nodule in the right retrosternal position, corresponding to the focus identified on scintigraphy (Fig. 4). This functional-anatomical correlation confirmed the diagnosis of a mediastinal ectopic parathyroid adenoma, providing crucial information for surgical planning.

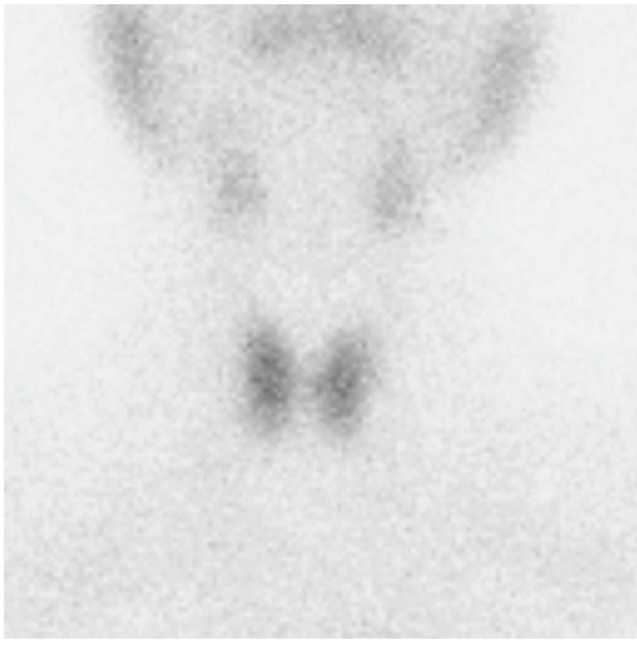


Figure 1. Thyroid acquisition performed 15 minutes after injection of 1.5 mCi of technetium pertechnetate.

Discussion

Mediastinal parathyroid adenomas are rare and show no gender predominance. The classic presentation of a parathyroid adenoma is PHPT associated with psychiatric symptoms, renal stones, skeletal manifestations, and gastrointestinal disturbances [8].

The main treatment consists of surgical removal of the hyperfunctioning parathyroid gland. Accurate preoperative identification of the hyperfunctioning gland(s) allows for a focused parathyroidectomy, reducing operative time, complications, and hospitalization [8].

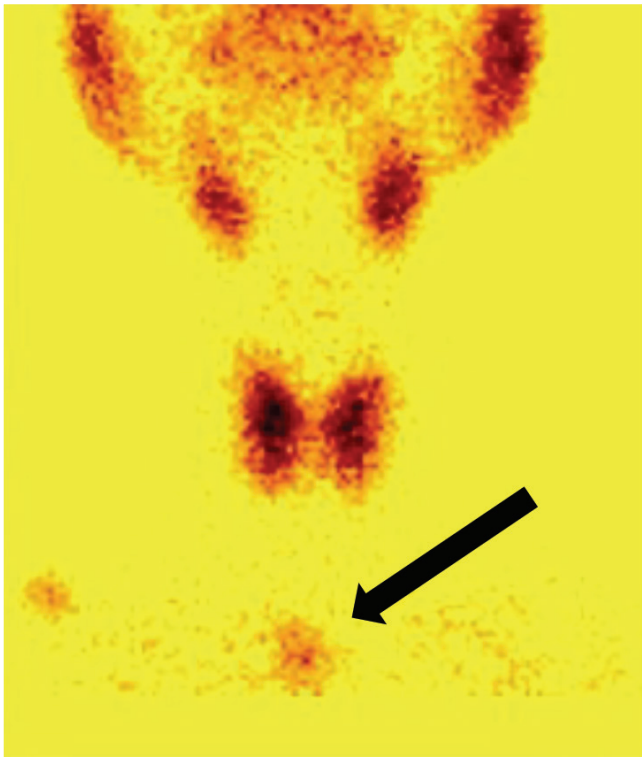


Figure 2. Early acquisition 10 minutes after injection of 18 mCi of [^{99m}Tc]Tc-MIBI.

Scintigraphy and ultrasonography are essential for identifying and localizing hyperfunctioning parathyroid glands. The advantage of parathyroid radionuclide imaging over ultrasonography lies in its ability to detect ectopic glands and facilitate recognition of posteriorly located superior glands [9]. Preoperative imaging is particularly valuable in guiding the surgeon to the exact location of one or more hyperfunctioning glands, especially in cases of ectopic glands not visualized by ultrasonography. Correct preoperative localization can shorten the duration of the procedure, which today is mainly a minimally invasive parathyroidectomy combined with intraoperative PTH measurement, particularly in single-gland disease [3].

[^{99m}Tc]Tc-MIBI is the most commonly used radiopharmaceutical for parathyroid scintigraphy. It is a lipophilic cationic complex that accumulates in hyperfunctioning parathyroid glands due to their increased mitochondrial content [10], primarily related to the abundance of oxyphil cells [11]. Moreover, it is generally cleared more rapidly from the thyroid than from hyperfunctioning parathyroid tissue, making it suitable for single-tracer dual-phase imaging. Dual-tracer scintigraphy with subtraction imaging has shown excellent performance in detecting and localizing hyperfunctioning parathyroid glands [12]. In a recent study, Woods et al. [13] reported high sensitivity and specificity for subtraction imaging (95% and 89%, respectively), with positive predictive value of 97% and negative predictive value of 83%. The accuracy for detection and localization of parathyroid adenomas was 94% and 92%, respectively.

Double-tracer subtraction scintigraphy uses 99mTc-sestamibi combined either with iodine-123 (^{123}I) or technetium-99m pertechnetate ($^{99m}TcO_4^-$) to remove the thyroid signal. The MIBI/^{123}I combination is generally considered to provide superior diagnostic performance, with increased sensitivity and specificity, due to the precision of

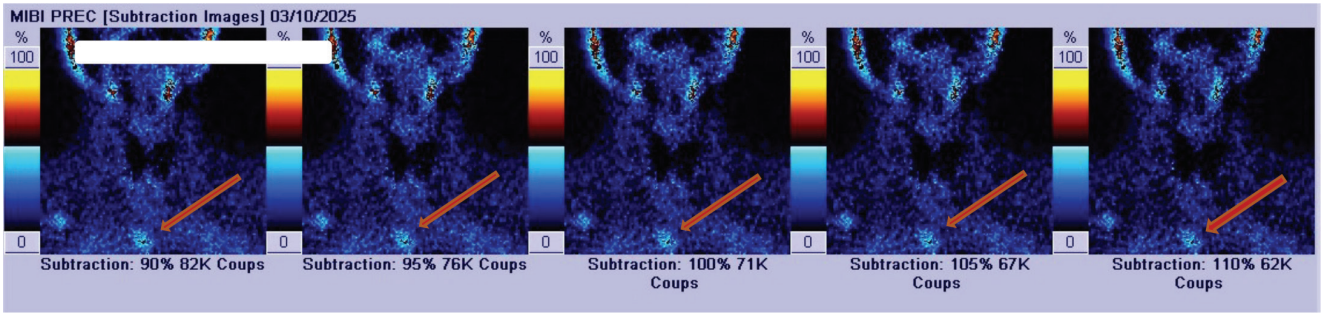


Figure 3. Subtraction image digital subtraction images, obtained by subtracting the Na[^{99m}Tc]TcO_4 image from the [^{99m}Tc]Tc-MIBI.

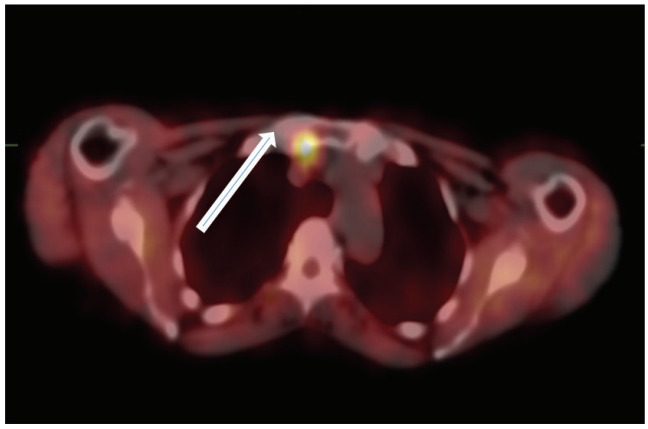


Figure 4. SPECT/CT acquisition showing a nodule capturing MIBI located in the right retrosternal position.

the dual-isotope subtraction technique [14,15]. The main difference between these methods lies in the physical properties of the isotopes and the acquisition principles. Pertechnetate offers several advantages over iodine-123: lower cost, greater availability, and rapid thyroid uptake, allowing imaging as early as 15 to 20 minutes after injection. In contrast, for iodine-123, thyroid imaging is usually performed about 2 hours after intravenous administration, and the acquisition protocol is more complex, requiring cameras capable of handling the different gamma photon energies of ^{123}I (159 keV) and ^{99m}Tc (140 keV) [14,15].

Not all hyperfunctional parathyroid glands retain [^{99m}Tc]Tc-MIBI, as its uptake and retention depend on several pathophysiological factors, including the phase of the cell cycle, parathyroid blood supply, capillary permeability, serum calcium levels, and the expression of P-glycoprotein [16]. Moreover, the presence of a thyroid pathology, such as a nodule or a multinodular goiter, represents a limiting factor for the interpretation of the examination, as these anomalies can take up MIBI, leading to false positives and reducing the sensitivity of double-tracer subtraction scintigraphy using 99mTc-sestamibi combined with technetium-99m pertechnetate ($^{99m}TcO_4^-$) [17]. Fluorocholine PET/CT ([^{18}F]choline) has shown promising results. In a comparative study of patients with PHPT, the diagnostic performance of fluorocholine PET/CT was superior to that of double-tracer parathyroid scintigraphy, with a sensitivity of 92% versus 65% for conventional scintigraphy [18]. Additionally, fluorocholine PET/CT offers several advantages over [^{99m}Tc]Tc-MIBI scintigraphy, including lower radiation exposure, better spatial resolution, and shorter acquisition times.

Conclusion

The high sensitivity of hybrid imaging enabled the detection of an ectopic parathyroid adenoma, facilitating precise preoperative localization and allowing for a focused parathyroidectomy, while reducing operative time and minimizing the risk of postoperative complications.

However, in cases of diagnostic uncertainty, choline PET/CT proves to be more sensitive and more specific, particularly in patients with a negative or inconclusive [^{99m}Tc]Tc-MIBI scintigraphy.

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Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval and Consent to participate

Ethical committee approval was not required, as this is a case report. The patient provided written informed consent for the publication of the data and images presented in this article.

Availability of data and materials

The data generated or analyzed during this case report are available from the authors upon reasonable request, subject to patient anonymity and any applicable legal or regulatory restrictions.

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