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Intrathyroidal Parathyroid Adenoma in Primary Hyperparathyroidism: Are We Overdiagnosing? Case Series and Learning Outcomes

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ABSTRACT

Intrathyroidal parathyroid (IP) adenoma as a cause of primary hyperparathyroidism (PHPT) presents a diagnostic challenge in localization and differentiating it from a thyroid nodule. We report here three distinct cases of PHPT where preoperative imaging findings were compared with surgical and histopathological findings. Case 1 was a typical true IP adenoma, as diagnosed by preoperative sestamibi and ultrasound, and confirmed at surgery and subsequent histopathology. Case 2 was diagnosed by sestamibi and ultrasound as bilateral lower pole IP adenomas which turned out to be thyroid nodules at surgery. Postsurgery, the serum PTH levels dropped only partially and PHPT persisted. Revision surgery was performed, and a right inferior parathyroid adenoma was removed, after which PTH was normalized. Case 3 had a preoperative sestamibi diagnosis of left inferior parathyroid. Preoperative ultrasound suggested a left thyroid nodule/IP along with an associated contralateral right inferior parathyroid nodule. Surgery and subsequent histopathology confirmed left follicular adenoma and right inferior parathyroid adenoma. We discuss the limitations of preoperative imaging modalities in these cases along with their learning outcomes. It is very essential that all the involved clinicians, radiologists, and surgeons are well aware of the diagnostic features and pitfalls associated with IPs so as to enable a correct diagnosis and appropriate surgical or medical management.

Key words: Follicular adenoma, hemithyroidectomy, intrathyroidal parathyroid adenoma, parathyroidectomy, primary hyperparathyroidism, revision surgery, sestamibi, thyroid nodule, ultrasound color Doppler

INTRODUCTION

Incidence of intrathyroidal parathyroids (IPs) is 0.5%–4%.^[1-3] True IPs account for less than 1% cases^[3] of hyperparathyroidism and are located completely within the thyroid gland, surrounded by thyroid parenchyma on all sides. There is no intervening thyroid capsule between the thyroid and parathyroid tissue. They result when the primordium^[4,5] of the parathyroid gets trapped into the thyroid during descent at the time of embryogenesis. As the inferior parathyroids have longer descent, they are more likely to get trapped; however, their site of entrapment in the thyroid varies. Recognition of the entity is important, both for localization of adenoma^[6] in primary hyperparathyroidism (PHPT) and conversely to prevent inadvertent hypoparathyroidism at the time of thyroidectomy.

CASE REPORTS

Case 1 (intrathyroidal parathyroid on imaging, confirmed at surgery and histopathology)

An 80-year-old male with PHPT had serum calcium of 11.5 mg/dl and serum PTH value of 756 pg/ml. Tc99m parathyroid scan [Figure 1a] showed increased uptake at the upper aspect of the right lobe of thyroid on the delayed scan, suggestive of a right superior parathyroid adenoma. Ultrasound [Figure 1b] localized a hypoechoic nodule measuring 25 mm × 18 mm within the upper part of right thyroid, completely surrounded by thyroid parenchyma on all sides with characteristic arc rim vascularity on color Doppler. An ultrasound diagnosis of an IP adenoma located at the upper pole of right thyroid was made. The patient was taken up for surgery at our institute. Intraoperatively,

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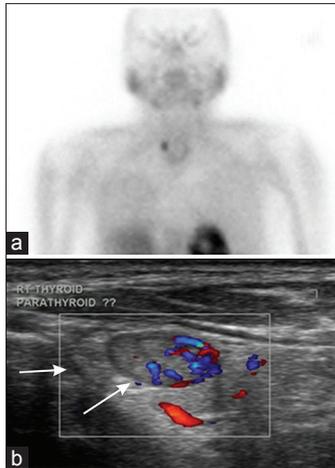


Figure 1: (a and b): Case 1: Sestamibi (a) showing increased uptake at the upper aspect of the right lobe of thyroid (thin arrow) on the delayed 2 h scan, suggestive of a right superior parathyroid adenoma. Ultrasound (b) right lobe thyroid (bold arrow) showing a hypoechoic nodule (thin arrow) measuring 25 mm × 18 mm in the upper part of the right thyroid gland with arc rim vascularity on color Doppler

adenoma was felt but there was no plane between thyroid lobe and parathyroid adenoma. A small normal right parathyroid was identified in the field and left *in situ*, likely right superior parathyroid. Right hemithyroidectomy was done and sent for [Figure 2], which confirmed parathyroid adenoma (size 10 mm × 10 mm) embedded within thyroid tissue. An operative diagnosis of right inferior IP, located at the upper part of thyroid gland, was made. Intraoperative PTH (IOPTH) assays were done. Preexcision IOPTH value of 762 pg/ml dropped to 34 pg/ml 10 min postexcision showing satisfactory drop as per Miami^[7-9] protocol. On 6-month follow-up, serum calcium and PTH remained within normal limits.

Case 2 (bilateral intrathyroidal parathyroid adenomas on imaging revealed to be thyroid nodules at surgery. Revision surgery done to remove an extrathyroidal parathyroid adenoma)

A 37-year-old female of PHPT had hypercalcemia for the past 10 years and a history of ulcerative colitis, recurrent pancreatitis, cholecystectomy, multiple intestinal polypectomies, and right adrenalectomy. Her serum calcium was 11.5 mg/dl and serum PTH 256 pg/ml. Sestamibi scan [Figure 3] showed increased uptake at both thyroid lower poles on the delayed scans, suggestive of double parathyroid adenomas, right inferior and a possible left inferior. Ultrasound [Figure 4a and b] showed a nonhomogeneous isoechoic to hypoechoic 28 mm × 21 mm × 13 mm nodule at the lower part of right thyroid and an 11 mm × 7 mm hypoechoic nodule at the lower pole of the left thyroid. Both the nodules showed increased peripheral and central vascularity [Figure 5a and b], likely IPs. FNAC of the right thyroid nodule showed follicular

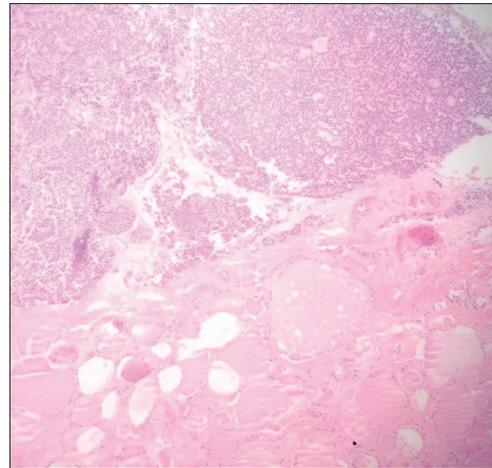


Figure 2: Case 1 Postsurgery histopathology: HPE section (×100) shows parathyroid tissue in-between the thyroid tissue. Mitosis is not seen. No atypia seen

atypia/Bethesda III and from left lobe as Bethesda I. PTH washout was not elevated. The patient underwent surgery at an outside center. Bilateral neck exploration (BNE) and a step-wise progressive resection of the right and left lobes of thyroid and left paratracheal clearance were done. Both the thyroid nodules were follicular adenoma and the para-tracheal tissue was fibro fatty on histopathology. A tiny 5 mm × 3 mm × 3 mm parathyroid removed from the left mid pole was reported as possible hyperplasia or adenoma on histopathology. The postoperative PTH was elevated (159 pg/ml) and kept increasing on follow-up to 278 pg/ml. Repeat Tc99m pertechnetate^[8] scan [Figure 6a] showed residual thyroid tissue in the right neck, and Tc99m sestamibi [Figure 6b] showed increased uptake below the right thyroid suggestive of small parathyroid adenoma. On ultrasound [Figure 6c], a 13 mm hypoechoic parathyroid nodule was noted in the right thyroid bed. Single photon emission computed tomography (SPECT) [Figure 7] showed a nodular 9 mm × 5 mm lesion in the right paratracheal region with postcontrast enhancement, suggestive of small right parathyroid adenoma. One year after her first surgery, radio-guided revision surgery was performed by a different surgeon at another center, and right inferior parathyroid adenoma was localized and removed. Furthermore, a microdissected small bit of normal parathyroid tissue was left *in situ* and another bit autotransplanted into the right sternocleidomastoid muscle. Postexcision, 30 min PTH levels decreased to 4.7 pg/ml and post 1.5 h to 1.7 pg/ml. On 6-month follow-up, the serum calcium and PTH remained within normal limits.

Case 3 (contralateral parathyroid nodule to sestamibi scan)

A 56-year-old male with PHPT had serum calcium level of 12.2 mg/dl and serum PTH 132.0 pg/ml. Sestamibi

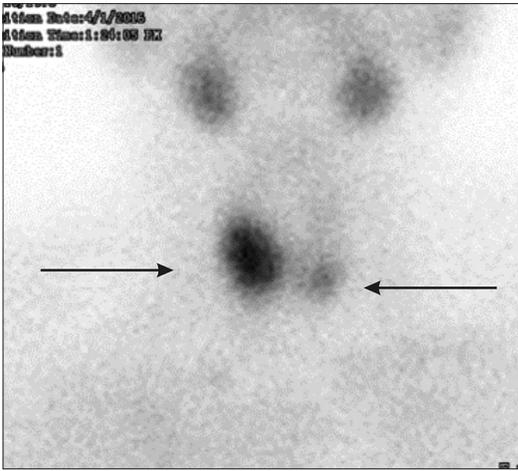


Figure 3: Case 2 Tc99m Parathyroid scan showing a large focus of increased uptake in relation to the entire right lobe of thyroid (bold arrow) with the right lobe not visualized separately? Intrathyroidal location of parathyroid, which persisted on delayed image while the thyroid gland showed normal washout. A similar smaller focus is also seen in the lower pole of left lobe (thin arrow). Scan suggestive of right parathyroid adenoma, with possibility of double adenoma and a smaller lesion at left inferior location

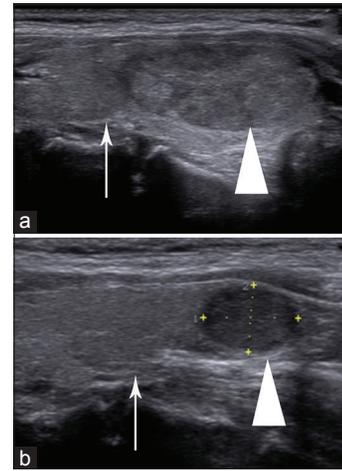


Figure 4: (a and b) Case 2 first ultrasound (a) right thyroid (thin arrow) showing a 28 mm x 21 mm x 13 mm isoechoic to hypoechoic, slightly nonhomogeneous ovoid nodule (arrowhead) with well-defined margins and partial halo around it. (b) Left thyroid (thin arrow) showing a well-defined rounded homogeneously hypoechoic nodule (arrowhead) measuring 11 mm x 7 mm at lower pole

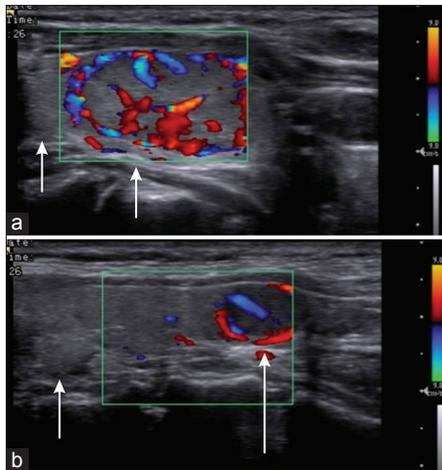


Figure 5: (a and b) Case 2 Ultrasound images with color Doppler (a) of the right thyroid nodule (thin arrow) and (b) left thyroid nodule (thin arrow) with significantly increased vascularity on color Doppler in both central and peripheral part

scan [Figure 8] showed persistent uptake of technetium contrast at the lower pole of left thyroid, suggestive of left inferior parathyroid adenoma. Ultrasound [Figure 9a and b] showed a corresponding hypoechoic nodule at left lower thyroid, well encapsulated by thyroid parenchyma and with significantly increased central and peripheral vascularity. Another well-defined homogeneously hypoechoic 8 mm x 6 mm nodule was identified posterior to the right (contralateral) lower pole which showed characteristic eccentric vascularity and a polar feeding vessel. An ultrasound diagnosis of the left thyroid nodule/IP and an associated right inferior parathyroid

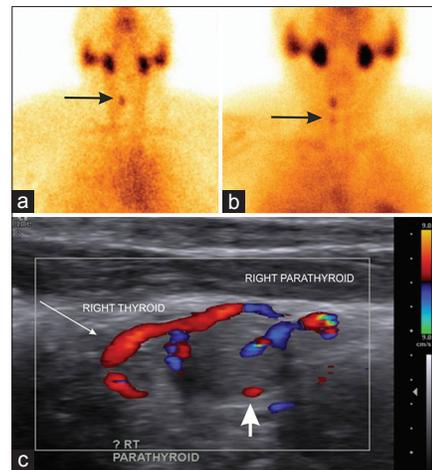


Figure 6: (a-c) Case 2 - postsurgery (a) Tc99m Pertechnetate scan showing thyroid tissue (long arrow) in the right neck (b) Tc 99m sestamibi parathyroid scan showing parathyroid adenoma (small arrow) below thyroid (c) Ultrasound showing an isoechoic area in right thyroid bed (long arrow) likely residual thyroid along with an hypoechoic parathyroid nodule (small arrow) measuring 13 mm x 8 mm x 7 mm in the lower part of right thyroid fossa region which shows arc rim vascularity on color Doppler

nodule was made. The patient was taken up for surgery at our center. Left hemithyroidectomy was performed and frozen section confirmed left thyroid nodule. There was an insignificant drop in IOPTH levels (128 pg/ml). Then, the right side was explored; an inferior adenoma was found and removed. Frozen section confirmed parathyroid tissue. Post 10 min excision, IOPTH levels dropped to 18.9 pg/ml and post 20 min to 13.2 pg/ml, showing satisfactory drop as per Miami protocol. Histopathology confirmed left thyroid nodule as follicular adenoma and right inferior parathyroid as parathyroid adenoma. On subsequent

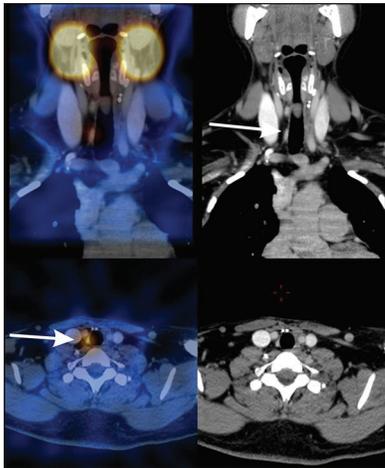


Figure 7: Case 2 - Postsurgery single photon emission computed tomography contrast-enhanced computed tomography neck showing a nodular lesion measuring 9 mm × 5mm in right paratracheal region (upper arrow) with postcontrast enhancement (lower arrow)

6-month follow-up, serum calcium and PTH remained within normal limits.

DISCUSSION

A detailed correlation of the diagnostic and surgical findings shows case 1 to be a correctly diagnosed IP, while case 2 and 3 both have been an overdiagnosis. These cases highlight the diagnostic pitfalls of the modalities used and present various learning outcomes for all the involved physicians and surgeons.

Case 1 represents a typical true intrathyroid parathyroid adenoma. Here, the preoperative sestamibi and ultrasound findings matched exactly with the surgical findings and the histopathology. Correlation of the sestamibi images with another imaging, ultrasound or cross-sectional contrast computed tomography (CT)/SPECT-CT is vital to recognize IP adenoma.

Case 2 – Preoperative imaging, both sestamibi and ultrasound, failed to correctly identify the adenoma. Despite extensive first surgery, PHPT persisted. Repeat postoperative imaging and functional studies correctly identified the offending adenoma, and a revision surgery had to be performed to remove it. By cytopathology, it is often difficult to distinguish between thyroid and parathyroid cells,^[10-12] and accurate preoperative imaging diagnosis is important. As per literature, Technetium-99m sestamibi scan is the investigation of choice^[13] for localization of parathyroids, but its pitfalls must be well remembered. Overdiagnosis on sestamibi may sometimes occur in any lesion in the area, which is hypermetabolic (usually hypervascular on imaging). Caution must be exercised in interpreting all cases where a thyroid nodule is



Figure 8: Case 3 Tc-99m Sestamibi scan showing an area of focal radiotracer concentration in the region of lower pole of left thyroid lobe, which persists on delayed image corresponding to a left inferior parathyroid adenoma

identified on ultrasound and especially if it shows increased vascularity, as metabolically active nodules will take up increased technetium contrast, and can be misinterpreted as parathyroid nodules. It must be remembered that IP s are rare, but thyroid nodules are far more common.^[14] In a case of PHPT, these thyroid nodules may mimic a parathyroid adenoma on imaging. Ultrasound evaluation of neck is limited inferiorly by clavicles, and in cases of thyroid enlargement, a tiny ipsilateral parathyroid can be displaced leading to its failed detection at ultrasound. Ultrasound features should be scrutinized carefully and interpretation must be unbiased with the sestamibi findings. Typical ultrasound features of a parathyroid nodule are a

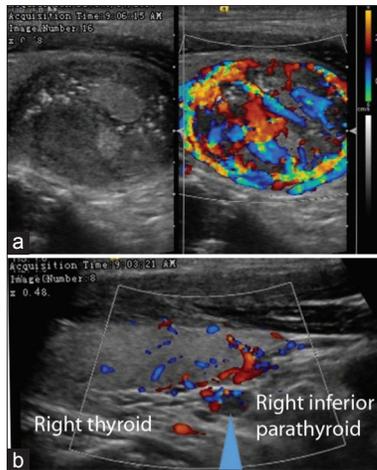


Figure 9: (a and b) Case 3 Ultrasound with color Doppler: (a) left lobe thyroid showing a well-defined rounded isoechoic to hypoechoic 27 mm × 18mm × 24 mm nodule in the lower half with significantly increased vascularity both centrally and peripherally. (b) Right side showing a well-defined homogeneously hypoechoic parathyroid nodule measuring 8.6 mm × 4.4 mm × 5.3 mm located posterior to the lower part of right thyroid gland (blue arrow), with characteristic arc rim vascularity on color Doppler

homogeneously hypoechoic well-defined nodule with an arc rim vascularity. Often, a feeding vessel may be identified at one pole and this is highly suggestive of an enlarged parathyroid. Further imaging with 4D CT or dual isotope subtraction sestamibi^[15,16] and SPECT may be performed to localize enlarged parathyroids lying adjacent to thyroid nodules. Availability of IOPH monitoring is a very important adjunct in such cases.^[17]

Case 3 – In this case of PHPT, sestamibi localized a left inferior parathyroid adenoma. Ultrasound findings, especially the color Doppler findings and search for other parathyroid nodules were timely and found the offending parathyroid adenoma, separate from the abnormality shown on sestamibi. This allowed for an effective management of this case. The examination and interpretation of the various diagnostic imaging modalities must be unbiased with respect to another. They may be all correlated together later to form a final diagnosis and formulate appropriate management plan.

CONCLUSION

It is important to remember IP adenoma as a diagnostic entity when evaluating a patient with hyperparathyroidism. However, these are rare, and a diagnosis of IP adenoma should always be viewed with skepticism as they can be overdiagnosed. Both the radiologist and the surgeon should keep an open mind and be ready to explore beyond. For the radiologist, overdiagnosis of IP must be kept in mind, and a thorough search must be done for an adenoma elsewhere in an extrathyroidal location. Care must be taken to avoid the

diagnostic pitfalls of any single modality.^[14] In patients with concomitant thyroid nodules, a sestamibi – SPECT CT/4D CT may provide localization of a missed extrathyroidal parathyroid adenoma. For the surgeon, when IP is suspected based on imaging (sestamibi alone or sestamibi and ultrasound), a potential search for a true extrathyroidal adenoma at another location must be kept in mind, if needed, with a BNE approach. Accurate preoperative diagnosis, and consideration of alternatives, avoids any unexpected surprises at surgery, obviating the need for any unplanned changes to be made on the operating table. Accordingly appropriate preoperative counseling and informed consent can be taken from the patient before the surgery. It helps reduce revision surgeries.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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