Localization of an Ectopic Parathyroid Adenoma by Double-Phase Technetium-99m-Sestamibi Scintigraphy

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Double-phase planar scintigraphy using ^{99m}Tc-MIBI has been introduced as a means to detect and localize parathyroid adenomas. Focal uptake on both early and delayed imaging is typical of these entities. We report a patient with persistent hypercalcemia following subtotal parathyroidectomy, who was found scintigraphically to have an ectopic parathyroid adenoma. Following initial detection within the mediastinum using planar scintigraphy, the adenoma was more precisely localized using SPECT imaging. This case suggests that double-phase parathyroid planar scintigraphy augmented with SPECT imaging, if needed, is cost-effective, and often necessary, in the assessment of primary hyperparathyroid patients before surgical re-exploration.

Key Words: parathyroid gland; hyperparathyroidism; ectopic parathyroid adenoma

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The incidence of primary hyperparathyroidism is now higher than previously suspected with the increasing physician awareness and relative ease with which accurate screening laboratory studies are obtained. Since the clinical presentation of primary hyperparathyroidism is widely variable, it is not unusual for patients to be identified with little, if any, concurrent hypercalcemic complications.

The previously described differential washout and optimal Anger camera characteristics of ^{99m}Tc-MIBI make it a promising agent for routine preoperative localization of parathyroid adenomas. In this patient, SPECT imaging augmented the planar findings in such a way that the surgical approach was appropriately altered to facilitate successful excision.

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CASE REPORT

A 32-yr-old woman with otherwise unremarkable past medical and family histories was found to have primary hyperparathyroidism based on markedly elevated serum calcium, hypercalciuria and elevated intact parathyroid hormone levels. Because of her young age, high urinary calcium levels and a possible risk for progressive bone loss, she was referred to surgery for neck exploration.

Intraoperatively, four hyperplastic parathyroid glands were visualized and pathologically confirmed. No adenoma was identified in the young patient. Near-total 3 ½-gland parathyroidectomy was performed without complications. Histopathologic examination confirmed the hypercellularity of four distinct parathyroid glands. Subsequent endocrinologic evaluation ruled out the possibility of multiple endocrine neoplasia syndrome.

Postoperatively, the patient remained biochemically hyperparathyroid, thus further localizing imaging modalities were performed to locate an ectopic parathyroid adenoma. Noncontrast CT of the neck and chest were negative as well as US of the neck. After intravenous administration of 740 MBq (20 mCi) ^{99m}Tc-MIBI, planar parathyroid scintigraphy, as described by Taillefer et al. (*1*), revealed a small focus of activity within the chest (Fig. 1). Repeat planar scintigraphy demonstrated similar findings.

Delayed SPECT of the neck was then performed with a dual-head, large field of view gamma camera. Low-energy all-purpose parallel-hole collimators were used for 360° acquisition at 30 sec/stop over 45 stops. A 128 × 128 word matrix was used to acquire the raw data obtained over a 20% symmetric energy window centered on 140 keV. The corrected data were reconstructed with a Butterworth filtered backprojection technique. Final filtered images produced 5.28 mm slices. SPECT imaging further localized a focus 7 cm deep within the anterior mediastinum at the T4 vertebral body (Fig. 2).

Subsequent high-resolution CT of the mediastinum revealed a possible ectopic parathyroid adenoma in the area of the remnant thymus. Fat-suppressed MRI did not corroborate this finding. Arteriogram of the internal mammary arteries revealed a "tumor blush" in the anterior mediastinum, fed by the second segmental branch of the right internal mammary artery (Fig. 3).

The patient was taken to surgery and a median sternotomy was performed. The ectopic parathyroid was found in the scintigraphic location (Fig. 4). After pathologic confirmation of a frozen specimen, it was excised and a total thymectomy performed. The

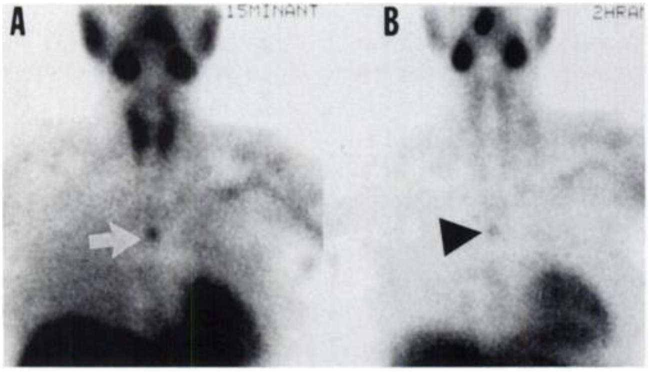

FIGURE 1. Images obtained 15 min (A) and 2 hr (B) postinjection show an abnormal focus of activity in the thorax (arrow and arrowhead, respectively). Increased intensity over time is suggestive of a parathyroid adenoma.

remaining parathyroid tissue was cryopreserved for possible future re-implantation.

Histopathologic examination of the fixed surgical specimen confirmed the tissue as a parathyroid adenoma. The patient's biochemical profile returned to normal postoperatively.

DISCUSSION

Primary hyperparathyroidism is the most common cause of hypercalcemia in adults. Autonomous parathyroid tissue leads to excessive parathyroid hormone concentrations, in spite of elevated serum calcium levels. Clinical manifestations are highly variable, and may be completely asymptomatic, insidious over many years, or accelerated and overt. Symptoms may range from recurrent renal stones and accelerated bone loss, to that associated with severe hypercalcemia or disabling fractures. Enlargement of a single parathyroid gland is the cause in approximately 85% of cases. Of these, the vast majority are due to adenomas, whereas parathyroid carcinomas are extraordinarily rare.

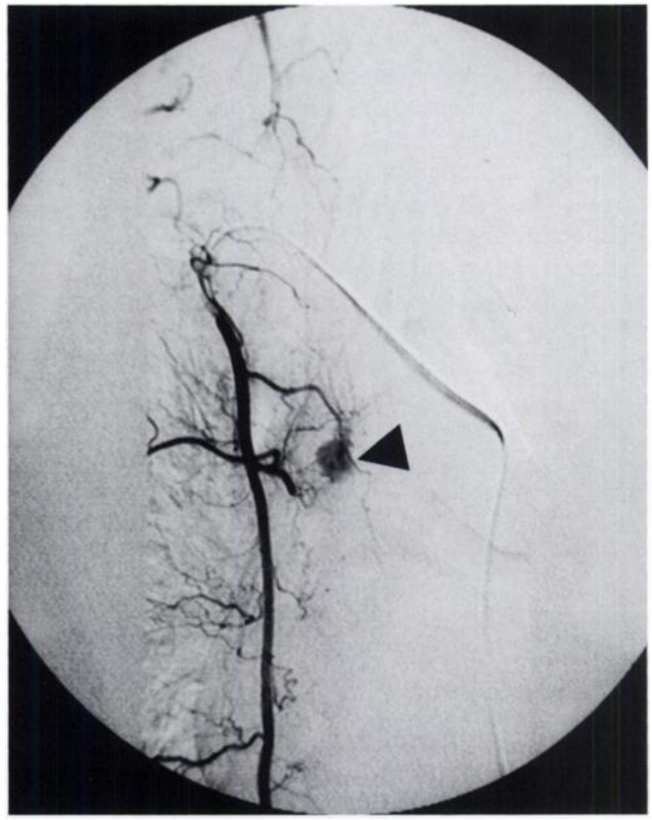

FIGURE 3. Arteriogram of the right internal mammary artery revealed a "tumor blush" (arrowhead) which corresponds to the scintigraphic findings.

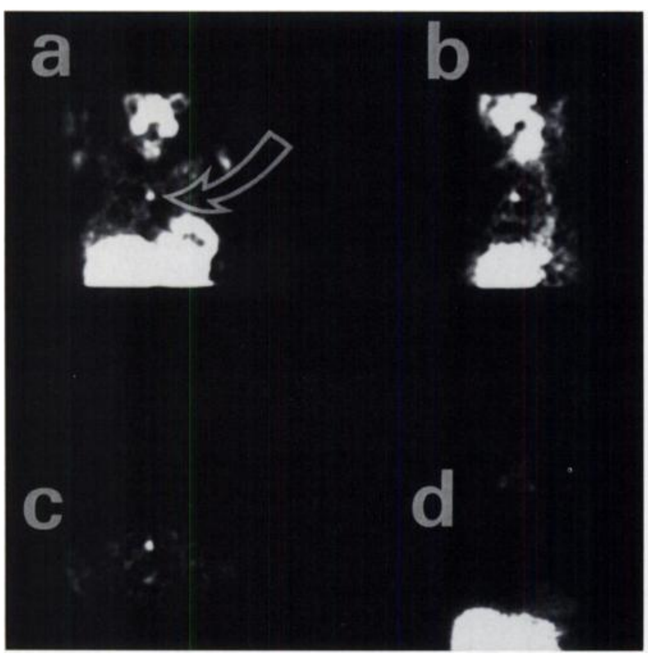

FIGURE 2. SPECT imaging was used to further localize an abnormal focus of activity before additional surgery. Representative slices from the coronal (A), sagittal (B) and transverse (C) projections pinpoint the abnormal focus within the anterior mediastinum (curved arrow). The remaining anterior planar image (D) was used as a reference.

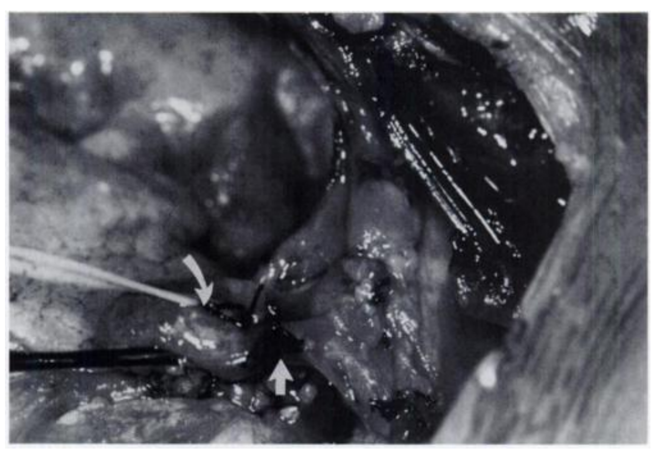

FIGURE 4. An ectopic parathyroid adenoma was found in the lower anterior mediastinum, as indicated scintigraphically. This intraoperative image shows a ligature around the adenoma's vascular pedicle (arrow) and ligatures on the dissected adenoma itself (curved arrow).

The remaining 15% are due primarily to chief-cell hyperplasia (*2*).

Disease incidence increases with age and occurs more often among women; peak incidence is between the third and fifth decades. The overall incidence of primary hyperparathyroidism appears greater than previously suspected, largely due to increased physician awareness, wider use of multichannel analyzers and increased accuracy in the biochemical assessment of parathyroid hormone levels (*2*).

Ectopic adenomas occur in 6%–10% of cases, in locations such as the thymus, thyroid, pericardium or behind the esophagus. The reported incidence of ectopic hyperplastic parathyroid glands ranges from 7% to 47% (*3*).

Although most cases of primary hyperparathyroidism are sporadic, those due to hyperplasia may be familial, inherited as an autosomal dominant trait. In some patients, hereditary primary hyperparathyroidism occurs as part of a complex of endocrinologic disorders: Type I multiple endocrine neoplasia (MEN I, Wermer's syndrome)—hyperparathyroidism, pancreatic islet cell tumor and pituitary tumor; or MEN II (Sipple's syndrome)—hyperparathyroidism, medullary carcinoma of the thyroid and pheochromocytoma (*2*).

Confirmed primary hyperparathyroidism often warrants surgical intervention. The success rate of an experienced endocrine surgeon in removing an adenomatous gland without preoperative imaging has been reported to be in the range of 85%–98% (*4,5*). Postoperative patients with persistent or recurrent hypercalcemia, however, usually undergo imaging studies to localize ectopic parathyroid tissue prior to repeat surgery (*5*).

Although no single imaging modality is clearly superior, a multimodality approach, including scintigraphy, CT, MRI and real-time sonography, improves localization accuracy (*5*). The primary strength of radionuclide parathyroid scintigraphy over anatomic imaging modalities is its unaffected sensitivity (~70%) and specificity (90%) following initial parathyroid surgery (*4*).

Computed tomography can visualize retrotracheal, retroesophageal and mediastinal parathyroid adenomas (*4*), but its postoperative images are diminished by metal clips and distorted tissue planes (*5*).

Postoperative MRI sensitivity is about 75% (*2*) and positive predictive values are between 77% and 95% (*5*). Potential disadvantages of this modality include its cost, potential for artifactual findings and low specificity (*5*).

There are two radionuclide techniques currently available to image parathyroid adenomas: (a) dual radionuclide subtraction scintigraphy with ^{201}Tl and [^{99m}Tc]pertechnetate (*6*) and (b) double-phase single radionuclide scintigraphy with ^{99m}Tc-MIBI (*1,7*).

Tumor size is an important consideration with regard to scintigraphic sensitivity. For adenomas greater than 500 mg, the reported sensitivity using the ^{201}Tl/[^{99m}Tc]pertechnetate subtraction technique is 90% (*4*). Using the double-phase ^{99m}Tc-MIBI technique, Taillefer et al. reported a 90% sensitivity in adenoma detection, with tumor size ranging from 150 mg to 8.0 g (*1*). In a subsequent study, O'Doherty reported a detection sensitivity of 98% for adenomas ranging from 194 mg to 5.02 g (*8*).

The ^{99m}Tc-MIBI technique offers several advantages over ^{201}Tl/[^{99m}Tc]pertechnetate:

1. Technetium-99m imaging characteristics are far superior than those of ^{201}Tl.
2. Differential washout over time allows for straightforward interpretation,
3. Patient throughout is optimized, without time-consuming, subtraction-related image acquisition and processing (*1*).

Localization of ^{99m}Tc-MIBI is presumably due to its cytoplasmic and mitochondrial sequestration in response to the negative membrane potentials generated across the respective bilayers (*1,8*). Sandrock et al. demonstrated that parathyroid adenomas had high concentrations of mitochondria (*9*). Parathyroid adenomas have a much greater avidity for ^{99m}Tc-MIBI than that of surrounding tissue; in addition, there is a slower differential washout from the adenomatous tissue. These processes together allow for an optimal target-to-background ratio and clear scintigraphic visualization on delayed images (*1,8*). The addition of SPECT imaging in our patient clearly demonstrated its utility in precisely localizing adenomas and proved helpful to the surgeon in pinpointing the operative site.

Although experienced surgeons possess extremely high initial surgical success rates without preoperative tumor localization, this case suggests that preoperative planar and SPECT scintigraphy is cost-effective in precisely localizing ectopic foci and thereby directing their surgical excision.

REFERENCES

1. Taillefer R, Boucher Y, Potvin C, Lambert R. Detection and localization of parathyroid adenomas in patients with hyper-parathyroidism using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study). *J Nucl Med* 1992;33:1801–1807.
2. Fitzpatrick LA, Bilezikian JP. Primary hyperparathyroidism. In: Becker KL, Bilezikian JP, Bremner WH, et al., eds. *Principles and practice of endocrinology and metabolism*, 1st ed Philadelphia: JB Lippincott 1990;430–437.
3. Liechty RD, Weil R, III. Parathyroid anatomy in hyperplasia. *Arch Surg* 1992;127:813–815.
4. Beierwaltes WH. Endocrine imaging: parathyroid, adrenal cortex and medulla, and other endocrine tumors: part II. *J Nucl Med* 1991;32:1627–1639.
5. Freitas JE, Freitas AE. Thyroid and parathyroid imaging. *Semin Nucl Med* 1994;24:234–245.
6. Erwin WD, Groch MW, Ali A, Fordham EW. Image normalization and background subtraction in T1-201/Tc-99m parathyroid subtraction scintigraphy. Effect on lesion detection. *Clin Nucl Med* 1992;2:81–89.
7. Coakley AJ, Kettle, AG, Wells CP, O'Doherty MJ, Collins RE. Technetium-99m-sestamibi—a new agent for parathyroid imaging. *Nucl Med Commun* 1989;10:791–794.
8. O'Doherty MJ, Kettle AG, Wells P, Collins REC, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: preoperative localization and tissue uptake studies. *J Nucl Med* 1992;33:313–318.
9. Sandrock D, Merino MJ, Norton JA, Neumann RD. Ultrastructural histology correlates with results of thallium-201/technetium-99m parathyroid subtraction scintigraphy. *J Nucl Med* 1993;34:24–29.