Rapid Washout of Technetium-99m-MIBI from a Large Parathyroid Adenoma

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We report a case of rapid ^{99m}Tc-methoxyisobutylisonitrile (MIBI) clearance from a parathyroid adenoma. A double-phase ^{99m}Tc-MIBI parathyroid scintigraphy was performed on a 62-yr-old female evaluated for primary hyperparathyroidism. A large parathyroid adenoma was visualized caudal to the left lobe of the thyroid gland with an unusually rapid washout of the tracer from tumor tissue. Histologic tissue examination confirmed the presence of a parathyroid adenoma and the absence of oxyphil cells. Care should be taken in interpretation of ^{99m}Tc-MIBI parathyroid scintigrams because some adenomas can present a rapid release of the radiotracer in a double-phase study. Technetium-99m-MIBI retention could be related to the number of mitochondria-rich cells in parathyroid adenomas or to hyperplasia.

Key Words: technetium-99m-MIBI; primary hyperparathyroidism

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Since it was originally reported, the use of ^{99m}Tc-MIBI for parathyroid imaging (*1*) using a subtraction method with ^{123}I-iodide continues to be suggested for preoperative evaluation of primary hyperparathyroidism (*2*). In 1992 Taillefer et al. proposed a double-phase (early and late) protocol to capitalize on the faster clearance of ^{99m}Tc-MIBI from normal thyroid tissue for better visualization of parathyroid adenomas or hyperplasias (*3*). This method does not use ^{123}I and obviates the need to obtain subtraction images. We report a case of rapid clearance of the ^{99m}Tc-MIBI from a large parathyroid adenoma.

CASE REPORT

A 62-yr-old female with a history of hypertension presented high serum calcium levels on routine blood chemistry evaluation for osteoporosis. Except for osteoporosis, she was completely asymptomatic on presentation and had no history of kidney stones, peptic ulcers or ectopic calcifications. Physical examination did not reveal any abnormal findings. No neck masses were found and the thyroid was normal on palpation.

Serum calcium was at 3.34 mmole/liter (normal values 2.10–2.54) and intact parathormone level was at 32 pmole/liter (normal values 0.9–5.8). A sonogram of the neck revealed a 3 × 1 × 2 cm neck mass slightly behind the left sternoclavicular joint. Technetium-99m-MIBI scintigraphy was performed and a large foci of radiotracer accumulation was seen caudal to the left lobe of the thyroid gland (Fig. 1A). However, the 3-hr scintigrams showed rapid release of the tracer from the mass (Fig. 1B). No other abnormalities were found on the parathyroid scan and it was felt that the mass was probably a large parathyroid adenoma. No radioiodine accumulated at that site on a thyroid scintigram done the next day.

To prevent further aggravation of her osteoporosis, surgery was performed and a large 4 × 2 × 1.2 cm parathyroid adenoma weighing 7 g was removed in the left lower neck. The tumor mass was well encapsulated but adherent to the upper part of the thymus. Serum calcium returned to normal after surgery. Histological examination of the specimen revealed an expansile growth that compressed surrounding parathyroid tissue. A thick fibrous capsule clearly demarcated the benign neoplasm. The architectural arrangement of cells was composed of numerous acinoglandular formations with some ribbons and sheets. Vasculature was dense. There was a marked predominance of water-clear cells with rare dark chief cells (Fig. 2). No oxyphil cells were present in the tumor.

DISCUSSION

Although standard thallium-technetium parathyroid scintigrams are useful in the preoperative localization of parathyroid adenomas (*4*), the single tracer double-phase ^{99m}Tc-MIBI technique is at least as accurate, easier to perform and produces images of higher quality (*3*). The typical pattern seen with a parathyroid tumor is a prolonged retention of ^{99m}Tc-MIBI in the adenoma with a rapid washout of the tracer from normal thyroid tissue.

The study done by O'Doherty et al. (*2*) first showed the differential washout of ^{99m}Tc-MIBI occurring in thyroid and parathyroid tissue as documented by dynamic time-activity curves obtained from scintigraphic data. Surgical excision of tissues in 20 patients showed that the absolute tracer uptake in these samples was higher with ^{201}Tl-chloride, but ^{99m}Tc-MIBI presented a higher parathyroid to thyroid ratio. Sandrock et al. (*5*) showed a clear correlation between the number of oxyphil cells and abnormal parathyroid tissue visualization in ^{201}Tl/^{99m}Tc subtraction scintigraphy. The absolute number of mitochondria was significantly higher in lesions detected by scintigraphy than in

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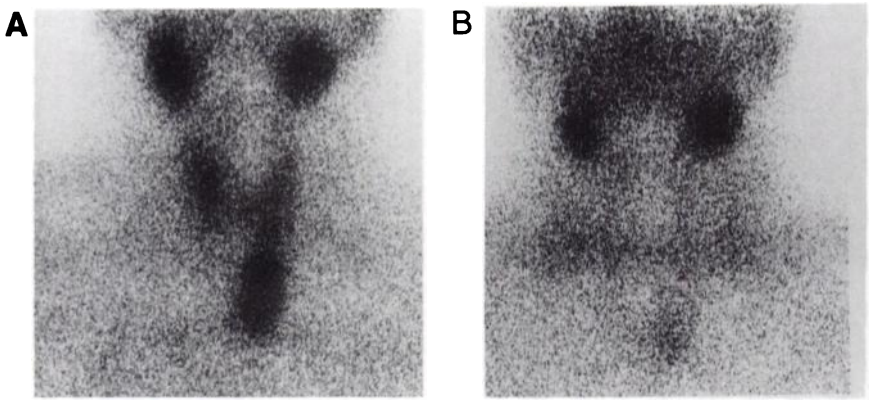

FIGURE 1. Double-phase ^{99m}Tc-MIBI study with early (A) and 3-hr (B) images of a parathyroid adenoma located caudal to the left lobe of the thyroid gland. There is a rapid washout of the tracer from both the adenoma and the thyroid gland compared to soft-tissue background and salivary gland activity.

those that were missed, the highest ratio of mitochondria per cell being found in oxyphil cells.

However, no definitive explanation has been provided for the uptake of ^{99m}Tc-MIBI in hyperplasias or in adenomas. Technetium-99m-MIBI binding in cultured mammalian cells is dependent on both plasma and mitochondrial membrane potentials. It was postulated that high numbers of mitochondria could contribute to the accumulation of the agent, as inhibition of the mitochondrial membrane potential produced a rapid release of the tracer from cultured cells (*6*). By using subcellular fractionation, ^{99m}Tc-MIBI has also been shown to bind to the mitochondrial fraction in tissues other than the heart, and we could assume this is also true for parathyroid tissue. In the same study, ^{99m}Tc-MIBI retention has been inversely correlated with Ca^{2+} concentration in mitochondrial fractions (*7*). Although variations in intracellular calcium content would be expected to influence sestamibi retention, it is doubtful that viable hyperplasia or adenoma cells could survive with the intracellular calcium concentrations (>1.5 m*M*) needed to reduce significantly the mitochondrial retention of ^{99m}Tc-MIBI.

Tissues with a low mitochondrial content would not be expected to significantly retain the tracer. We can therefore hypothesize that mitochondria-rich oxyphil cells make a logical target for the prolonged retention of ^{99m}Tc-MIBI usually observed in abnormal parathyroids. The absence of these cells in the studied adenoma could explain the lack of ^{99m}Tc-MIBI retention on late-phase imaging. Presumably, the observed initial uptake relates to increased flow or cellularity in the tumor. In addition to the size of the adenoma or hyperplasia, the presence and number of oxyphil cells might be important for adequate visualization on the 3-hr images.

Although rapid washout did not prevent adequate localization of the adenoma in the present case, smaller intrathyroidal tumors with similar behavior would be missed on scintigraphic evaluation. This could explain the occasional false-negative study observed with ^{99m}Tc-MIBI parathyroid scintigraphy. The subtraction method using ^{123}I-iodide and ^{99m}Tc-MIBI would be superior in such cases since the ^{99m}Tc-MIBI scintigram is obtained immediately after injection when there is maximal tissue uptake in parathyroid adenomas or hyperplasias. The superiority of either technique remains to be determined, however, balancing the additional information provided by the subtraction method with the simplicity and convenience of the double-phase technique.

We believe that ^{99m}Tc-MIBI parathyroid scintigraphy is currently the best available imaging technique for preoperative localization of abnormal parathyroid tissue in primary hyperparathyroidism, using either the double-phase or the subtraction method. However this case illustrates that slow washout of the radiotracer is not invariable and that more rapid release can be observed in some adenomas when using the double-phase technique.

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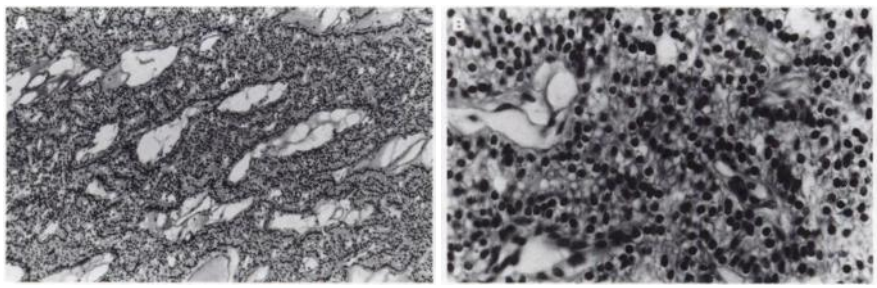

FIGURE 2. H & E staining of a specimen from the adenoma seen in Figure 1. Magnification is at 100× (A) and 400× (B). There is a complete absence of oxyphil cells and a large number of water-clear cells.

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