NONEQUIVALENT RESULTS OF TETROFOSMIN AND SESTAMIBI IMAGING OF PARATHYROID TUMORS

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Case Report

NONEQUIVALENT RESULTS OF TETROFOSMIN AND SESTAMIBI IMAGING OF PARATHYROID TUMORS

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ABSTRACT

Objective: To report the case of a patient with a large parathyroid carcinoma missed by dual-phase technetium Tc 99m tetrofosmin (TETRO) parathyroid scanning.

Methods: We present the clinical findings, laboratory results, imaging studies, and surgical pathology report in a man with parathyroid carcinoma and review the literature regarding the use of TETRO scintigraphy in patients with hyperparathyroidism.

Results: In an 83-year-old man with hyperparathyroidism, severe hypercalcemia developed in the context of nephrolithiasis. An in-office ultrasonographic evaluation of the neck revealed a partially calcified mass (2.3 by 1.3 by 1.6 cm) at the inferoposterior border of the left thyroid lobe. Technetium Tc 99m sestamibi (MIBI) scanning was requested and reported as "negative." In fact, TETRO scanning had been substituted for MIBI scanning by the management of the nuclear medicine facility. Before neck exploration, performance of dual-phase MIBI parathyroid scintigraphy revealed radionuclide retention in the left lower neck area at 120 minutes, in the same site as the ultrasonographically visualized mass. A limited left inferior parathyroidectomy was performed, and intraoperative parathyroid hormone levels declined from 254 pg/mL to 28 pg/mL 10 minutes after near-complete resection of the mass. Pathology evaluation of the surgical specimen revealed a 2,000-mg parathyroid carcinoma.

Conclusion: Although both agents incorporate the same technetium Tc 99m radionuclide, TETRO and MIBI parathyroid scanning are not equivalent in the detection of parathyroid tumors with use of the dual-phase technique. We do not recommend substitution of TETRO for MIBI as a cost-control measure in the evaluation of hyperparathyroidism. **(Endocr Pract. 2006;12:179-182)**

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Abbreviations:
MIBI = technetium Tc 99m sestamibi; **PTH** = parathyroid hormone; **TETRO** = technetium Tc 99m tetrofosmin

INTRODUCTION

Since the 1990s, nuclear imaging of parathyroid glands has been used by endocrine surgeons, nuclear radiologists, and endocrinologists in the evaluation of parathyroid gland hyperfunction and in planning for curative, minimally invasive parathyroidectomy (1-4). In conjunction with preoperative neck ultrasonography and intraoperative chemiluminescent parathyroid hormone (PTH) assays, nuclear imaging of hyperfunctioning parathyroid tissue can diminish the need for time-consuming full neck exploration. Unfortunately, nuclear parathyroid scanning compounds are limited by a substantial false-negative rate, particularly in the setting of multiple parathyroid adenomas and parathyroid hyperplasia (5). In addition, the use of new, less expensive parathyroid scanning agents such as technetium Tc 99m tetrofosmin (TETRO) with a dual-phase scanning technique may be associated with an unforeseen loss of sensitivity (6-8). The following report describes such a case.

CASE REPORT

An 83-year-old man presented to one of us (R.M.H.) with a 12-year history of hypercalcemia and elevated plasma PTH levels. He complained of progressive fatigue, excessive nocturnal urination, and a 3.2-kg weight loss. The past medical history was remarkable for diffuse atherosclerosis, hyperlipidemia, a coronary bypass grafting procedure, atrial fibrillation and pacemaker implantation, and refractory hypertension. His current medications were sotalol, furosemide, potassium, simvastatin, enalapril, digoxin, amlodipine, and tamsulosin. The family history was notable for the absence of hypercalcemia or parathyroid disease.

Physical examination revealed a blood pressure of 194/92 mm Hg, loud bilateral carotid bruits, an aortic outflow murmur (3 on a scale of 1 to 6), a sternotomy scar from previous coronary artery bypass grafting, and diminished pulses in the feet. The metacarpophalangeal joints and right knee exhibited joint swelling and effusion.

Laboratory evaluation revealed a serum calcium concentration of 12.9 mg/dL, a phosphorus level of 2.0 mg/dL, and an albumin value of 3.1 g/dL. The serum intact PTH level was 163 pg/mL (normal range, 10 to 65). Renal ultrasonography demonstrated intraparenchymal nephrolithiasis. An office neck ultrasound examination clearly identified a partially calcified, hypoechoic mass (2.3 by 1.3 by 1.6 cm) behind the left lower pole of the thyroid.

A technetium Tc 99m sestamibi (MIBI) parathyroid scan was ordered to confirm the location of the mass seen on ultrasonography. The patient's insurance plan required that parathyroid scanning be performed at a freestanding nuclear medicine facility. Despite the direct request for MIBI as the scanning agent, a TETRO dual-phase scan was performed, which demonstrated only thyroid retention of radionuclide at 120 minutes (Fig. 1 *A*).

Because of progressive dehydration attributable to advancing hypercalcemia, the patient was hospitalized and given fluids intravenously for 48 hours before MIBI-guided parathyroidectomy. On the day of the surgical procedure, the patient demonstrated appreciable MIBI uptake in the area of the left lower neck mass at 120 minutes after injection of the radionuclide (Fig. 1 *B*). After careful dissection, a densely fibrotic mass was exposed and found to exhibit high radioactive emission, as shown by our gamma probe. Intraoperative intact PTH levels decreased dramatically from 254 pg/mL to 28 pg/mL 10 minutes after near-complete resection of the mass, which surrounded the left recurrent laryngeal nerve. Serum calcium levels declined rapidly into the normal range postoperatively, and they remained normal after the patient was dismissed from the hospital. Pathology evaluation of the surgical specimen revealed a 2,000-mg parathyroid carcinoma with cellular atypia and extensive fibrosis.

DISCUSSION

Preoperative scintigraphic scanning of the neck has revolutionized the treatment of hyperparathyroidism during the past 15 years and has facilitated the advent of minimally invasive parathyroid surgical procedures (1-4). Several radiopharmaceutical agents such as MIBI, TETRO, and thallous chloride Tl 201 have been used in parathyroid imaging because of their unique uptake and retention characteristics in parathyroid tissue.

Parathyroid scintigraphy is performed by using two different techniques. The first technique (dual-phase scanning) involves intravenous injection of the radionuclide (MIBI or TETRO) and subsequent imaging at 10 to 20 minutes and 120 minutes. Both thyroid and parathyroid tissues take up the scanning agent at 10 to 20 minutes, with subsequent tissue-specific washout during a period of 60 to 120 minutes. Parathyroid tissue is more likely to retain the radionuclide at 120 minutes. Thus, the typical single parathyroid adenoma is demonstrated scintigraphically by retained radionuclide activity at 120 minutes in association with radionuclide washout in the overlying thyroid parenchyma. Dual-phase scanning with MIBI is the method of choice in the United States, even though

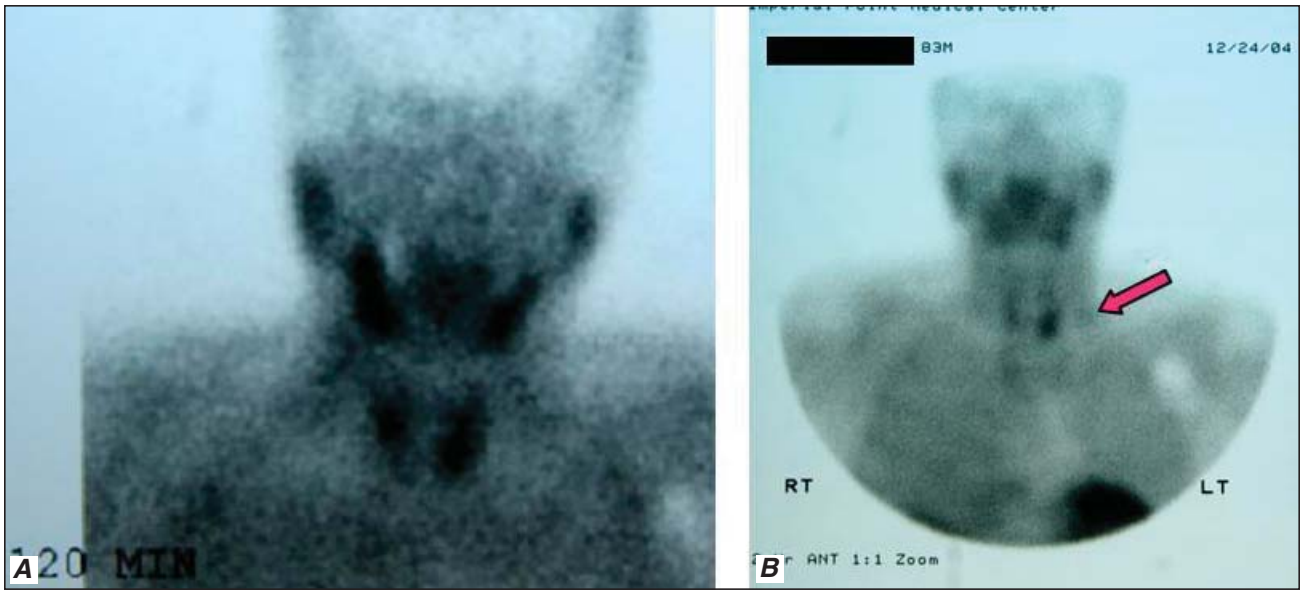

Fig. 1. Comparison of technetium Tc 99m tetrofosmin scan of neck area of study patient at 120 minutes after injection of the radionuclide (*A*) and perioperative technetium Tc 99m sestamibi scan at 120 minutes (*B*). Note retention of radioactive tracer in area of left lower parathyroid gland in sestamibi study (*B, arrow*) in conjunction with radionuclide washout in overlying thyroid tissue. *LT* = left;

TETRO is less expensive to manufacture (9). At least 3 investigative groups in Europe have found TETRO to be less desirable than MIBI in dynamic studies because of its long washout times in both thyroid and parathyroid tissues (6-8).

The second technique involves the staged use of a thyroid imaging radionuclide (for example, iodine 123 or technetium Tc 99m pertechnetate) and a parathyroid imaging agent (MIBI, TETRO, or thallous chloride Tl 201), with subsequent subtraction scanning at a predetermined time depending on the agents used. This technique is technically more demanding (the patient must remain absolutely still) and more expensive than dual-phase scanning with a single parathyroid imaging agent. On the basis of studies performed in Japan and Europe, MIBI and TETRO subtraction scans seem to be equivalent in their ability to distinguish parathyroid adenomas (10,11). The improved performance of TETRO in this context is presumably due to its pronounced avidity for parathyroid tissue. Despite this encouraging preliminary data, the Society of Nuclear Medicine in the United States does not suggest the use of TETRO as a parathyroid scanning agent in its June 2004 imaging recommendations (9).

In our patient, TETRO was retained in parathyroid and thyroid tissues throughout the scanning sequence and especially at 120 minutes (Fig. 1 *A*). Thus, even though TETRO had high avidity for our patient's parathyroid cancer, the similar retention characteristics in the proximate thyroid gland made parathyroid visualization impossible. In contrast, the MIBI imaging at 120 minutes clearly corroborated the ultrasonographic localization of the patient's left lower pole parathyroid carcinoma (Fig. 1 *B*) because of the prolonged retention of MIBI in parathyroid tissue and early washout from the overlying thyroid.

Decision making in modern medicine is frequently driven by cost considerations. Both MIBI and TETRO are readily available from nuclear supply companies because both radionuclides are used for cardiac imaging. In our hospital, the MIBI radionuclide costs $99.30 per parathyroid imaging dose, whereas TETRO is only $64.80 (35% cost savings). The third-party reimbursement for parathyroid scanning is the same regardless of the agent (or agents) used; thus, a financial incentive is created for TETRO substitution. In Florida, because of contractual restrictions, 2 of our 3 radionuclide suppliers do not handle MIBI; therefore, MIBI parathyroid scanning is effectively unavailable to exclusively contracted hospitals and freestanding nuclear facilities.

Although subtraction scanning with synchronous use of TETRO and technetium Tc 99m pertechnetate may be useful in the research setting (10,11), several studies suggest that the more commonly used dual-phase scanning with TETRO alone is less sensitive than MIBI for parathyroid gland localization (6-8). In our case, resection of a large parathyroid carcinoma was delayed for several days as we puzzled over the "negative" parathyroid scintigram. Typical causes for false-negative parathyroid nuclear scans, including upper gland adenoma, parathyroid hyperplasia, multiglandular disease, and small lesion size (12), were not present in our patient. Only after careful review of the radiology report did we discover that the freestanding nuclear facility had substituted TETRO for the MIBI requested. This substitution resulted in a false-negative scan that, in another setting, could have considerably delayed or prevented surgical resection of the parathyroid carcinoma.

CONCLUSION

Our review of the nuclear medicine literature suggests that although MIBI and TETRO have the same technetium Tc 99m radiolabel, they are not equivalent when used as dual-phase parathyroid scanning agents. We describe a patient with parathyroid cancer whose large (2,000-mg) carcinoma was missed by TETRO parathyroid scanning and easily recognized with neck ultrasonography and MIBI scanning. We would caution all endocrine physicians and endocrine surgeons to be alert for radionuclide substitutions with parathyroid scintigraphy, particularly if the dual-phase technique is used. Before allowing free substitution of TETRO for MIBI in dual-phase parathyroid scanning, we should, at the very least, demand a head-to-head, prospective, dual-phase scanning trial in patients with hyperparathyroidism.

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