PRELIMINARY NOTE

New Perspectives in Localizing Enlarged Parathyroids by Technetium-Thallium Subtraction Scan

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Double-tracer scanning (Tc-99m as pertechnetate and Tl-201 as chloride) with an Anger camera and computerized image subtraction was performed in 61 patients whose clinical and biochemical findings had suggested primary hyperparathyroidism. This study showed intra- or extrathyroidal focal uptake of thallium in 37 cases. Among these, 24 patients underwent surgery, and 18 parathyroid adenomas, five carcinomas, and one hyperplastic gland were found exactly in the sites predicted by scintigraphy. Among 24 patients with negative scans, only two underwent surgery; a hyperplastic parathyroid gland (diam < 0.5 cm) was found in both. The success rate was 92% in the cases in which operation was performed. We believe that the new method may be useful in the preoperative detection of parathyroid enlargements.

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The preoperative location of enlarged parathyroids—a most important step in the surgical approach to primary hyperparathyroidism—has always presented difficulties. For this reason numerous diagnostic procedures have been proposed and used, including scintigraphy.

The traditional scintigraphic methods, which use Se-75 methionine as an indicator, have not given satisfactory results (*1*). Moreover, the double-tracer and image-subtraction techniques have not greatly improved the detection of the enlarged parathyroids, whether they use Se-75 methionine and I-125 (*2*), Se-75 methionine and I-131, (*3*), or Se-75 methionine and pertechnetate, with a gamma camera as the examining instrument (*4*). Recently we reported positive scintigraphic patterns using cesium-131 (*5*) and in some of the same patients, thallium-201 (*6*); the latter makes it possible to perform the study with a computerized gamma camera, with two tracers and image subtraction.

This method has been applied in a large number of patients with suspected primary hyperparathyroidism, and in this note we report the results.

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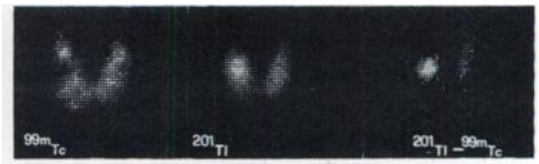
MATERIALS AND METHODS

We examined 61 selected patients (41 females and 20 males, aged 21 to 83, average 51) whose clinical and biochemical data (calcemia, phosphoremia, calciuria, phosphaturia, alkaline phosphatase, peripheral PTH) suggested that they had primary hyperparathyroidism. Only two of these patients had a palpable node in the neck.

For this investigation a gamma camera was equipped with a pinhole collimator and an on-line computer. One mCi of $^{99m}TcO_4^-$ was injected i.v. 20 min before the patient was placed under the camera with the neck extended. A 50,000-count static image was recorded using the Tc-99m photopeak, after which 1 mCi of thallium-201 was injected. For the next 25 min, two images were stored per minute in a 64 by 64 matrix, with a 25% window centered at 80 keV. The technetium image was then recalled on the computer display. A region of interest was marked over the whole thyroid image. Subsequently the thallium image series was displayed and normalized to that of the technetium. With appropriate subtraction it is possible to recognize extra- or intrathyroidal areas of increased thallium uptake if it is present.

LEFT INFERIOR PARATHYROID ADENOMA

FIG. 1. Focal uptake of Tl-201 (b) is evident below left inferior pole of Tc-99m thyroid image (a). This area is better visualized after subtraction (c).



RIGHT SUPERIOR PARATHYROID ADENOMA

FIG. 3. A case in which increased thallium uptake (b) corresponds to photopenic area in pertechnetate image (a), better seen in subtraction image (c).

RESULTS

In 24 patients the scintigrams were considered negative, whereas they were positive in 37 cases where they showed abnormal thallium uptake.

The scintigraphic patterns were as follows: In 12 patients focal uptake of thallium was found in an extrathyroidal site: in 11 immediately below the right or left inferior pole of the thyroid (Fig. 1), and in one completely outside in an ectopic site (Fig. 2 below). In 15 other cases Tl-201 uptake areas corresponded to photopenic technetium areas (Fig. 3). In ten patients we observed a relatively high thallium uptake corresponding to diminished areas of technetium area (Fig. 4). In all cases, thallium areas were more prominent after subtraction of the Tc-99m image (Figs. 1c,3c,4c).

Twenty-four out of 37 positive patients underwent surgery, and in all cases there was correspondence between the scintigraphic location and the anatomical site. Table 1 shows the results of the scintigraphic examination and the gross and histological findings obtained by surgery. The microscopic findings were checked by pathologists in two institutions and the results, identical in each case, were as follows: one hyperplastic gland, five carcinomas, 17 chief-cell adenomas, and one oxyphilic-cell adenoma.

The scintigram was also positive in a case of oxyphilic-cell adenoma (Fig. 2, above) which neither TCT nor ultrasonography located in spite of its considerable mass of 4 grams. We had a similar result in a case of adenoma in an ectopic site (Fig. 2, below), namely high in the mediastinum, not found during previous exploratory neck surgery. Another patient showed increased activity in the right inferior pole of the thyroid and partially outside it, whereas surgical neck exploration gave a negative report. Since biochemical and clinical findings were persistently abnormal, a second scan was performed. This (Fig. 5, top) confirmed the previous result and a retrograde phlebography, taken in the course of venous sampling, showed an adenoma in the same site as that indicated by scintigraphy. In one case among those considered scintigraphically positive, surgery revealed a macrofollicular adenoma of the thyroid, a small parathyroid adenoma in the thyroid, and a small parathyroid adenoma immediately above it (Fig. 5, bottom).

LEFT INFERIOR PARATHYROID ADENOMA(in a retroclavicular site)

ECTOPIC PARATHYROID ADENOMA

FIG. 2. Above: oxyphilic-cell adenoma in retroclavicular site. Below: adenoma in an ectopic site.

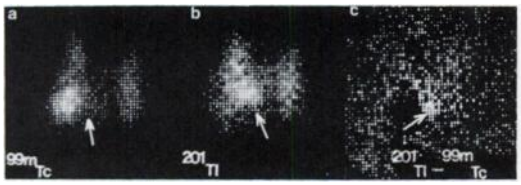
Two out of 24 thallium-negative patients underwent surgery on the basis of results obtained from other tests, particularly serum PTH, obtained either peripherally or through specific venous sampling. A hyperplastic gland was found in both, though it was less than 0.5 cm in diameter.

Of the other patients with positive scintigrams as with the patients found negative with thallium, some have refused surgery while others are still under observation. In eight patients whose scintigrams proved negative, diagnosis of hyperparathyroidism was not confirmed in subsequent check-ups because of the spontaneous normalization of the calcemia and peripheral PTH, or normal selective PTH measurements, and also because of an improvement in clinical symptoms. Since a pattern of "a poussées" is typical of primitive hyperparathyroidism, which alternates phases of parathyroid hyperactivity and normal functioning, we have kept these eight patients under clinical and biochemical observation.

DISCUSSION

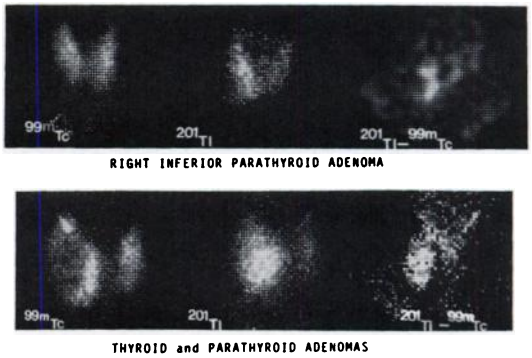
Up to now, it has not been possible to evaluate the real sensitivity and accuracy of the method because not all patients underwent surgery; we can affirm, however, that scintigraphy with radiothallium using our procedure has correctly identified 24 out of 26 pathological parathyroids—a 92% success rate. This is better than our results with cesium-131 (*5*) or those reported by others (*3,4*).

The two false-negative results were due to the rather small dimensions of the glands, which in both cases were



RIGHT INFERIOR PARATHYROID ADENOMA

FIG. 4. Prominent thallium uptake (b,c) corresponds to decreased area of activity in Tc-99m thyroid image (a).



RIGHT INFERIOR PARATHYROID ADENOMA

THYROID and PARATHYROID ADENOMAS

FIG. 5. Above: right inferior parathyroid adenoma not found during previous neck surgery. Below: macrofollicular adenoma of thyroid with small parathyroid adenoma immediately above it.

less than 0.5 cm in diameter. This appears to be the resolution limit of the method.

It can be assumed that thallium accumulation, even if not clearly understood, seems to be related to an increased regional blood flow (*7*) or to its biological distribution analogous to that of potassium (*8*,*9*). These properties probably explain thallium uptake in areas of high cellular density such as enlarged parathyroids. For this reason we observed the same scintigraphic pattern in the one positive case of hyperplasia, in the carcinomas, and in the adenomas; consequently this technique does not enable us to differentiate between benign and malignant parathyroid tumors. One drawback of our method lies in the fact that thallium also accumulates in photopenic thyroid masses with high cellular density (*9*); thus it is not possible to distinguish clearly between parathyroid and thyroid nodular disease. This, however, is the limitation of other indicators used in parathyroid scintigraphy such as Se-75 methionine (*4*) and Ga-67 citrate (*10*). In our study this difficulty occurred in one case, considered partially positive, in which both parathyroid and thyroid adenomas existed and could not be

TABLE 1. CORRELATION OF THE PARATHYROID SCAN WITH SURGICAL FINDINGS

Patient	Sex	Age	Scintigraphy	Correl.	Size (cm)	Histology
1	F	42	LI	Corr.	1.5 × 1.5 × 1.2	Carcinoma
2	F	63	RI	Corr.	1.0 × 0.8 × 0.5	Carcinoma
3	F	51	RI	Corr.	1.2 × 1.0 × 0.5	Chief-cell ad.
4	F	54	LI	Corr.	2.5 × 2.0 × 1.5	Chief-cell ad.
5	F	49	RI	Corr.	2.0 × 1.5 × 1.5	Chief-cell ad.
6	F	69	RS	Corr.	2.0 × 1.5 × 1.5	Chief-cell ad.
7	M	29	LI	Corr.	2.0 × 1.5 × 1.5	Carcinoma
8	F	44	RI	Corr.	0.5 × 0.5 × 0.5	Chief-cell ad.
9	M	57	RI	Corr.	9.0 × 4.0 × 3.0	Chief-cell ad.
10	F	43	RI	Corr.	0.8 × 0.5 × 0.5	Hyperplasia
11	F	59	LI	Corr.	1.5 × 1.2 × 1.0	Chief-cell ad.
12	F	70	RI	Corr.	2.5 × 1.5 × 1.0	Carcinoma
13	M	54	RI	Corr.	2.0 × 2.0 × 1.5	Chief-cell ad.
14	M	40	neg.	Incorr.	0.5 × 0.2 × 0.2	Hyperplasia
15	F	40	LI	Corr.	2.0 × 1.8 × 1.5	Chief-cell ad.
16	F	69	LI	Corr.	1.5 × 1.5 × 1.0	Chief-cell ad.
17	M	55	LI	Corr.	1.5 × 1.0 × 1.0	Chief-cell ad.
18	F	51	LI	Corr.	1.5 × 0.8 × 0.8	Chief-cell ad.
19	F	59	LI	Corr.	2.0 × 2.0 × 1.5	Chief-cell ad.
20	F	54	LI	Corr.	1.5 × 1.5 × 1.0	Chief-cell ad.
21	M	68	LI	Corr.	3.0 × 2.0 × 2.0	Carcinoma
22	M	53	neg.	Incorr.	0.4 × 0.4 × 0.2	Hyperplasia
23	F	59	LI	Corr.	1.5 × 0.8 × 0.5	Chief-cell ad.
24	M	51	RI	Corr.	2.0 × 1.8 × 1.5	Oxyphil. cell ad.
25	F	45	LI	Corr.	2.0 × 2.0 × 1.8	Chief-cell ad.
26	M	45	ectopic	Corr.	2.0 × 2.0 × 1.5	Chief-cell ad.

R = right; L = left; S = superior; I = inferior.

distinguished on the basis of scintigraphy (see Fig. 5). It must be stressed, however, that this type of examination is to be performed only in selected patients in whom clinical and biochemical data suggest parathyroid hyperactivity.

We believe this simple, noninvasive method, with its low radiation dose, is useful in the detection of enlarged parathyroids prior to surgery.

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