

Tc-99m-MIBI scintigraphy for recurrent hyperparathyroidism after total parathyroidectomy with autograft

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The aim of this study is to assess the sensitivity of Tc-99m-MIBI for the pre-operative localization of hyperfunctioning parathyroid glands in patients with persistent or recurrent hyperparathyroidism (HPT) after total parathyroidectomy (PTX) with autograft. **Patients and Methods:** Tc-99m-MIBI scintigraphy was performed on 7 patients (3 men and 4 women; aged 32 to 62) on hemodialysis with persistent or recurrent HPT after PTX due to secondary hyperparathyroidism. Tc-99m-MIBI of 370 MBq was injected intravenously. Double-phase planar images were acquired at 15 min and 120 min-postinjection. SPECT images of the chest in an early phase were also obtained. **Results:** All patients underwent surgery after scintigraphy. The enlarged parathyroid grafts were removed in 4 patients. An unusual location of parathyroid hyperplasia was found in 2 patients. In one patient, the abnormal graft coexisted with an ectopic parathyroid in the mediastinal region. Tc-99m-MIBI was able to identify all hyperfunctioning parathyroids correctly (100% sensitivity). In one case, a focus of the increased uptake in SPECT was considered as a false positive. The remnant of ectopic parathyroid in the mediastinum was only detected by SPECT images. **Conclusion:** Tc-99m-MIBI parathyroid scintigraphy is useful for the pre-operative localization of persistent or recurrent HPT following total PTX with autograft.

Key words: Tc-99m-MIBI, hyperparathyroidism; recurrent, autograft, ectopic

INTRODUCTION

SECONDARY HYPERPARATHYROIDISM (HPT) is a common problem in patients on hemodialysis for end-stage renal disease. Most of the patients are controlled medically but a subset of them develops severely symptomatic secondary HPT that requires total parathyroidectomy (PTX) with/without autografting or subtotal PTX for hyperfunctioning parathyroid.^{1,2} The necessity of pre-operative localization of these abnormal parathyroids is controversial because of the high success rate of 95% achieved by experienced surgeons.³ In contrast, once persistent and recurrent HPT after PTX is confirmed by clinical symp-

toms and laboratory tests, localization of the source of excessive parathyroid hormone (PTH) secretion which may be caused by ectopic, supernumerary, missed or grafted parathyroid should be identified by imaging techniques.^{4,5}

Tc-99m-MIBI scintigraphy has been used in the localization of hyperfunctioning parathyroid tissue in patients with primary or secondary HPT^{6–10} as well as recurrent HPT after the operation.¹¹ We evaluated the diagnostic accuracy of scintigraphy in the pre-operative localization of abnormal parathyroid tissue in patients with persistent or recurrent HPT following PTX with autograft.

PATIENTS AND METHODS

Seven patients (3 men and 4 women; aged 32 to 62) were enrolled in the present study. They were treated on hemodialysis for end stage renal disease and were suspected of having persistent or recurrent hyperparathyroidism after PTX with autograft.

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Table 1 Clinical, laboratory, surgical and histological profiles of the patients studied

Case No.	Gender	Age	Re-operation after previous surgery	Laboratory Tests						Surgical Exploration		
				Intact PTH (pg/ml)		Ca (mg/dl)		P (mg/dl)		location	weight (mg)	histology
				pre	post	pre	post	pre	post			
1	man	49	6.5 years	990	96	9.7	7.5	5.5	4.1	graft	1430	hyperplasia
2	man	36	3 years	820	110	10.1	9.6	2.7	2.9	RLR	1530	hyperplasia
3	woman	58	7.3 years	1000	42	11.8	8.9	6.3	3.9	graft	4750	hyperplasia
4	woman	58	5 years	540	160	10.4	8.1	—	5.6	graft	2210	hyperplasia
5	woman	62	9.6 years	470	120	10.1	8.9	5.5	3.8	graft	450	hyperplasia
6	woman	48	2.5 years	600	42.6	11.3	10.4	4.2	3.2	graft	1134	hyperplasia
			3 months	610	170	12.5	9.6	4.9	3.4	AM	5000>	hyperplasia (cystic)
7	man	32	1 year	360	250	10.3	8.0	4.8	3.6	LUM	460	hyperplasia

Abbreviations; pre: pre-operation, post: post-operation, RLR: right lower region of the thyroid gland, AM: anterior mediastinum, LUM: left upper mediastinum

Normal range: intact PTH = 10–65 pg/ml, Ca (calcium): 8.7–10.1 mg/dl, P (phosphorus): 2.4–4.3 mg/dl

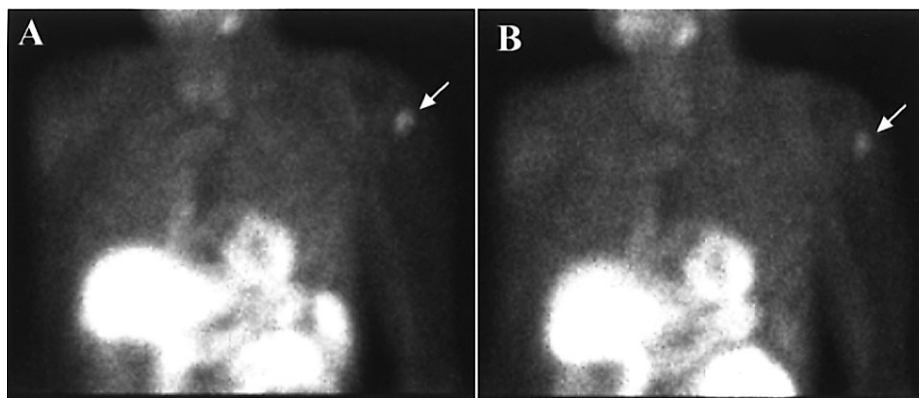


Fig. 1 Early-phase (A) and delayed-phase (B) planar images with Tc-99m-MIBI in a patient (case No. 1) with autograft-dependent hyperparathyroidism. Both left anterior oblique images demonstrate increased uptake in the autograft in the left upper arm (arrows). An early-phase image is clearer in the positive delineation of abnormal graft than a delayed-phase one.

Double-phase parathyroid scintigraphy^{7,12} was performed at 15 and 120 minutes after injection of 370 MBq Tc-99m-MIBI (Daiichi Radioisotope Laboratories, Ltd., Tokyo, Japan). Each image was obtained by a dual-headed gamma camera (E.CAM plus GMS-5500A/P, Toshiba, Tokyo, Japan), low-energy high-resolution parallel-hole collimator, $\pm 10\%$ window at 140 keV, scatter correction with triple energy window (TEW) and 256×256 matrix. Magnified images by 2.23 for the neck and 1.23 for the chest were taken at the preset time of 5 minutes and 4 minutes, respectively. SPECT was also performed only in the early phase. Thirty 15-second images were taken by each head over 180 degree step-wise rotation and stored in a 128×128 matrix of a frame mode. Images were reconstructed using Butterworth pre-filter, Ramp post-filter and mathematical algorithm of ordered subsets expectation maximization (OSEM).

Double-phase planar and early-phase SPECT images were interpreted visually by one observer (K.I.). If increased focal uptake more than the surrounding tissues

such as thyroid, chest and arm muscle was observed, the study was interpreted as positive.

RESULTS

All patients were operated on approximately one month following scintigraphy (Table 1). The interval of re-operation after the previous PTX ranged from 3 months to 9.6 years with an average of 4.4 years. Pre-operative intact PTH level was elevated in the range of 360–1000 pg/ml with an average of 673.8 pg/ml (normal range: 10–65 pg/ml). Post-operative PTH level was significantly decreased to the range of 42–250 pg/ml with an average of 123.8 pg/ml ($p < 0.0001$ in the paired t-test). The weight of the removed specimens ranged from 450 mg to 5,000 mg with an average of 2,120 mg. Histological examination proved hyperplasia in all.

All 8 removed parathyroid glands demonstrated increased uptake by Tc-99m-MIBI scintigraphy. The graft was positive in 4 patients (case No. 1, 3, 4, 5) (Fig. 1). In

one patient (case No. 3), the graft was a true positive but an increased uptake in the left upper mediastinum in the SPECT image was considered to be a false positive (Fig. 2). In 2 patients (case No. 2, 7), the graft did not show increased uptake. A focal area of increased uptake in case No. 2 was observed in the right lower pole of the thyroid. The removed gland was considered a supernumerary parathyroid because four parathyroids had already been

removed at the previous operation. In case No. 7, 2 abnormal glands in the lower poles of the thyroid were removed at the initial surgery, while other glands were not identified. The removed glands showed increased uptake in the pre-operative Tc-99m/Tl-201 subtraction scintigraphy. Tc-99m-MIBI scintigraphy (Fig. 3) was performed 6 months and 11 months after the initial PTX, because elevated PTH level persisted. These studies demonstrated

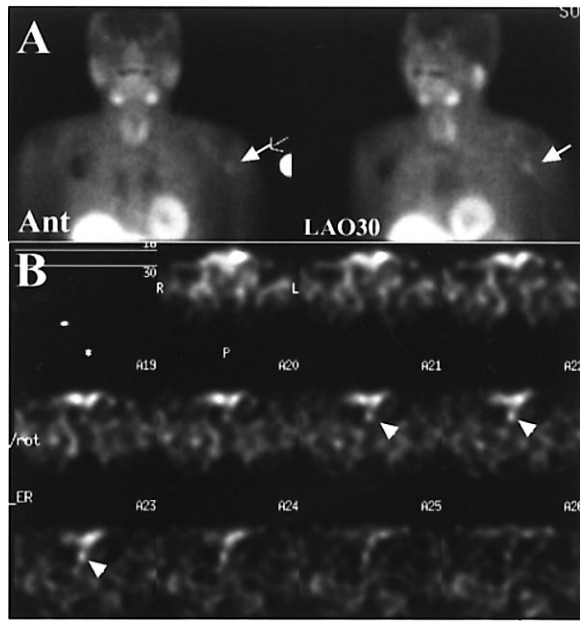


Fig. 2 Early-phase planar (A) and SPECT (B) images with Tc-99m-MIBI in a patient (case No. 3) with autograft-dependent hyperparathyroidism. Planar images demonstrate increased uptake in the autograft in the left upper arm medially (arrows). SPECT images shows increased focus in the left upper mediastinal region adjacent to the trachea (arrowheads). This was considered as a false-positive because clinical symptoms and PTH improved promptly after the removal of the enlarged autograft and no recurrence was observed.

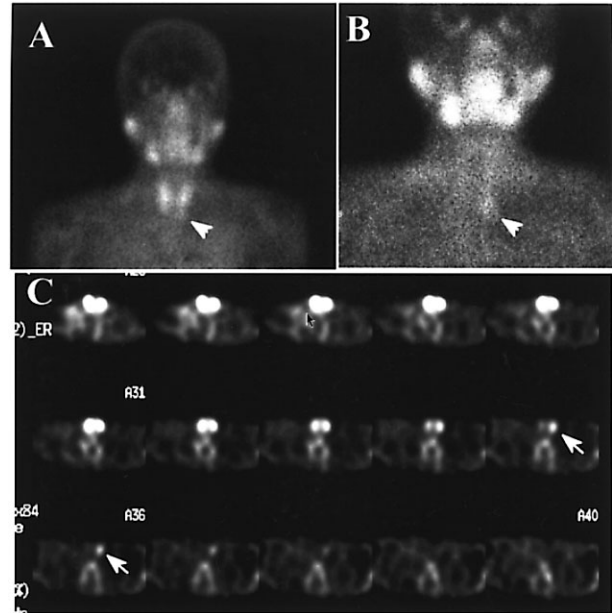


Fig. 3 Tc-99m-MIBI parathyroid scintigrams in a patient (case No. 7) with secondary HPT due to the missed parathyroid hyperplasia. The planar image A and B were obtained 6 months after the PTX with the autograft. A delayed-phase image (B) is better in the positive delineation of abnormal gland (arrowheads) than an early-phase image (A). The early-phase SPECT image (C) shows a focus of increased uptake (arrows) just below the lower region of the left thyroid.

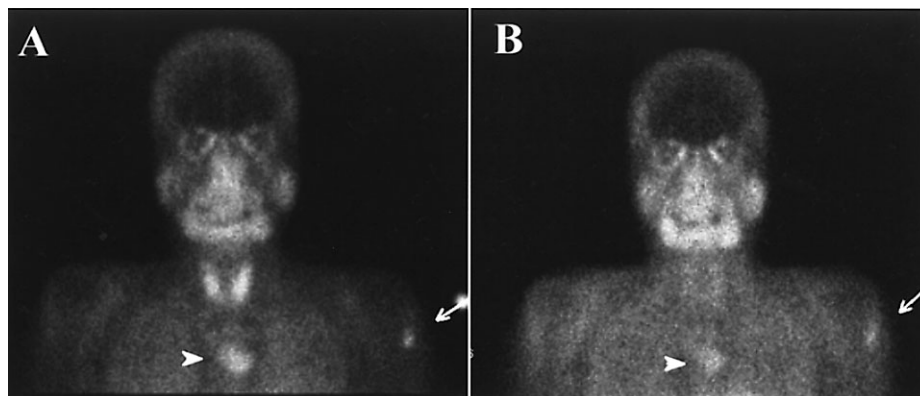


Fig. 4 Early-phase (A) and delayed-phase (B) planar images with Tc-99m-MIBI in a patient (case No. 6) with recurrent HPT caused by co-existence of hyper-functioning autografted (arrow) and ectopic (arrowhead) parathyroid glands.

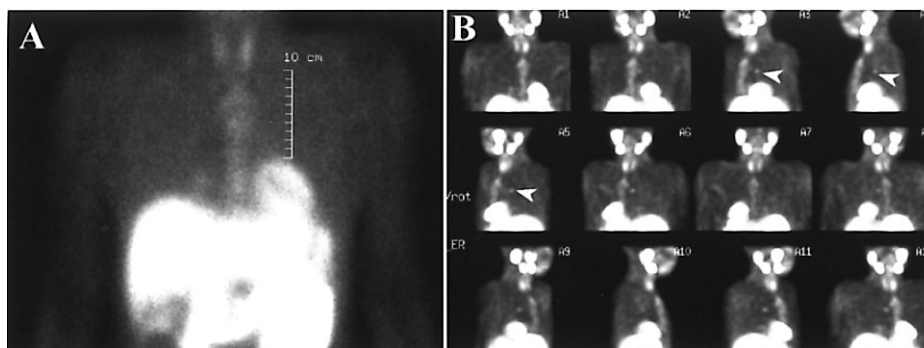


Fig. 5 An early-phase planar image (A) and 3 dimensional MIP image (B) in the same patient of Figure 3. These images were obtained 1 month after the removal of the ectopic parathyroid in the mediastinum. The repeated scintigram 8 months later also showed the same findings.

increased uptake in the left upper mediastinum just below the inferior pole of the left thyroid lobe. A focus of parathyroid hyperplasia in the left upper mediastinum was removed by the re-operation.

Case No. 6 showed 2 foci of increased uptake in the autograft in the left upper arm and in the mediastinal region (Fig. 4). This patient underwent two separate operations: the first for removal of the abnormal autograft and the second for a mediastinal tumor 3 months later. Tc-99m-MIBI scintigraphy was repeated 1 month and 8 months following the removal of the mediastinal ectopic parathyroid which showed cystic degeneration because of persistent elevation of intact PTH. Repeat studies showed focal uptake in the same region of the mediastinum, only identified in the SPECT image (Fig. 5). This finding highly suggested the existence of a remnant of the ectopic parathyroid. The patient has been followed up for further surgical intervention.

In comparing positive delineation of abnormal parathyroid glands, early-phase images were superior or equal to delayed-phase images in 7 foci in 6 patients. Incidentally, sternal uptake was observed in 6 of 7 patients.

DISCUSSION

The main reasons for unsuccessful PTX for primary HPT and necessity for re-operation were summarized in 102 patients⁴: 1) parathyroid tumor located in an atypical position (ectopic) in 53%, 2) incomplete resection of multiple abnormal parathyroid glands (supernumerary) in 37%, 3) missed resection of parathyroid tumor in normal position in 7%, 4) regrowth of a partially resected parathyroid tumor in 3%. In patients with PTX with autograft, hyperfunction of the graft should be added to the above reasons.^{13,14} Although the exact recurrence rate of autograft-dependent HPT is not known, it is presumed to range from 3% to 10%.¹⁴⁻¹⁶ Preoperative localization of the excessive PTH source is important to a patient with

recurrent HPT after previous neck surgery, because scarring and distortion of normal tissue, as well as a high incidence of ectopic location render surgical neck exploration difficult. If recurrent HPT is due to the autograft, the surgery for this is simpler than neck operation.

In our present study, 4 of 7 patients (57%) had autograft-dependent HPT. In the other 3 patients, persistent and recurrent HPT was caused by either a supernumerary gland, or unrecognized location of the glands, or co-existence of an ectopic parathyroid and the graft. Tc-99m-MIBI parathyroid scintigraphy identified all abnormal parathyroid glands preoperatively (100% sensitivity). According to a review on parathyroid scintigraphy by Pattou et al.,¹⁷ the sensitivity of Tc-99m-MIBI scintigraphy for pre-operative localization of primary, secondary and recurrent HPT after previous operation are 71% to 100% with an average of 87% in collected 984 patients, 8% to 67% with an average of 29% in collected 303 patients and 59% to 100% with an average of 75% in 240 patients, respectively. The sensitivity of Tc-99m-MIBI parathyroid scintigraphy is affected by the functional status of hyperplastic parathyroid rather than the weight of the gland.¹⁸ Positive uptake in the autograft is also reported to be correlated well with the gradients in PTH levels.¹¹

Several technical manipulations from the first report by Coakley et al.⁶ have been studied: double-phase,⁷ factor analysis of dynamic structure,¹⁹ subtraction (Tc-99m-pertechnetate or I-123),^{20,21} parallel or pinhole collimation¹² and planar and SPECT imaging techniques.⁹ Intraoperative scanning has recently been proposed for enhancement of sensitivity and for minimally invasive surgery.²² In the present study, an early-phase planar image with a parallel-hole collimator was able to demonstrate all abnormal autografts. The results indicate that the early-phase image may be sufficient to identify autograft abnormality. SPECT in an early phase appears to enhance the detectability of abnormal ectopic parathyroid in the mediastinum,⁹ while we experienced a false positive

result in the left upper mediastinal region. The reason is not known but indicates that SPECT may also produce a false positive result.¹⁷ Several causes of errors for the interpretation of SPECT images are thought to exist: technical and image-processing differences, inadequate experience of the diagnostic physicians, and unexpected distribution of Tc-99m-MIBI. We often observed sternal uptake which was due to an unexpected distribution which tended to lead to a wrong interpretation of unusual location of the parathyroid. These findings in SPECT image of Tc-99m-MIBI in the chest seem to be important to avoid a false positive result.

Although our experience is limited to a small number of patients, recurrent HPT was related to autografts implanted 2.5 to 9.6 years (average 6.1 years) following the previous PTX. In contrast, persistent and recurrent HPT caused by an abnormal parathyroid gland rather than the transplanted graft was operated on in an average 1.4 years. The parathyroid autograft may take a longer time than ectopic or missed parathyroid to act as a source of excessive PTH after removal of hyperfunctioning parathyroids. Hemodialysis itself is considered to be a stimulator to parathyroid gland hyperfunction.^{1,2}

CONCLUSION

Causes of persistent or recurrent HPT after total PTX with autograft are variable. Autograft-dependent HPT may be more frequent than ectopic gland HPT. For the identification of abnormal autograft, early-phase planar imaging seems to be better than a delayed-phase imaging. SPECT in an early phase is helpful in disclosing ectopic parathyroid glands in the mediastinum. Tc-99m-MIBI parathyroid scintigraphy is useful for the pre-operative localization of hyperfunctioning parathyroid glands in patients with persistent or recurrent HPT after PTX with autograft.

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