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Tc-99m-MIBI scintigraphy for detecting parathyroid adenoma and hyperplasia

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We performed scintigraphy with technetium-99m-methoxyisobutylisonitrile (MIBI) in 10 patients with parathyroid adenoma (7 lesions) or hyperplasia (9 lesions). Correlation between an amount of accumulation of MIBI and histological types of the lesions were evaluated with special reference to an amount of oxyphilic cell in the lesions. Selected lesions were also evaluated for mitochondrial density by electromicroscopy and showed increased mitochondrial density in the oxyphilic cells. All lesions equal to or above 220 mg showed positive scintigraphic results despite differences in cell types. Undetected lesions were all equal to or below 100 mg. The scintigraphic results for 2 lesions with abundant oxyphilic cells were both positive although those for 11 lesions with abundant chief cells only 6 were positive, probably because these lesions were smaller in the hyperplasia group. In conclusion, MIBI uptake in parathyroid lesions was not dependent on the cell type but either on the size or functional state of the lesions.

Key words: Tc-99m-MIBI, parathyroid adenoma, parathyroid hyperplasia, hyperparathyroidism, parathyroid scintigraphy

INTRODUCTION

Tc-99m-methoxyisobutylisonitrile (MIBI), a myocardial perfusion imaging agent used as an alternative to Tl-201, is now being widely used to visualize various tumors.[1] Among these, parathyroid adenoma or hyperplasia is considered a good candidate for imaging by this agent.[2–4] The usefulness of MIBI in parathyroid imaging is thought to be due to the relationship of the cellular uptake mechanism of MIBI to mitochondrial membrane potentials,[5,6] although recent studies have shown that MIBI uptake is also related to the cell membrane Na^+/H^+ antiport system and may involve the Na^+,K^+-ATPase system.[7] Parathyroid adenoma, especially with oxyphilic cells, is thought to possess abundant mitochondria.[8] MIBI is therefore thought to accumulate strongly in parathyroid adenoma or hyperplasia.[2]

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In this study we precisely evaluated the histological findings in parathyroid lesions including electromicroscopic findings and compared them with the findings obtained by MIBI scintigraphy.

MATERIALS AND METHODS

Altogether 16 lesions were evaluated, including 7 adenomas in 7 patients (6 females and 1 male, 32–74 years old) and 9 hyperplastic lesions in 3 patients (3 males, 11–59 years old). All lesions were confirmed histopathologically after surgery. Parathyroid scintigraphy was performed 2–4 weeks before surgery. After injecting a dose of 740 MBq of Tc-99m-MIBI (Cardiolite, Daiichi Radioisotopes Laboratory Co. Ltd., Tokyo, Japan), the images were obtained with a Toshiba GCA-10A gamma camera (Tokyo, Japan) fitted with a low energy, parallel hole high resolution collimator and a 20% energy window centered on the 140 KeV peak. Five-minutes anterior neck images were obtained at 5 minutes, 1 hour and 2 hours after injection of the tracer. The scintigraphic findings were interpreted as positive (+) when the accumulation of MIBI in lesions was apparent and separable from the residual thyroid activity at 1 or 2 hours, equivocal (±)

Table 1 Details of the patients, weight/size, cellular component and scintigraphic findings of parathyroid lesions

Age (yrs)	Sex	Weight/Size	Cellula component	MIBI scintigraphy
Adenoma				
40	F	2,500 mg	70–80% chief cells	+
57	M	1,410 mg	Mostly chief cells	±*
32	F	500 mg	Mostly chief cells	+
56	F	420 mg	70–80% chief cells	+
74	F	380 mg	70–80% chief cells	+
48	F	15 × 10 × 7 mm	Mostly chief cells	+
44	F	13 × 13 × 8 mm	Mostly oxyphilic cells	+
Hyperplasia				
41	M	7,200 mg	Mostly chief cells	+
		900 mg	70–80% oxyphilic cells	+
		100 mg	Mostly chief cells	–
		100 mg	Mostly chief cells	–
11	M	220 mg	Mostly chief cells	+
		60 mg	Mostly chief cells	±
		50 mg	Mostly chief cells	–
59**	M	1,100 mg	Mostly chief cells	+
		780 mg	Mostly chief cells	–

F = female, M = male, * = The lesion became (+) 6 hours after RI injection, ** = Patient was treated with ethanol injection before scintigraphy.

Table 2 Image interpretation in relation with time of acquisitions

2 hours images = early and 1 hour images in 4 lesions
2 hours images > early and 1 hour images in 7 lesions
2 hours images < early and 1 hour images in 1 lesion

when accumulation in the lesions was more than the surrounding background activity but was not easily separable from residual thyroid activity, and negative (–) when there was no apparent activity in the lesions.

Postoperative specimens were evaluated for their weight or size, and histological cellular types, especially an abundance of oxyphilic cellular components. The histological types of the lesions were evaluated by an experienced pathologist without any knowledge of MIBI scintigraphic results.

To evaluate mitochondrial abundance, selected lesions with chief and oxyphilic cells were prepared for electromicroscopic evaluation by a standard preparation method and was analyzed under a 75 KeV, H-6000 electron microscope of Hitachi, Japan.

RESULTS

Table 1 shows details of patients, lesions, histological types and MIBI scintigraphic results. All cases of adenoma showed (+) scintigraphic results, while only 4 of 9 hyperplastic lesions, showed (+) scintigraphic results. One large lesion (780 mg) was (–), probably because the patient was treated with ethanol injection before MIBI scintigraphy. One very small lesion (60 mg) showed (±) scintigraphic results. The smallest lesion detected clearly was 220 mg. The scintigraphic results for 2 lesions with abundant oxyphilic cells and lesion sizes of 13 × 13 × 8 mm and 900 mg each, were both (+), but the scintigraphic results for 11 lesions with abundant chief cells and lesion sizes varying from 50 mg to 7,200 mg in weight were (+) in 6 lesions. The scintigraphic results for the remaining 3 lesions, which had a 70–80% predominance of chief cell were (+) in all three.

Table 2 shows the advantage of a time intervals for clear visualization of the lesions. Of 12 lesions detected, 4 showed similar visualization at all time intervals, 7 showed better visualization after 2 hours, and only 1 showed better visualization on the early image. Of 2 lesions with abundant oxyphilic cells, one showed similar visualization at all time intervals and the other showed better visualization after 2 hours.

Figure 1 shows typical electromicroscopic findings for chief and oxyphilic cells. Oxyphilic cells contained noticeably abundant mitochondria compared to those of the chief cells. Figure 2 shows a case of oxyphilic cell adenoma (13 × 13 × 8 mm) in a 44-year-old woman. Later images showed better visualization of the lesion. Figure 3 shows images of chief cell adenoma (500 mg) in a 32-year-old woman. The early image showed better visualization of the lesion. Figure 4 shows images of parathyroid hyperplasias weighing 7,200, 900, 100 and 100 mg. Only the two larger lesions were visualized. The 7,200 mg lesion was primarily chief cells, but the 900 mg lesion

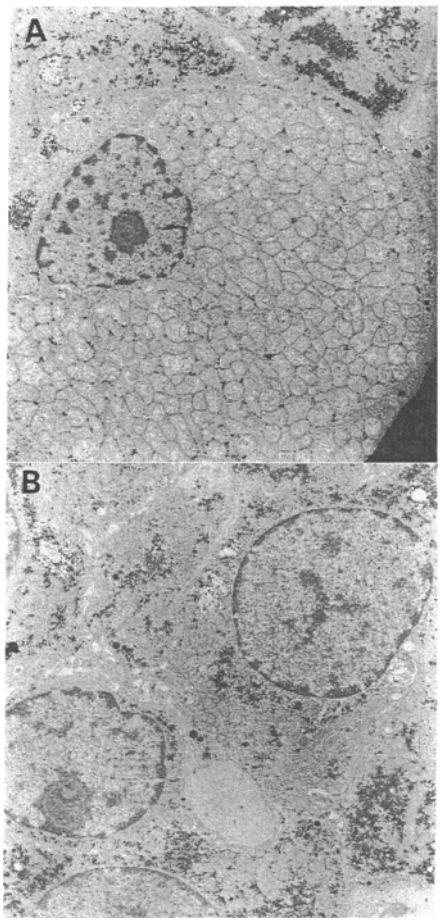

Fig. 1 Shows electromicroscopy of (A) oxyphilic cells (× 4,000) and (B) chief cells (× 5,000). Note the size and mitochondrial density in both cells. Despite higher magnification, the chief cells were smaller than oxyphilic cells and the oxyphilic cells were fully packed with mitochondria inside the cytosol with a smaller nucleus.

(arrow) showed a 70–80% predominance of oxyphilic cells.

DISCUSSION

To date many reports have shown the superiority of MIBI imaging in the detection of parathyroid lesions compared to the Tl-201 and Tc-99m pertechnetate subtraction technique.[3,9] Irvin III et al.[10] reported that MIBI scintigraphy of parathyroid lesions had improved the management of parathyroid surgery and was cost effective. Regarding the uptake mechanism, O'Doherty et al.[2] suggested that the uptake in the parathyroid lesion could be due to mitochondrial abundance in these lesions but, there is no published paper relating the findings of MIBI scintigraphy to cellular types, especially mitochondrial density in the cells. In this report, we precisely evaluated the cellular type of each lesion and related the results to the scintigraphic findings.

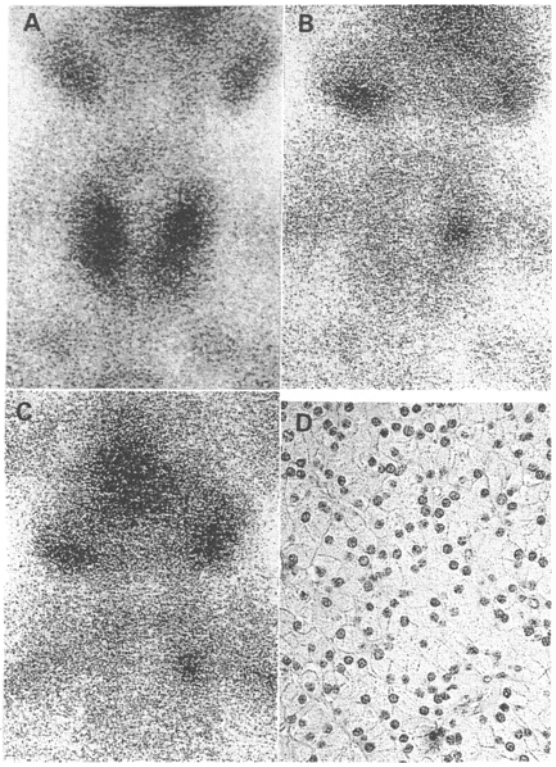

Fig. 2 Shows oxyphilic cell adenoma. (A) 5-minute, (B) 1-hour and (C) 2-hour images. Note that both 1-hour and 2-hour images showed better visualization. (D) Histopathology of the adenoma showed mostly oxyphilic cells.

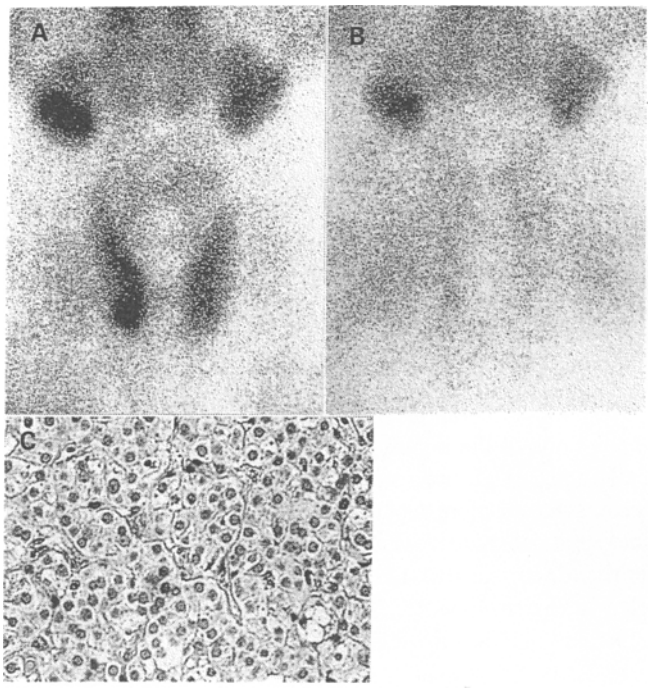

Fig. 3 Shows chief cell adenoma. Early image (A) showed better visualization of the tumor than the 2-hour image (B). Histopathology of the tumor showed mostly chief cells (C).

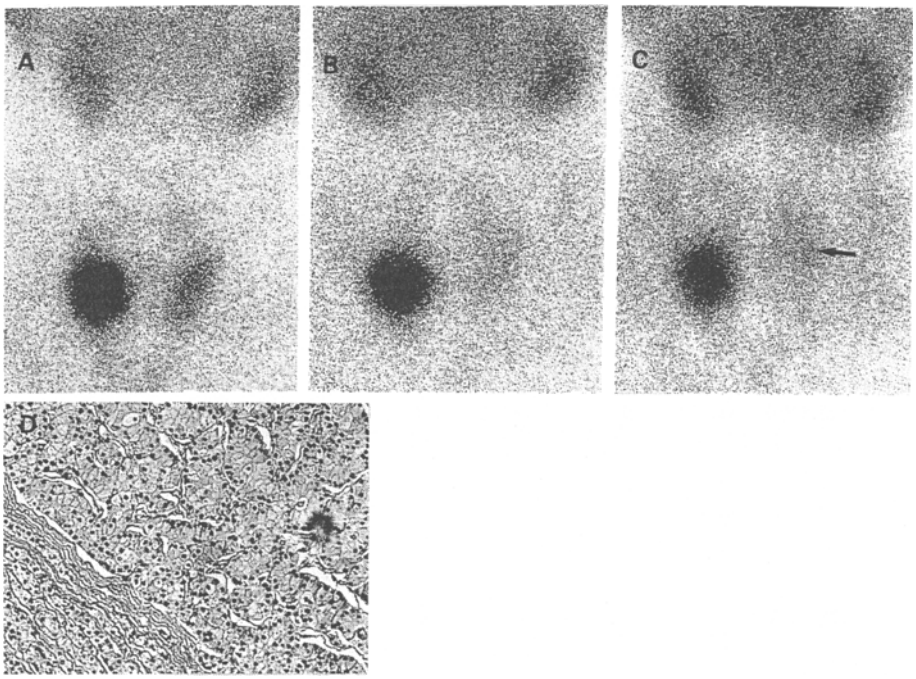

Fig. 4 Shows parathyroid hyperplasias weighing 7,200, 900, 100 and 100 mg. Only the two largest lesions were visualized. (A) 5-minute, (B) 1-hour and (C) 2-hour images. Note that the 2-hour image showed better visualization of the lesion with oxyphilic cells (arrow). (D) Histopathology of the 900 mg lesion. The upper part shows an oxyphilic cell component and the lower left corner shows a chief cell component.

Oxyphilic cells are known to be abundant in mitochondria[8] and because our electromicroscopic findings in selected lesions confirmed more mitochondria in the oxyphilic cells than in the chief cells, parathyroid lesions with predominantly oxyphilic cells were thought to show signs of more prominent uptake of MIBI than those with predominantly chief cells. Though not all lesions were electromicroscopically evaluated and there were only two lesions with abundant oxyphilic cells, the uptake patterns indicated that the uptake of MIBI to the parathyroid lesions might not be related to the cell type but rather to either the lesion size or disease state (functional autonomy), which has also been suggested by others.[11] This is because all adenomas (which has functional autonomy) showed (+) scintigraphic results, but the oxyphilic cellular component was present only 4 of 7 adenomas. All except one of the hyperplastic lesions had mostly chief cells, and 5 of 9 lesions were detected. Visualization of the lesions may be more dependent on the size or weight of the lesions and the size or weight of the gland may be a marker of the functional state of the lesions. The smallest lesion clearly visualized was 220 mg and faint visualization was observed in a lesion weighing 60 mg. Due to the greater size of the adenomas or their functional autonomy, all lesions were detected, but the smaller hyperplastic lesions were missed. This may be due to the suppressive effect of the large hyperfunctioning hyperplastic lesions. A 60 mg lesion in an 11-year-old boy was faintly visualized, and this might have been due to the hyperactivity of the cells because the smallest clearly visualized lesion was also observed in this boy.

Although 2-hour images detected more lesions than 1-hour images, both phases of images were important, especially in delineating the thyroid gland which is also suggested by others.[3] For a single phase study, the late 2-hour images are sufficient but may miss a lesion that show early washout which was observed in one case in this study, and the early images facilitated the interpretation. Similar phenomena were also reported in a case of adenoma.[12]

In conclusion, with this small number of lesions with oxyphilic cells, the results indicated that the uptake and retention of MIBI in parathyroid lesions may not be dependent on the cellular type, but rather on the size or functional autonomy of the lesions. Further study is necessary especially in view of the abundance of oxyphilic cells in the lesions.

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