USEFULNESS OF TECHNETIUM-99M-METHOXYISOBUTYLISONITRILE IMAGING AND INTRAOPERATIVE STAINING TECHNIQUE USING METHYLENE BLUE FOR LOCALIZATION: TWO CASES OF HYPERFUNCTIONING PARATHYROID LESIONS


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Abstract: Two patients with primary hyperparathyroidism in whom it was difficult to search the location of abnormal parathyroid tissues are presented. Both patients, 35-year-old woman and 49-year-old man, had experienced several episodes of urolithiasis. A right lower (the former case) or right upper (the latter) parathyroid tumor was suspected by ultrasonography, but 201Tl-Cl and 99mTc-pertechnetate subtraction scintigraphy (TTSS) demonstrated no abnormal accumulation in the thyroid bed or mediastinum. At operation, no abnormal parathyroid gland was found in both patients. 99mTc-methoxyisobutylisonitrile scintigraphy revealed the presence of elusive parathyroid lesion in the mediastinum or at the lower position of the left thyroid lobe. At reoperation, intraoperative staining with methylene blue was useful to find out the lesions in both patients. The histological diagnosis was hyperplasia of the parathyroid in both. The normal calcium level was obtained promptly after the removal of these tissues.

Key words: 99mTc-MIBI, Hyperparathyroidism, Methylene blue staining, Ectopic parathyroid gland, Preoperative localization

INTRODUCTION

For searching preoperative localization of a parathyroid tumor, ultrasonography (US), computed tomography (CT), and thallium-201 chloride (201Tl-Cl) and technetium-99m pertechnetate (99mTcO4−) subtraction scintigraphy (TTSS) are useful. However, these examinations are sometimes of no use, especially for a small or an ectopic hyperfunctioning lesion. A new parathyroid imaging agent, technetium-99m-methoxyisobutylisonitrile (99mTc-MIBI), has been recently reported to be useful for such cases. We report two patients with elusive hyperfunctioning parathyroid lesions, whose localizations were detected by preoperative 99mTc-MIBI...
imaging and by intraoperative staining with methylene blue.

**CASE REPORTS**

**Case 1**

A 35-year-old woman diagnosed as primary hyperparathyroidism was introduced to our hospital in October, 1990. She had experienced several episodes of urolithiasis since she was 23 years old. A right lower parathyroid tumor was suspected by US and CT scan, whereas TTSS demonstrated no abnormal accumulation in the thyroid region and mediastinum (Fig.1). At intraoperative cervical exploration, no abnormal parathyroid gland was found on both sides. A part of the right thyroid lobe including fatty tissues was resected. However, only one normal parathyroid gland was histologically identified in the specimen. The patient had had a persistent hyperparathyroidism. In spite of various examinations including US, CT scan, magnetic resonance imaging (MRI), and TTSS, we failed to localize the pathological parathyroid gland. The patient had been followed up and received symptomatic treatments. In June, 1994, 99mTc-MIBI imaging revealed the presence of a tumor in the mediastinum (Fig.1). A thin slice CT scan of the chest was reexamined and a small nodular lesion was noted at the right side of the right atrial appendage. At the time of reoperation, 5mg/kg body weight of methylene blue diluted in 200ml solution was intravenously adminis-

![Fig.1 Case 1. 201TI-C1 and 99mTcO4− subtraction scintigraphy demonstrated no abnormal accumulation in the thyroid region and mediastinum (left). 99mTc-MIBI and 123I subtraction scintigraphy showed an increased accumulation (arrow) in the mediastinum (right). The right thyroid lobe had been resected at the first cervical exploration.](image1)

![Fig.2 Case 1. Surgical specimen. A blue-stained nodule, 1.6×1.2×0.8cm in size, was seen in the right lobe of the thymus (arrow).](image2)
Hyperfunctioning Parathyroid Lesions

Case 1
A 62-year-old man with the diagnosis of primary hyperparathyroidism was introduced to our hospital in October, 1992. He had experienced several episodes of urolithiasis. US demonstrated a right upper parathyroid tumor. TTSS confirmed the presence of a parathyroid adenoma on the right side of the neck (Fig.3). At operation, a solid mass, 1.6 x 1.2 x 0.8 cm in size, was found in the right lobe of the thymus, which was identified as parathyroid adenoma. The histological diagnosis was hyperplasia of the parathyroid. The normal calcium level was obtained promptly after the removal of the tumor.

Case 2
A 49-year-old man with the diagnosis of primary hyperparathyroidism was introduced to our hospital in August, 1993. He had experienced several episodes of urolithiasis. A right upper parathyroid tumor was suspected by US. TTSS demonstrated no abnormal accumulation in the thyroid region and mediastinum (Fig.3). At operation, the parathyroid gland was not swelling. The right thyroid lobe including two right parathyroid glands and the left superior parathyroid gland were resected. No pathologic parathyroid gland was histologically identified in the resected specimen. Hyperparathyroidism still persisted after surgery. US, MRI, or whole body thallium scan failed to localize the remaining or ectopic parathyroid gland. After receiving symptomatic therapy for a while, 99mTc-MIBI imaging performed in June, 1994 demonstrated the presence of a tumor at the lower position of the left thyroid lobe (Fig.3). A thin slice CT scan of the neck was reexamined, but no nodular lesion was identified. At a second cervical exploration in Takasaki National Hospital in February, 1995, intraoperative methylene blue staining was employed in the same way as case 1. A blue-stained nodule was identified at the left side of the esophagus, and was excised. The specimen mea-

Fig.3 Case 2. 201Tl-CI and 99mTcO₄⁻ subtraction scintigraphy. No abnormal accumulation was seen in the thyroid region and mediastinum (left). 99mTc-MIBI and 123I subtraction scintigraphy showed an increased accumulation (arrow) at the lower position of the left thyroid lobe (right). The right thyroid lobe had been resected at the first cervical exploration.

Fig.4 Case 2. Local appearance at the second cervical exploration (top). The left inferior parathyroid gland (arrow) stained to be blue. Surgical specimen (bottom; cut surface). A blue-stained gland measuring 1.4 x 0.9 x 0.5 cm.
Horii, Iino, Maemura, Takei, Horiguchi, Koibuchi, Yokoe, Oriuchi, Inoue, Endo, Ishida, Morishita

sured 1.4×0.9×0.5cm and weighed 1020mg (Fig.4). The histological diagnosis was hyperplasia of the parathyroid (Fig.5). His serum calcium level resumed the normal level promptly after surgery.

DISCUSSION

For searching the preoperative localization of hyperfunctioning parathyroid tumor, non-invasive studies such as US, CT, and TTSS are most popular. Furthermore, MRI and selective venous sampling are occasionally performed, but these tests are costly and invasive. More than one of these studies are usually performed before surgery. TTSS is an accepted radionuclide method for imaging abnormal parathyroid tissues, and is particularly useful in searching for ectopic parathyroid glands located around the clavicles or in the mediastinum. However, TTSS is of no use for a small nodule. In Case 1, the hyperfunctioning parathyroid tissue was in the mediastinum. In Case 2, the size of a resected parathyroid lesion was not so small, however, the lesion was undetectable with TTSS. False-negative results such as both cases are often encountered because of various conditions including not only the size of gland but also the interference of back ground. An improved parathyroid imaging agent had been desired.

A new agent, $^{99m}$Tc-MIBI, has been recently reported to be useful for the detection of abnormal parathyroid glands in patients with hyperparathyroidism. $^{99m}$Tc-MIBI is a cationic complex introduced for myocardial perfusion imaging as an alternative to $^{201}$Tl, and was subsequently applied to parathyroid scintigraphy. We first tried this agent in 1994 for the two cases presented herein, and since then we have used $^{99m}$Tc-MIBI for the patient with primary or secondary hyperparathyroidism. The diagnostic sensitivity of $^{99m}$Tc-MIBI imaging for hyperfunctioning parathyroid lesions is superior to that of TTSS.

Localization of $^{99m}$Tc-MIBI in the tissue will be dependent not only on the size of the gland but also on blood flow to the tissue, the concentration of $^{99m}$Tc-MIBI presented to the tissue, and the binding mechanism in various tissues. Chiu et al. and Carvalho et al. suggested that the tissue with a large number of mitochondria might take up $^{99m}$Tc-MIBI more avidly than one with less. O'Doherty et al. reported that the uptake per gram of parathyroid tissues of $^{99m}$Tc-MIBI was higher than the uptake per gram of thyroid tissues, but no difference in uptake was observed between $^{201}$Tl in these tissues. They reported also that $^{99m}$Tc-MIBI activity in the parathyroid tissue remained relatively constant following the peak activity, whereas the $^{201}$Tl activity steadily declined and activity over the thyroid fell with both tracers, suggesting that the localization would be superior with $^{99m}$Tc-MIBI because of the higher target-to-background ratio.

Intraoperative staining using methylene blue is useful to detect abnormal parathyroid glands visually. In our study, all 21 glands with primary hyperparathyroidism were stained with methylene blue. This method is safe and useful for identifying the abnormal gland and discovering the supernumerary glands.

Fig.5 The histological diagnosis of both cases was hyperplasia of the parathyroid (Figure of Case 1. H.E. stain; original magnification ×35 and ×350).
REFERENCES


