

RADIONUCLIDE IMAGING IN PRIMARY HYPERPARATHYROIDISM USING ^{99m}Tc SESTAMIBI - FOUR CASE REPORTS

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ABSTRACT

Radionuclide imaging using the ^{99m}Tc sestamibi either singly or as a subtraction technique with pertechnetate is a recent and reliable method in localising parathyroid adenomas prior to surgery. This is of use in pre-operative planning, as well as in failed first neck exploration. Four local patients with primary hyperparathyroidism whose parathyroid adenomas were localised by this scintigraphy are presented. The value and limitations of this imaging modality are discussed.

Keywords: technetium, sestamibi, parathyroid, imaging, adenoma

SINGAPORE MED J 1996; Vol 37: 585-587

INTRODUCTION

Primary hyperparathyroidism is increasingly being recognised because of the widespread use of general multiphasic screening. In the United States alone, approximately 100,000 new cases are reported each year⁽¹⁾. A study done locally at one of the largest tertiary hospital showed 15 patients with primary hyperthyroidism over a 9-year period from 1974-1982⁽²⁾.

Several reports have stated that in experienced hands, some 90% - 95% of parathyroid adenomas will be localised during an initial neck exploration^(3,4). Parathyroid imaging still has a role for three reasons. Firstly, in localities with a rather low incidence of primary hyperparathyroidism, the level of surgical experience may not be as high as that in the large tertiary referral centres. It may be of help to localise any abnormal glands so as to increase the probability that an initial neck exploration would be successful. Secondly, some surgeons may find pre-operative imaging useful in planning the sequence of the operation⁽⁴⁾. Thirdly, when the initial operation has failed to locate the source of the primary hyperparathyroidism, there is a definitive role for diagnostic imaging to localise any abnormal glands, which may be ectopically located, before a second neck exploration.

In the past, various tracers such as ^{75}Se selenomethionine, ^{131}Cs cesium chloride and ^{201}Tl thallous chloride have been used but none gained widespread acceptance due to lack of reliability and poor imaging properties. ^{201}Tl thallium- ^{99m}Tc pertechnetate as a subtraction technique subsequently became the standard scintigraphic modality for parathyroid scanning in the 1980s⁽⁵⁾. Recently, the myocardial-imaging agent ^{99m}Tc sestamibi, used as a single agent or with pertechnetate subtraction, has been reported to be as reliable and sensitive as the thallium-pertechnetate subtraction method⁽⁶⁾. This report highlights 4 local

patients with parathyroid adenomas detected using ^{99m}Tc sestamibi prior to surgery in the last 2 years.

METHODOLOGY

Double tracer images were obtained using ^{99m}Tc as sodium pertechnetate for thyroid scanning and ^{99m}Tc -labelled sestamibi (hexakis 2-methoxy isobutylisonitrile) for both thyroid and parathyroid imaging. Images were acquired using gamma cameras with a low energy general purpose parallel hole collimator. 15 mCi (555 MBq) of ^{99m}Tc sestamibi was given intravenously. Anterior images of the neck were taken at 5-minute intervals up to 20 minutes. Where necessary, this was followed by 5 mCi (185 MBq) of ^{99m}Tc pertechnetate intravenous injection and images were again acquired up to 20 minutes at 5-minute intervals, with the patient remaining absolutely still during the whole procedure. Subtraction of the two images was done digitally by calculating and normalising the total counts within the thyroid ROI (region of interest) before subtraction of the pertechnetate image from the sestamibi image.

CASE 1

CTK, a 42-year-old Chinese male, first presented with a pathological fracture of the right femur. Subsequently he developed generalised bone aches, became bedridden for 2 years and defaulted follow-up. At a later time, he presented with the above symptoms and was referred to a hospital for medical evaluation. Biochemical tests revealed primary hyperparathyroidism (Table I). Skeletal survey showed advanced demineralization of the bones in the axial and appendicular skeleton with florid brown tumours, mainly in the humeri, femora, right hand, ischii, pelvis and skull vault. There was subperiosteal resorption in the phalanges and tufts of the fingers. Bone scan showed multiple hot spots in the extremities. A ^{99m}Tc sestamibi single agent study of the neck showed a focus of tracer uptake at the right side of the superior mediastinum, highly suggestive of a parathyroid adenoma. Subsequent CT scan of the neck and the superior mediastinum revealed a 6.3 x 3.9 x 5 cm nodule behind the right lobe of the thyroid and extending inferiorly to behind the right clavicle medially. Parathyroid venous sampling gave a very high PTH level (> 1500 pmol/L) from the inferior thyroid vein. During surgical exploration, a large 4 cm cystic lesion at the inferior pole of the right thyroid lobe was found. The histological diagnosis was parathyroid adenoma with haemorrhage.

CASE 2

TCS is a 74-year-old Chinese lady who presented to a doctor in

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Table I – Blood biochemical profiles

	patient 1	patient 2	patient 3	patient 4	Normal range
PTH (intact) pg/mL	497.5	106.5	222.5	72.7	4.7-48.5
ionized calcium (corrected for albumin) mmol/L	2.73	2.35	3.01	2.69	2.1-2.6
Phosphate mmol/L	0.47	0.54	0.92	0.71	0.77-1.38
Serum alkaline phosphatase (U/L)	1274	124	92	90	32-103
Urea (mmol/L)	2.8	4.9	4.5	2.8	2.8-7.7
Creatinine μ mol/L	40	68	105	91	44-141

Australia while on holiday, with severe pain in her lower legs, calves and pelvis, causing walking difficulty. X-rays of the pelvis showed Looser's zones in both superior and inferior pubic rami bilaterally. Results of biochemical tests are listed in Table I. ^{99m}Tc sestamibi- ^{99m}Tc pertechnetate scan of the neck revealed a focus of activity at the region of the lower pole of the left thyroid lobe. Neck exploration located an enlarged nodule at that site measuring 0.5 cm in diameter. The other parathyroid glands appeared normal macroscopically as well as on frozen section. Subtotal parathyroidectomy was done. Histology of the enlarged nodule showed a parathyroid adenoma.

CASE 3

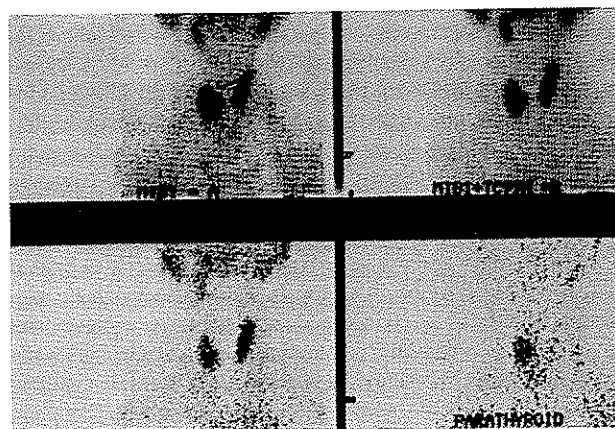
KKH, a 60-year-old Chinese female, first presented with haematuria and lower abdominal pain. Abdominal X-ray showed a left renal calculus. IVU revealed a small left kidney with calculi in its upper pole and small calculi in the right lower ureter. Some biochemical investigations are shown in Table I. In view of elevated PTH levels, a ^{99m}Tc sestamibi- ^{99m}Tc pertechnetate subtraction scan of the neck was carried out and it showed a residual focus of tracer activity in the region of the lower pole of the right thyroid lobe. Ultrasonography of the neck, done at the same sitting, showed a hypoechoic nodule (1.0 x 0.9 x 0.9 cm) posterior to the right lower pole of the thyroid. A concurrent CT scan of the neck, however, did not reveal any abnormalities in the thyroid or any enlargement of the parathyroids. Neck exploration revealed an enlarged right inferior parathyroid, measuring 2 x 1 x 1 cm. Three and half parathyroids were removed. Histological diagnosis was a right inferior parathyroid adenoma. The rest of the parathyroid glands appeared normal histologically.

CASE 4

LAS, a 59-year-old Chinese male, diagnosed to have multi-infarct dementia, Parkinson's disease and hypertension, was admitted twice within 1 year for falls, confusion and faecal incontinence. CT head showed diffuse cerebral atrophy which appeared inconsistent with the severity of his confusional state. Skull X-ray showed several small lytic areas in the vault. Biochemical tests were done and results are shown in Table I. Bone scan showed 'hot spots' in the left greater trochanter, L1 vertebra and the left shoulder. Investigations for multiple myeloma were negative. ^{99m}Tc sestamibi- ^{99m}Tc pertechnetate subtraction scan showed focal tracer uptake in the region of the right thyroid lobe lower pole which corresponded to a hypoechoic nodule 1.5 cm in diameter with irregular low attenuation areas, in the same location. Surgical exploration showed a 2 cm nodule, posterior to the mid aspect of the right

thyroid lobe. Histology of the nodule showed an encapsulated parathyroid tissue with 2 cell types, most likely a parathyroid adenoma.

Figure 1 – The panel shows 4 images: (a) ^{99m}Tc sestamibi image (see top left diagram); (b) combined ^{99m}Tc sestamibi image and ^{99m}Tc pertechnetate image (top right diagram); (c) subtracted image of the above ie: (b) - (a) which gives the ^{99m}Tc image (lower left diagram). (d) ^{99m}Tc sestamibi ^{99m}Tc pertechnetate subtracted image ie (a) - (c) (lower right diagram). The latter shows a residual focus of tracer activity at the region of the lower pole of the right thyroid lobe.



DISCUSSION

Previous experience with ^{201}Tl thallium- ^{99m}Tc pertechnetate subtraction scintigraphy showed a reported sensitivity of 89% to 95%^(5,7,8) in localising parathyroid adenomas. Another study, employing 4 imaging modalities, reported that in 100 patients with parathyroid adenomas, the thallium-technetium subtraction method gave a sensitivity of only 73%, which compares favourably with the sensitivities of 68% for CT scanning, 55% for high resolution ultrasonography and 57% for magnetic resonance imaging. In the same study, the combination of CT scanning and radionuclide imaging achieved a sensitivity of 90% and the combination of radionuclide imaging and ultrasound, 85%⁽⁹⁾. In one study reported, CT scan showed a sensitivity of 76%⁽¹⁰⁾. MRI had been reported to give a sensitivity of 50% - 93%⁽¹¹⁾. Hence overall, ^{201}Tl thallium- ^{99m}Tc pertechnetate subtraction scintigraphy appears to have a comparatively high sensitivity in imaging parathyroid adenomas.

Recently, O'Doherty found that using sestamibi in the subtraction scanning with ^{99m}Tc pertechnetate gave a better sensitivity of 97% (39/40 parathyroid adenomas) compared to 92.5% (37/40 parathyroid adenomas) using thallium⁽¹²⁾. In addition to better sensitivity, there are 3 reasons why ^{99m}Tc -sestamibi is preferable to thallium. Firstly, the use of ^{99m}Tc sestamibi is associated with a more favourable radiation dosimetry than thallium (Table II). Secondly, the principal gamma photons of ^{99m}Tc (0.142 Mev) as derived from decay from ^{99}Mo is more suited to conventional gamma cameras than that of ^{201}Tl thallium (0.069-0.083Mev). Thirdly, the higher energy gamma photons from technetium are able to penetrate the sternum and the thick overlying tissues in cases of ectopic glands in the superior mediastinum. Therefore, ^{99m}Tc sestamibi gives better image resolution and is expected to become more frequently used than thallium in parathyroid scintigraphy.

One additional advantage is that sestamibi may be used alone as a dual phase study. The rationale is that sestamibi is relatively more concentrated in parathyroid tissue than thyroid tissue, unlike thallium, and the time-behaviour of sestamibi uptake in parathyroid is slower and more sustained.

Table II – Dosimetry associated with parathyroid imaging

	Activity(MBq)	EDE* (mSv)
^{99m} Tc (pertechnetate)	75	1.0
²⁰¹ Thallium	75	25
^{99m} Tc sestamibi	200	2.4 (males) 3.0 (females)

* estimated dose equivalent

Various conditions influence the sensitivity of sestamibi-pertechnetate or thallium-pertechnetate subtraction scintigraphy: (a) drugs, (b) presence of thyroid nodules and enlarged cervical lymph nodes, (c) size and weight of the parathyroid adenoma, and (d) nature of the enlargement of the parathyroid (adenoma or hyperplasia). Drugs reducing the sensitivity include L-thyroxine, iodine-containing cough mixtures and herbal concoctions, and iodinated contrast agents. These would render the thyroid image extremely faint and decrease the effectiveness of the subtraction. When such constraints exist, one may consider using ^{99m}Tc sestamibi alone as a dual phase study.

Multinodular goitres or thyroid adenomas are well known to give rise to false positive results. False positives have also been reported due to a lymph node affected by sarcoidosis, and to lymphomas and thyroid carcinomas. The size or weight of the gland also affect sensitivity. In general, it is felt that an adenoma less than 0.5g would give a fairly high false negative rate. Hyperplastic parathyroid glands, which may also be present in MEN I and IIa syndromes, are usually multiple and are known to give a much lower sensitivity. Thus, scintigraphy is usually not indicated in patients with suspected hyperplastic glands such as may occur with secondary hyperparathyroidism.

As ultrasonography of the neck further increases the sensitivity and specificity of locating any parathyroid adenoma, a combination of ^{99m}Tc sestamibi scintigraphy and high resolution ultrasonography is employed by our department. ^{99m}Tc sestamibi scintigraphy, with the addition of high resolution ultrasonography, is of reliable and good utility in the pre-operative assessment of primary hyperparathyroidism in our local context.

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