ORIGINAL ARTICLE

Preliminary Report on Somatostatin Receptor Imaging in Rare Endocrine Tumours

B J J Abdullah, FRCR*, M Paramsothy, FRCP, A S M Khir, FRCP**, S P Chan, MRCP**, *Department of Radiology, **Department of Medicine, University of Malaya, 50603 Kuala Lumpur**

Summary

Our preliminary experience of Somatostatin Receptor Positive Tumour Scintigraphy (SRPTS) in the management of some rare neuroendocrine tumours is highlighted. Six patients were evaluated using SRPTS. A single patient each with Zollinger-Ellison syndrome, recurrent medullary carcinoma of thyroid and Stage IV neuroblastoma. Two patients with phaeochromocytoma, and one patient with suspected insulinoma were evaluated. SRPTS was useful in three of the six patients studied i.e. patient with gastrinoma, recurrent medullary carcinoma of thyroid and metastatic neuroblastoma. SRPTS although expensive is a useful and cost-effective approach of rare endocrine tumours and it role as a first line tool in the diagnosis is discussed.

Key Words: Neuroendocrine tumours, Somatostatin receptor scintigraphy, MIBG, MDP, CT and Ultrasound

Introduction

Both primary and recurrent neuroendocrine tumours e.g. gastrinoma, insulinomas, phaeochromocytomas are rare and pose a difficult diagnostic and management problem. There have been numerous imaging modalities (magnetic resonance imaging {MRI}, computed tomography {CT}, endoluminal ultrasound, and scintigraphy) and protocols which have been advocated to assist in the management of these tumours. The sensitivities and specificities of these vary but we discuss a cost-effective approach using Somatostatin Receptor Positive Tumour Scintigraphy (SRPTS) in the management of this difficult group of patients.

Materials and Methods

Between April 1992 and March 1995, 6 patients were investigated for a variety of rare neuroendocrine tumours using Indium-111 labeled DTPA-D-Phe'octreotide or Pentreotride somatostatin receptor scintigraphy (SRPTS)(Octeoscan, Mallinckrodt Diagnostica, Holland). The dose injected was 216 MBq (5.8mCi). The octreotide therapy, if any, was discontinued for at least 3 days prior to SRPTS. Adequate hydration was maintained. Imaging was done at 4, 24 and 48 hours after injection. Whole body planar image from head to feet was done at 8cm/sec. In addition static anterior and posterior views of the head, neck and thorax (excluding the liver) was done followed by a second of the abdomen to the level of the thigh. The images were taken for 600, 000 counts. Sinle photon computed tomographic (SPECT) were done of any abnormal area of activity.

There were four females and two males. The clinical information of the six patients is as summarized in Table I.

Table I
Summary of Patients and Investigative Findings

Age, Sex & Ethnic Group	Clinical History	Physical Findings	Clinical Diagnosis	Laboratory Chemistry	Other Investigations	Computed Tomography	Angiography	111In-SRPTs	Operative Diagnosis
43 yr. Chinese female	3 yr. h/o recurrent diarrhoea with duodenal ulcers	Normal	Zollinger Ellison syndrome		Recurrent duodenal ulcers confirmed on endoscopy	Normal	Normal	"Hot" lesion seen in region of the head of the pancreas	Metastatic gastrinoma in lymph node
39 yr. Chinese female	Known medullary carcinoma thyroid treated with surgery & radiotherapy. On max. doses of octreotide. Presenting with raised levels of serum calcitonin	Palpable masses in the neck	Recurrent medullary carcinoma	Serum calcitonin greater than 1000µg/l	MIBG negative on 2 occasions. 2nd study done with 5 times normal dose	Mediastinal and neck lymphadenopathy ?scar or recurrent disease	Not applicable	Increased uptake in the mediastinum and neck	Recurrent medullary carcinoma of thyroid
1 yr. Chinese boy	Stage IV neuroblastoma with negative marrow extension. Post chemotherap developed liver microabscesses. Presented with pain & swelling in the left femur	Swollen & tender proximal femur	Osteomyelitis	Not applicable	Not applicable	Not applicable	Not applicable	Showed diffuse uptakein proximal 2/3rd femur	No post mortem
16 yr. old Chinese male	Known MEN syndrome with bilateral phaeochromocytoma treated with surgery presenting with persistent hypertension	BP 150/110 mmHg	Ectopic phaeochro -mocytoma	Negative post-op. Pre-op study was also negative	MIBG negative. Pre-operative study was also normal	Not applicable	Not applicable	No uptake	Not re -operated
59 yr. Chinese male	Father of above patient with hypertension	BP 150/105 mmHg	MEN syndrome	Urine metanephrine 30.7µg/24hr	MIBG concentrated in both adrenals	Initial study normal. Repeat showed R adrenal mass (2.0 x 2.8cm). L adrenal bulky but no focal mass	Not applicable	No uptake	Refused surgery
31 yr. old Chinese female	Presenting with repeated bouts of hypoglycemia	Normal	Insulinoma	Random glucose 6.2mmol/l, fasting gluocse 2.1 mmol/l/. Insulin levels 5.3-89.0, ratio to fasting bld. 2.5-26.2	Not applicable	2 studies done, one showed questionable mass in the neck of pancreas	Normal	No uptake	No tumour found at surgery. Well controlled on medication

Results

The results are summarized in Table I.

In the first patient, the anterior and posterior planar SRPTS images of the abdomen obtained at 4 hours showed a small "hot" lesion located just medial to the right kidney and projected on the right renal pelvis (Fig. 1). The 24-hour SPECT images demonstrated very clearly the location of the tumour to be situated just ventero-medial (antero-medial to the right kidney) compatible with a tumour situated in the head of the pancreas. No other abnormal areas of focal concentration of pentetreotide seen in the body to indicate other multiple tumour sites. On surgery a 2cm x 1cm tumour was found posterior to the pancreatic head.

In second patient, a whole body planar and SPECT SRPTS study showed lesions clearly located in the middle mediastinum (Fig. 2). This confirmed that the CT changes were due to tumour rather than scarring. In addition, another focal "hot" lesion was detected in the upper anterior cervical region of the neck, which corresponded to the palpable masses in the neck. These masses were clinically considered to be related to radiation fibrosis. She had surgical excision of the mediastinal nodes.

In the third patient (Stage IV neuroblastoma), the planar SRPTS images showed diffuse accumulation in the proximal two thirds of the left femur corresponding to the abnormality seen on the methylene diphosphonate (MDP) bone scan.

The fourth and fifth patients had phaeochromocytoma. The SRPTS study did not show any abnormal uptake. In the last patient suspected to have an insulinoma, the SRPTS study was negative. She subsequently had surgery based on a questionable lesion in the neck of the pancreas but the histology did not show any insulinoma.

Four lesions out of the seven lesions imaged by plain films, CT and conventional angiography were identified in the six patients studied with SRPTS. One lesion was a solitary gastrinoma, two separate lesions of recurrent medullary carcinoma in the neck and mediastinum and a solitary secondary bony metastasis in a patient with stage IV neuroblastoma. In the other 3 patients, one with biochemical evidence of insulinoma, one patient

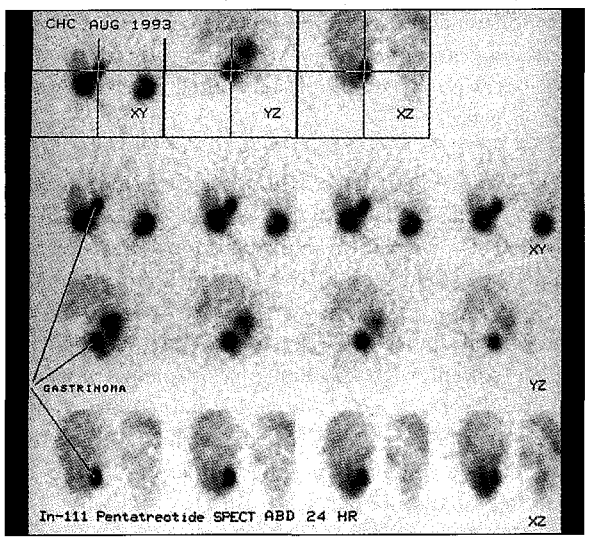

Fig. 1: Gastrinoma in the abdomen. SPECT study of the abdomen 24 hours shows focal "hot" spot on the axial [a], sagittal [b] and [c] coronal reconstructions.

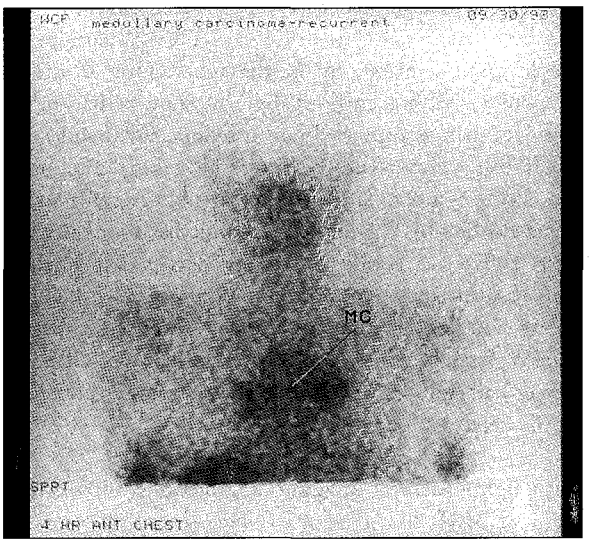

Fig. 2: Recurrent medullary of the thyroid. Planar SRPTS study of the chest shows an area of increased concentration in the mediastinum. This corresponded with the enlarged lymph nodes seen on the CT of the chest.

with bilateral phaeochromocytoma (based on CT and meta-iodobenzylguanidine {MIBG}) and the third with post-operative hypertension and raised levels of VMA were negative.

The CT was able to detect four of the six lesions imaged in five patients. There was a case of a false positive lymph node involvement in the para-aortic area based on CT in the patient with bilateral phaeochromocytoma.

The MIBG studies in three patients were only positive in one patient with bilateral phaeochromocytoma i.e. able to detect two out of the four lesions studied. There was no uptake in the patient with the recurrent medullary carcinoma of the thyroid despite having the study repeated twice once with a higher high dose.

Discussion

The persistence of high affinity receptors on neuroendocrine tumours permits imaging of these tumours using radiolabelled somatostatin analogues. These receptors have been found present in most of the growth hormone producing pituitary adenomas and in most of the metastatic pancreatic and carcinoid tumours[1]. Lamberts *et al*[2] first used I-123 TYR3-octreotide for whole body scintigraphy in the functioning pituitary adenomas. Subsequently it has be shown that other tumours such as primary brain tumours, small and non-small cell tumours of the lung, Hodgkin's and non-Hodgkin's lymphoma as well as sarcoidosis concentrate pentreotride[3]. In-111-pententetreotide has supplanted I-123 TYR3 octreotide as the preferred radiolabelled somatostatin analogue for whole body imaging because of its simpler labeling technique, lower cost, better binding and less interference from biliary activity and longer half life[4]. However, this has not made a difference in the detection rate[5].

Although structural imaging (angiography, ultrasound, CT and MRI) has good resolving power compared to SPECT, it has limitations in the detection of functioning neuro-endocrine tumour. This is because detection on structural imaging depends on a change in configuration, density or vascularity while the vast majority of these tumours are small at presentation[6]. Therefore, it is not suprising that CT, MRI, angiography and trans-abdominal ultrasound[7-10] have a low sensitivity and specificity in the diagnosis of neuroendocrine tumours (primary and secondary) to SRPTS[11-14]. The role of positron electron imaging (PET) with fluoro-deoxyglucose (FDG) in the evaluation of functioning neuroendocrine tumours appears to be promising though availability of PET centers is limited.

Lamberts *et al*[15] using SRPTS revealed localization of primary tumour or its unknown metastases in 86% of patients while de Kerviler *et al*[11] was able to detect 50% of previously unimaged lesions. SRPTS has a sensitivity of between 57% to 85% for medullary carcinomas of the thyroid and is excellent for lung secondaries[12,16]. However, it is not useful for the detection of the liver secondaries from medullary carcinoma of thyroid[17]. Krenning *et al*[13] showed SRPTS has a sensitivity of 100% for the detection of gastrinomas, glucagonamas, carcinoids, small cell carcinomas of the lung as well as the pituitary adenomas. SRPTS also detected more tumour sites compared to conventional imaging techniques. However, they found for insulinomas, medullary carcinomas of the thyroid and nonfunctioning adenomas SRPTS have a sensitivity of between 50% to 70 %. The low detection rate of insulinomas with SRPTS[5,13,14] may be related to the tracer accumulation in the gastrointestinal tract.

The advantage of SRPTS is that a whole body survey can be carried out unlike CT where only one or two regions can be examined and with similar radiation doses[18]. SRPTS is a good cost-effective modality for the surveillance of patients with known primaries and follow-up of those with known disseminated disease to evaluate their response to treatment. SRPTS also has the potential benefit of treating these candidates with tumours that are positive for the presence of somatostatin receptors with octreotide therapy[19] as well as the possibility of tumour ablation with I-131 tagged somatostatin receptor analogues[20]. Schirmer *et al* have used I-123- TYR [3] octreotide to locate the pancreatic endocrine tumour intra-operatively even when the SRPTS SPECT was negative[20,21]. They showed that the majority of patients with a known tumour but negative whole body SRPTS were found to have positive uptake intra-operatively (87.5% intra-operatively compared to 25% at whole body SPECT). They concluded that a negative whole body study is not a reliable indicator of presence of somatostatin receptors within the tumour.

Although SRPTS costs approximately 5 - 6 times that of the CT scan, it is more cost-effective in the detection of rare neuroendocrine tumours. This can be achieved using a single whole body procedure compared to assessment by conventional methods where a minimum of 2 - 3 different imaging procedures with significant saving in terms of working days lost and patient discomfort. Results of SRPTS can also be used to plan treatment of these patients if surgery is not curative or if the patients are poor surgical candidates.

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