^{111}In-Pentetreotide Scintigraphy in the Detection of Insulinomas: Importance of SPECT Imaging

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The aim of this study was to determine whether the systematic use of SPECT can increase the reported low sensitivity of somatostatin receptor scintigraphy (SRS) in detecting insulinomas. **Methods:** Fourteen patients were evaluated. After ^{111}In-pentetreotide injection (~250 MBq intravenously), abdominal SPECT images were obtained at 4 h and multiple planar images were obtained at 4 and 24 h. MRI and CT were performed within 1 mo of SRS. Sixteen tumors were histologically verified after surgery in 14 patients. **Results:** SPECT revealed 14 lesions in 12 patients (sensitivity, 87.5%), both planar SRS and MRI revealed 7 tumors in 7 patients (sensitivity, 43.8%), and CT revealed only 5 lesions in 4 patients (sensitivity, 31.3%). Moreover, in 4 patients SPECT was the only examination with positive findings. **Conclusion:** SPECT at 4 h is mandatory for preoperative detection of insulinomas using SRS because the images are more sensitive than planar images and are superior to images from other conventional methods.

Key Words: somatostatin receptor scintigraphy; insulinomas; SPECT

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Insulinomas are insulin-secreting tumors that usually originate in the pancreas and are rarely malignant. The diagnostic triad of the insulinoma syndrome (Whipple's triad) consists of characteristic hypoglycemic symptoms, the presence of hypoglycemia, and relief of symptoms after glucose administration. However, the symptom complex is relatively nonspecific, and diagnosis is often delayed (*1*).

Surgical resection is the treatment of choice. Because most tumors are solitary and benign, accurate diagnosis and preoperative localization are crucial. Numerous tests and procedures have been advocated to aid in locating insulinomas. Noninvasive imaging techniques such as CT, sonography, and MRI would be preferred, but they are successful in only 30%–60% of patients. Angiography with hepatic venous sampling is more sensitive but requires considerable expertise, is time consuming, and is invasive (*1*). Recent data suggest that endoscopic sonography in experienced hands can be useful in localizing intrapancreatic insulinomas (*2*).

Somatostatin receptor scintigraphy (SRS) has emerged as an easy and noninvasive technique to detect small neuroendocrine tumors and metastases not visualized with conventional imaging methods. Nevertheless, its role in the localization of insulinomas is controversial because SRS has been reported to have a lower detection rate for insulinomas than for other pancreatic endocrine tumors (*3,4*). However, usually only planar images have been obtained. This prospective study aimed to evaluate the sensitivity of ^{111}In-pentetreotide scintigraphy (planar and tomographic images) in comparison with conventional imaging methods in detecting insulinomas.

MATERIALS AND METHODS

Fourteen patients (6 women, 8 men; age range, 18–69 y; mean age, 46.6 ± 15.5 y) were studied. In all, an insulinoma was suspected on the basis of recurrent hypoglycemia and positive fasting-test findings, and the diagnosis was confirmed histologically after surgery. Informed consent was obtained from each patient for each procedure performed.

SRS was performed after an intravenous injection of ~250 MBq ^{111}In-pentetreotide (Mallinckrodt Medical BV, Petten, The Netherlands). To reduce background bowel activity, a laxative was administered to all patients 1 d before the injection of ^{111}In-pentetreotide and was continued for 48 h, according to the manufacturer's recommendations. Moreover, the patients were encouraged to drink amply after injection of the radiopharmaceutical to promote both bowel cleansing and renal excretion.

Images were obtained with a γ camera (Starcam 2000; General Electric Medical Systems, Milwaukee, WI) having a large field of view and equipped with a medium-energy collimator. Two 20% energy windows were centered on the ^{111}In photopeaks (173 keV and 247 keV). One-million-count planar images (128 × 128 word matrix) of the chest and abdomen were acquired in anterior and posterior projections 4 and 24 h after injection. Images of the rest of the body (500,000 counts or a 15-min acquisition, anterior and posterior) including the head and neck and the lower abdomen (to the mid thigh) were obtained 24 h after injection. SPECT was performed over the abdomen at 4 h using a 64 × 64 word matrix, 64 projections with a rotation of 360°, and a 60-s acquisition time per projection. The original SPECT data underwent Wiener prefiltration, and the filtered data were then reconstructed with a ramp

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filter. The scintigraphic images were interpreted independently by 2 nuclear medicine physicians who were unaware of the results of any prior investigations.

CT and MRI of the abdomen were performed within 1 mo of scintigraphy. For CT, contiguous scans of 5-mm thickness were obtained before and after an intravenous bolus injection of contrast medium. MRI was performed with contiguous 5- to 10-mm-thick sections using fast T1- and T2-weighted sequences with fat suppression.

Because the patient population was small, statistical analysis was not performed.

RESULTS

Table 1 summarizes the results. The SRS interpretation of the 2 readers agreed for each patient.

Sixteen tumors were histologically verified in 14 patients. Fifteen tumors were intrapancreatic (patient 14 had 2 pancreatic tumors), and 1 tumor was in the liver (patient 12 had a pancreatic tumor with a single hepatic metastasis).

In 12 patients, 14 abnormal sites of ^{111}In-pentetreotide uptake were found by SPECT (sensitivity, 87.5%), which localized 13 pancreatic lesions and the single liver metastasis in patient 12. Only 7 of 16 tumors could be detected by planar SRS (sensitivity, 43.8%), 5 of 16 by CT (sensitivity, 31.3%), and 7 of 16 by MRI (sensitivity, 43.8%). No imaging technique could reveal the pancreatic lesions in patient 4 (7 mm in diameter, in the pancreatic head) and patient 13 (8 mm in diameter, in the pancreatic tail). The smallest tumor revealed by SRS, measuring 8 mm in diameter, was in the pancreatic tail and visible only on SPECT images (patient 1).

In particular, in 4 patients SPECT was the only examination positive for tumor (Fig. 1), and SPECT was the only method able to detect both the pancreatic lesions in patient 14 and the liver metastasis in patient 12. The 5 pancreatic tumors detected by SPECT but not by planar imaging were in the tail. SPECT was positive for tumor in 12 of 14 patients (sensitivity, 85.7%), both planar imaging and MRI were positive for tumor in 7 of 14 patients (sensitivity, 50%), and CT was positive for tumor in 5 of 14 patients (sensitivity, 35.7%).

DISCUSSION

SRS has recently proved useful in the visualization of most endocrine pancreatic tumors. Nevertheless, detection of insulinomas by this scintigraphic method has been less sensitive, with a false-negative rate of approximately 50% (*3*).

Our prospective study yielded a detection rate higher than previously reported rates; this difference can be explained by several factors that can negatively affect the sensitivity of SRS. In the European trial reported by Krenning et al. (*4*), 3 of 8 patients with negative scan findings were injected with a low dose of ^{111}In-pentetreotide (~103–123 MBq), and no abdominal SPECT was performed. Schillaci et al. (*5*) previously reported that SPECT is mandatory for abdominal localization with SRS. In patients with carcinoids, tomography was more sensitive than either planar imaging or both CT and MRI not only in detecting primary tumors but also in assessing hepatic involvement and abdominal extrahepatic involvement. SPECT is particularly useful when tumors are small, are in the pancreatic head or tail, and are not seen on planar scans because of superimposition of other tissues or of organs such as the kidneys, liver, and spleen, in which ^{111}In-pentetreotide uptake always varies. In fact, we visualized 5 tumors in the pancreatic tail with SPECT but not with

TABLE 1
Overview of Results

Patient no.	Sex	Age (y)	Tumor location within pancreas	Tumor diameter (cm)	Planar SRS	SPECT SRS	MRI	CT
1	M	32	Tail	0.8	–	+	–	–
2	M	60	Tail	1.5	–	+	–	–
3	F	18	Head	1.2	+	+	+	–
4	M	59	Body and tail	1.3	–	+	–	–
5	M	34	Tail	1.0	–	+	–	–
6	M	52	Head	0.7	–	–	–	–
7	M	54	Body and tail	1.4	+	+	–	–
8	F	24	Head	2.0	+	+	+	+
9	M	51	Head	2.2	+	+	+	+
10	F	69	Tail	1.8	+	+	+	+
11	F	45	Body	2.0	+	+	+	+
12*	M	67	Head	2.3	+	+	+	+
13	F	48	Tail	0.8	–	–	–	–
14	F	39	Body/tail	1.2/0.9	–/–	+/+	+/–	–/–

*Patient also had liver metastasis detected only by SPECT SRS.
+ = positive; – = negative.

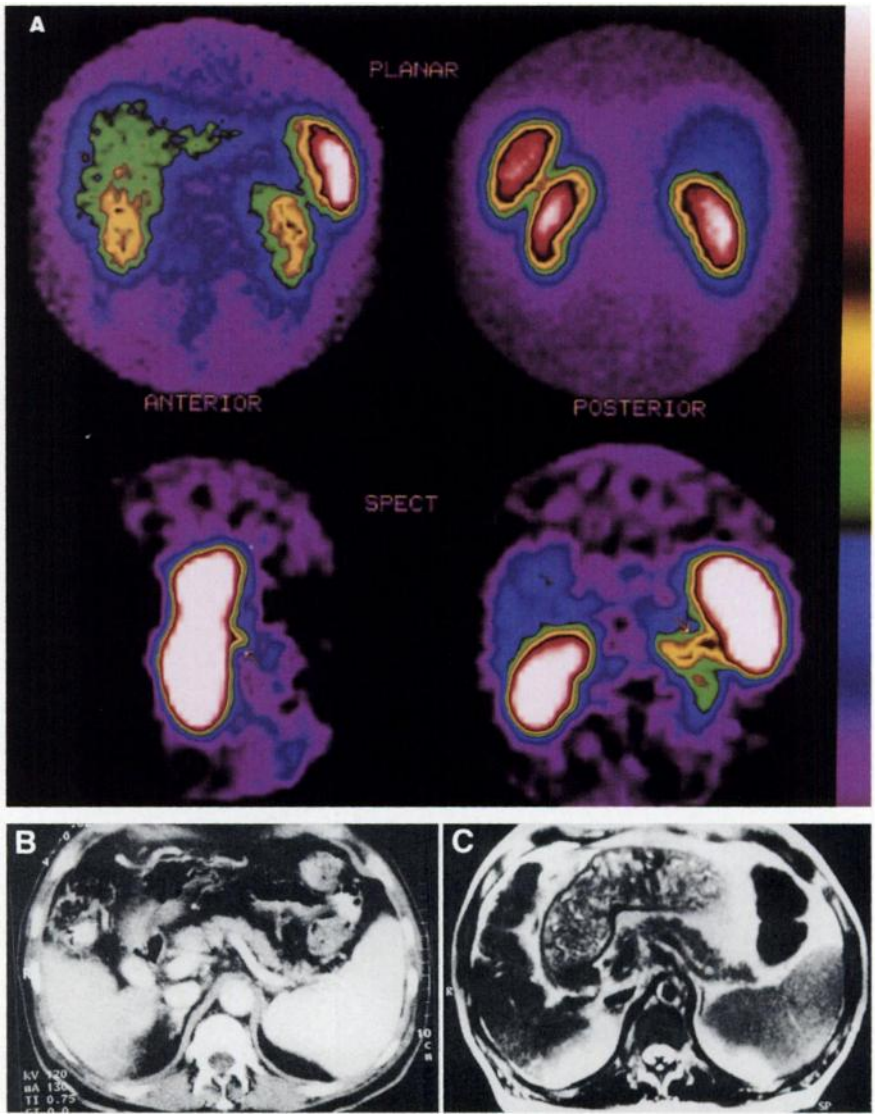

FIGURE 1. SRS of patient 5. (A) Abdominal planar scans (top, anterior and posterior views) show no abnormal uptake, whereas SPECT images (bottom, sagittal slice on left and coronal slice on right) localize 1 focus (arrow) between spleen and upper pole of left kidney. CT scan (B) and MR image (C) show no tumor site. One week after scintigraphy, surgery revealed insulinoma in pancreatic tail.

planar SRS, probably because of high uptake in the spleen. In our opinion, SPECT is also more important for patients with a suspected insulinoma, because in vitro autoradiographic results have shown that many tumors of this type express somatostatin receptors with a lower affinity for octreotide, mainly subtype III rather than subtype II (*3*). Furthermore, because somatostatin receptors in insulinoma cells can have a low affinity for ^{111}In-pentetreotide, an adequate dose (~250 MBq) of this tracer and a long acquisition time per projection are imperative. In fact, the more numerous the counts collected, the greater is the chance of localizing all receptor-expressing tumors, including those with low receptor density or low-affinity receptors (*4*). Our findings indicate that SPECT is essential for detecting insulinomas with SRS, and our routine use of SRS might explain the higher sensitivity yielded in this study compared with the results of studies in which SRS was performed only occasionally.

Among preoperative imaging methods, endoscopic sonography has recently been reported as highly sensitive in detecting pancreatic insulinomas, especially those in the pancreatic head (*2*). However, endoscopic sonography of the pancreas can be difficult, experienced interpreters are few, and detection rates for tumors in the tail are low, even for skilled interpreters. In addition, endoscopic sonography is useful only for primary tumor localization, whereas SRS is also able to show distal metastases because it allows whole-body examination and is easy to perform. Moreover, use of an intraoperative γ probe as an adjunct to preoperative SRS may help surgeons seeking the primary tumor and its metastases, thus possibly improving the sensitivity of external scintigraphy and guiding therapy.

CONCLUSION

Although our series included a relatively small number of patients, the data indicate that performing SPECT 4 h after injection of ^{111}In-pentetreotide is essential for preoperative localization of insulinomas by SRS. In fact, SPECT is more sensitive than both planar imaging and other conventional imaging methods in detecting pancreatic and liver tumors.

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