

Somatostatin Receptor Scintigraphy of Malignant Somatostatinoma with Indium-111-Pentetreotide

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This article describes the visualization of a pancreatic somatostatinoma and liver metastases using ^{111}In -pentetreotide imaging in a patient with somatostatinoma syndrome. A 61-yr-old woman with gallbladder stones, diabetes, weight loss, diarrhea and steatorrhea, immunohistochemical diagnosis of somatostatinoma (liver biopsy) and high plasma values of somatostatin was studied by somatostatin receptor scintigraphy. Six sites of focal abnormal ^{111}In -pentetreotide hyperfixation were found: three in the liver and three in the pancreatic area. This case report demonstrates that *in vivo* detection of somatostatinoma with somatostatin receptor imaging is possible in the presence of high levels of circulating somatostatin, suggesting that receptor downregulation has not occurred.

Key Words: somatostatinoma; somatostatin receptor imaging; indium-111-pentetreotide

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Somatostatin-producing tumors are rare gastroenteropancreatic neuroendocrine neoplasms. The diagnosis is difficult because the symptoms are generally nonspecific and mild. Metastases are found in most patients on presentation (1-3).

In vitro identification of a high number of somatostatin receptors in many tumors of various origins has permitted *in vivo* scintigraphy with ^{111}In -pentetreotide, a radiolabeled somatostatin analog with high affinity for somatostatin receptors subtype 2 (4,5). However, among 78 neuroendocrine tumors tested, Reubi et al. (6) reported that two somatostatinoma patients were somatostatin receptor-negative in binding assays and autoradiography. These findings have suggested that downregulation of somatostatin receptors after chronic exposure to high endogenous somatostatin levels may occur, and this may lead to false-negative results *in vitro* receptor evaluation and scintigraphy (7).

Krenning et al. (8) and Lambert et al. (9) have previously reported successful visualization of a somatostatinoma using ^{125}I -Tyr3-octreotide, but no data are provided on the levels of circulating somatostatin.

We describe the visualization of both the primary pancreatic somatostatinoma and liver metastases using ^{111}In -pentetreotide scintigraphy in a patient with somatostatinoma syndrome and elevated plasma levels of somatostatin.

CASE REPORT

A 61-yr-old woman was admitted because of diabetes, diarrhea and weight loss. She had had a diagnosis of gallbladder stones during the previous year. On admission, fecal fat excretion was elevated (21 g/day); serum protein electrophoresis was normal, as well as serum values of creatinine, total bilirubin, alkaline phosphatase, transaminase, total protein, calcium and phosphorus. Laboratory tests of thyroid hormones, serum gastrin, vasoactive intestinal polypeptide, urinary 5-hydroxyindolacetic acid and serotonin were all normal. Radiographical examination of the small

intestine and colonoscopy with histological evaluation of biopsy specimens were negative. Ultrasonography of the abdomen demonstrated a 4-cm mass in the tail of the pancreas and a 3.4-cm lesion in the liver. CT of the abdomen confirmed these findings. Histologic examination of a liver mass was chromogranin A-positive. Immunohistochemical analysis demonstrated somatostatin-like immunoreactivity. Subsequent determination revealed high plasma levels of somatostatin and neuron-specific enolase: 67.5 pg/ml (n.v. <15) and 24 ng/ml (n.v. <12), respectively. She was not under octreotide treatment.

Somatostatin receptor scintigraphy was performed. Five hundred thousand count planar images (128 × 128 word matrix) were acquired for the chest and abdomen in the anterior (A) and posterior (P) projections at 4 and 24 hr after injection (~250 MBq ^{111}In -pentetreotide) (10). Images of the rest of the body (500,000 counts or 15 min acquisition time, A and P) including the head/neck region and the lower abdomen (down to the midhigh region) were also performed 4 and 24 hr after injection; 360° SPECT (64 × 64 word matrix, 64 projections of 1 min each) were acquired over the abdomen at 4 hr.

No side effects were observed after intravenous injection of the radiopharmaceutical. Six sites of focal abnormal ^{111}In -pentetreotide uptake were detected: three in the liver and three over the pancreatic area (Fig. 1). All lesions showed intense and almost exclusive accumulation of the radiopharmaceutical so that the abdominal organs (liver, spleen and kidneys), which usually show some variable individual uptake of ^{111}In -pentetreotide, were scarcely visualized in the scans.

DISCUSSION

Somatostatin receptor scintigraphy has emerged as a promising imaging method. It is based on the specific binding of radiolabeled analogs to high affinity somatostatin receptors—mainly subtype 2—expressed by a variety of human tumors. Most pancreatic neuroendocrine tumors express somatostatin receptors and can be visualized using ^{111}In -pentetreotide scintigraphy when conventional imaging modalities have failed (11,12). If associated with a clinical syndrome due to hormone release by the tumor, they are classified as functional, or if not associated with elevated plasma level of any known peptide, as nonfunctioning. Therapy with octreotide, a somatostatin analog, has been shown to be beneficial in the treatment of the clinical symptoms in patients with functional tumors (13).

Studies that directly compare somatostatin receptor imaging *in vivo* with somatostatin receptor status *in vitro*, on the resected tumor from the same individual, have shown an excellent correlation between *in vivo* and *in vitro* data, especially in neoplasms with high density and homogeneous distribution of somatostatin receptors, such as gastroenteropancreatic neuroendocrine tumors (5,14). Nevertheless, among 78 neuroendocrine tumors tested *in vitro*, Reubi et al. (6) found that the two somatostatinomas were somatostatin receptor-negative in binding assays and in receptor autoradiography experiments.

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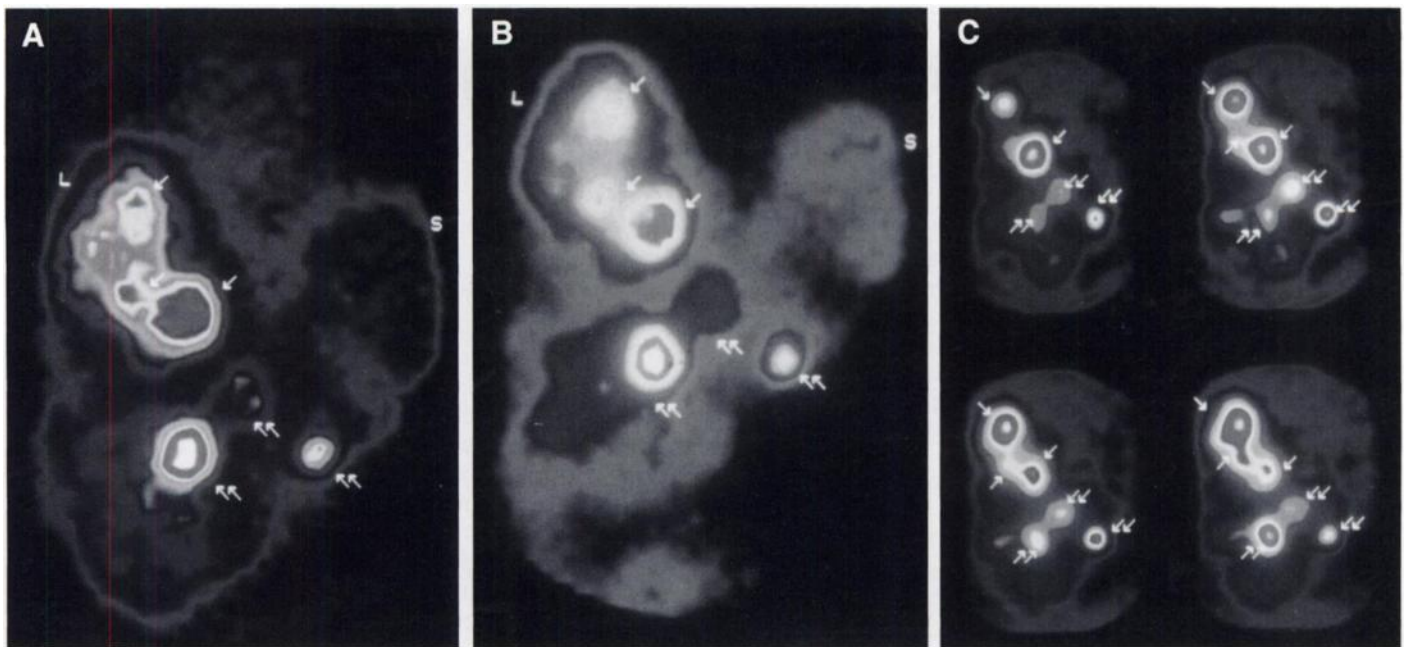


FIGURE 1. Indium-111-pentetreotide planar scintigraphy at 4 (A) and 24 hr (B) and 4-hr SPECT imaging (C), coronal slices, show three foci of abnormal uptake over the pancreatic area (double arrow) and three hepatic hot spots (single arrow). L = liver; S = spleen.

Moreover, the two somatostatinoma samples contained the highest levels of somatostatin messenger ribonucleic acid of all tumors considered, suggesting that the high levels of somatostatin secreted may downregulate somatostatin receptors. This observation as well as occupancy of the available receptors by endogenous somatostatin may lead to false-negative in vivo results using scintigraphy (7).

In vivo visualization of somatostatinoma with ^{111}In -pentetreotide scintigraphy is possible even in the presence of high levels of circulating somatostatin. In this patient, somatostatin receptor imaging clearly detected both the pancreatic tumor sites and the metastatic lesions in the liver, and intense tumor uptake of the radiopharmaceutical was observed. Moreover, scintigraphy demonstrated more somatostatinoma lesions than other conventional imaging methods consistent with the results obtained in larger series (9,12,15).

CONCLUSION

Indium-111-pentetreotide scintigraphy can successfully localize primary and metastatic somatostatinoma.

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