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Visualization of Myocardial Metastasis of Carcinoid Tumor by Indium-111-Pentetreotide

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We present a case of metastatic carcinoid tumor metastatic to the heart, presenting as ventricular arrhythmia and diagnosed by ¹¹¹In-pentetreotide scintiscan despite negative endocardial biopsy. The incidence and diagnosis of carcinoid heart disease is discussed, as well as the complementary role of high-resolution anatomical images (CT, MRI) with functional images (SPECT, PET) to determine the correct diagnosis of this rare condition.

Key Words: carcinoid tumor, indium-111-pentetreotide; heart

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Carcinoid tumor is a rare disease that originates from argentaffin cells of the gastrointestinal tract. Only 4% of these tumors lead to the carcinoid syndrome, which is characterized by flushing, telangiectasias, diarrhea, bronchoconstriction and right sided cardiac disease (1,2). Carcinoid heart disease occurs in up to 50% of the patients with carcinoid tumor, usually comprising endocardial and valvular lesions in the right heart (3,4). This is thought to be a result of excess circulating serotonin secreted by the liver metastasis. The left heart is relatively spared because serotonin is deactivated by enzymes found in the lungs (1,5,6).

In contrast, tumor metastasis to the myocardium is exceedingly rare. Less than ten cases have been reported in the past 30 yr (3,7-9).

We report here a case of malignant carcinoid tumor with metastases involving the right ventricle, presenting as ventricular arrhythmia detected during preoperative cardiac assessment.

CASE REPORT

A 54-yr-old man was admitted initially in May 1989 for observation of abdominal trauma due to a motor vehicle accident. At that time, an abnormality of the ileo-cecal region was found on the CT scan which was considered to be most likely a hematoma secondary to trauma. However, close follow-up revealed that the mass was persistent and increasing in size; these findings were also confirmed on subsequent gastrointestinal series and barium enema. Surgical exploration was performed, revealing a large tumor in the ileo-cecal region extending inferiorly into the pelvis and superiorly to the second part of the duodenum. The omentum as well as

multiple mesenteric lymph nodes were also involved. Extensive right hemicolectomy with resection of 2 feet of the terminal ileum and primary anastomosis was performed. The pathology report was consistent with carcinoid tumor of the distal ileum with metastasis extending into the omentum and involving four of six lymph nodes.

The patient was followed with yearly CT scans of the abdomen for the next 3 yr. In July 1992, abdominal CT revealed a 2 × 2-cm nodular lesion anterior to the liver suggestive of metastasis. Urinary 5-hydroxyindolacetic acid levels were also determined and showed significant elevation with abnormal results of 59.4 mg in 24 hr (normal values = 0-6 mg/24 hr). The patient also complained at that time of episodes of diarrhea together with the presence of periodic flushing of the face.

The patient underwent a second explorative laparotomy in August 1992, and the findings were consistent with extensive metastatic disease involving the small and large bowel with multiple nodules involving the entire mesentery. The patient was followed expectantly off therapy until September 1993 when he was started on 5-fluorouracil (5-FU) for impending bowel obstruction.

His disease remained stable on 5-FU until July 1994, when he presented with an episode of bowel obstruction. A palliative colonic bypass was subsequently performed.

At the time of surgery for his bowel obstruction, the patient was found to have ventricular arrhythmia. Echocardiogram revealed a large (5-cm) right ventricular mass protruding into the ventricular cavity. Mitral valve prolapse was also noted, with mild aortic insufficiency and moderate tricuspid insufficiency. Endocardial biopsy of the mass was reported as "normal heart muscle".

In September 1994, the patient was referred to the nuclear medicine department for evaluation of the extent of his disease and to determine whether or not the cardiac mass was indeed related to the carcinoid tumor.

After intravenous injection of 6 mCi ¹¹¹In-pentetreotide, anterior and posterior whole-body images were obtained at 4 and 24 hr. SPECT imaging of the abdomen and pelvis were also obtained at 4 hr and of the chest at 24 hr. The whole-body images showed multiple abnormal focal uptake in the abdomen, liver, mediastinum, neck, both thighs and the region of the heart just above the diaphragm (Fig. 1). Fusion of the SPECT and CT images confirmed the presence of somatostatin receptors in the right ventricular mass (Fig. 2).

Based on this information, the diagnosis of myocardial metastasis was made. In view of the strategic position of the tumor in the

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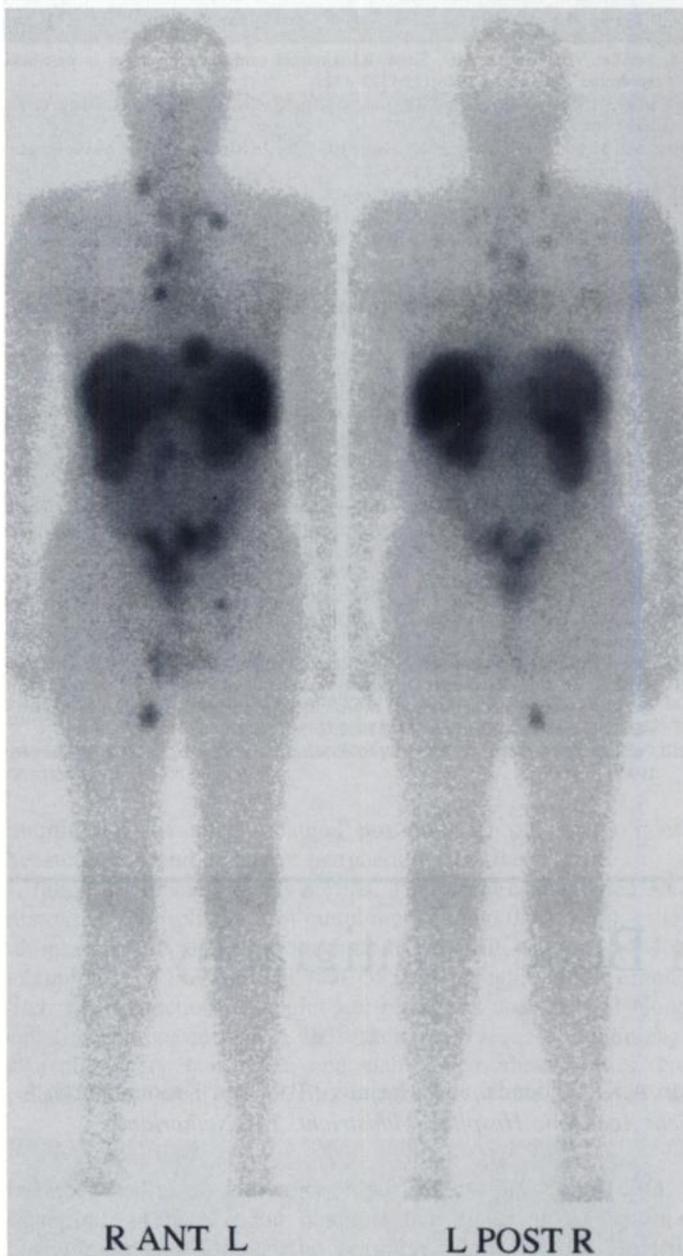


FIGURE 1. Anterior and posterior planar images 4 hr postinjection of 6 mCi ^{111}In -pentetreotide show multiple abnormal focal uptake in the abdomen, liver, mediastinum, neck, both thighs and the region of the heart just above the diaphragm.

right ventricle, it was felt that this mass, as it enlarged, could significantly shorten the patient's life. Therefore, the patient underwent open-heart surgery in October 1994 for resection of the right ventricular mass. Pathological diagnosis was metastatic malignant carcinoid tumor invading the myocardium. He made a quick and uneventful recovery and is currently maintained on Sandostatin suppression.

DISCUSSION

Historically, tumors of the heart were difficult to detect and final diagnosis were often made at autopsy, if at all. With the advent of modern imaging modalities such as ultrasound, CT and MRI, myocardial mass lesions can be readily visualized (10), but preoperative characterization of these mass lesions remain problematic. Sometimes even endocardial biopsy is not helpful, presumably due to sampling error, as exemplified in this case. With the introduction of high-affinity, receptor-directed radiopharmaceuticals labeled with various radionu-

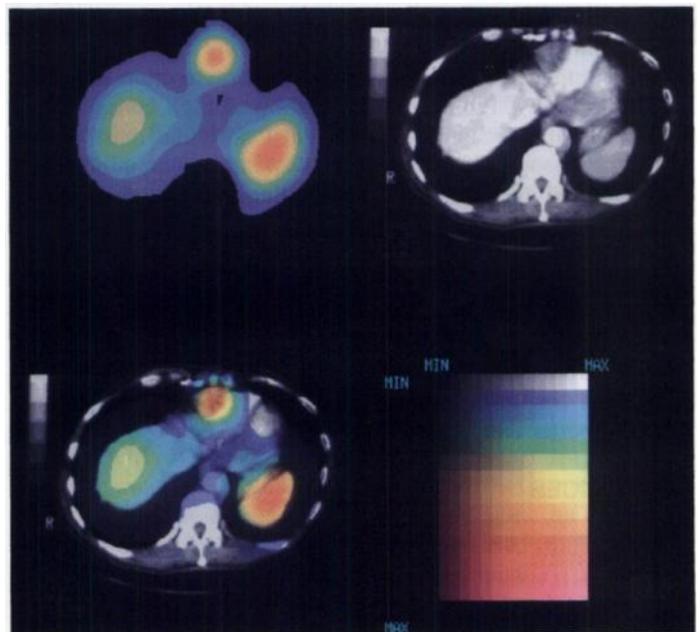


FIGURE 2. Co-registration of SPECT and CT images at the level of the heart. (Top left) SPECT transverse image, (Top right) CT image and (bottom left) registered image with the SPECT image superimposed on the CT in a "colorwash" display. There is precise localization of the focal area of ^{111}In -pentetreotide uptake in the right ventricular myocardial mass lesion seen on CT scan.

clides, nuclear medicine provides the unique opportunity for in vivo characterization of lesions on a functional and molecular level. The image co-registration (fusion) technique (11) offers the advantage of combining the high-resolution anatomic images from CT or MRI with the functional strength of nuclear medicine images (SPECT/PET), thus allowing precise anatomic localization of the functional abnormalities seen on nuclear medicine images.

Localization of carcinoid tumors by conventional imaging methods, such as transabdominal ultrasonography, CT, angiography and MRI is sometimes difficult. This is mainly due to their small size and their proximity to hollow organs (12). The recent introduction of somatostatin receptor imaging adds an important tool in the armamentarium of carcinoid detection. On the basis of in vivo and in vitro studies showing the presence of a high number of somatostatin binding sites on neuroendocrine tumors in comparison with normal tissue, Reubi et al. (13) developed a radioiodinated somatostatin analog, ^{125}I -Tyr3-octreotide, suitable for in vivo somatostatin receptor imaging. The method has been successfully used to image patients with somatostatin receptor-bearing tumors, including gastroenteropancreatic and neuroendocrine tumors (14-16). More recently, an ^{111}In -labeled analog, pentetreotide, has been developed (14,17). This latter compound has been shown to be very sensitive for carcinoid tumor, being positive in over 85% of reported cases (18,19). In the right clinical context, pentetreotide imaging has been very helpful in the evaluation of patients with carcinoid syndrome, both in the localization of the primary tumor as well as screening for metastatic sites. Also, since radiopharmaceutical uptake has been correlated with tumor responsiveness to somatostatin therapy (20,21), the imaging studies have allowed clinicians to predict the effectiveness of the nonradiolabeled somatostatin analog in patients with carcinoid symptoms.

In this report, our patient with known metastatic carcinoid tumor had a myocardial mass lesion. Although carcinoid involvement of the heart as a consequence of high serotonin

levels is a common finding, actual tumor growth in the myocardium is rare. In our patient, despite the finding of a negative endocardial biopsy, the ^{111}In -pentetreotide scan, co-registered with CT, unequivocally showed high concentration of somatostatin receptors in the right ventricular mass lesion, providing strong evidence that this was indeed carcinoid tumor metastatic to the heart. These findings were subsequently confirmed at surgery.

CONCLUSION

This case illustrates the usefulness of ^{111}In -pentetreotide and fusion imaging to evaluate metastatic carcinoid tumor. This technique represents a safe and powerful tool for noninvasive in vivo tissue diagnosis and results in a more rational management plan and better care for the patient.

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Lung and Gastric Uptake in Bone Scintigraphy of Sarcoidosis

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We report on $^{99\text{m}}\text{Tc}$ -MDP uptake in lungs and stomach in a patient with hypercalcaemia and renal failure due to elevated $1,25(\text{OH})_2\text{vitD}_3$ because of sarcoidosis. Presently, this typical scan pattern has only been described in patients with malignancies, parathyroid adenoma and drug-induced vitamin D intoxication. We offer possible explanations for the findings in our patient.

Key Words: sarcoidosis; lung; stomach; bone scintigraphy

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Extraosseous fixation of activity in organs can sometimes be seen in bone scintigraphy. This phenomenon is usually associated with microscopic calcifications due to an abnormality of calcium metabolism and occurs most often in the lungs. Hypercalcaemia and renal failure are often present but are not necessarily prerequisites to observe this phenomenon (1). Sometimes multiple organs are involved (2). Concomitant lung and gastric uptake is rare. Published reports describe the occurrence in patients with malignancy: multiple myeloma (3-8), breast cancer (9), Hodgkin's disease (10) and bladder carcinoma (11).

Of special interest are the reports that describe increased activity in the lungs and stomach not related to malignant disease. Those articles reported on patients with parathyroid adenoma (12), Paget's disease and vitamin D intoxication in conjunction with high calcium intake (6,13).

We report on a patient with sarcoidosis who had the same rare combination of lung and gastric uptake on a $^{99\text{m}}\text{Tc}$ -methylene diphosphonate (MDP) bone scan.

CASE REPORT

Clinical Data

A 70-yr-old man was admitted to our hospital because of slowly progressive dyspnea, orthopnea, edema and decreased diuresis. His medical history reported acute rheumatic fever in childhood and repeated cardiac surgery for aortal, mitral and tricuspidal valve replacement between 1980 and 1992. Five years before admission, a CT scan of the thorax showed massive hilar and mediastinal lymphomas. Sarcoidosis was diagnosed after lymph node biopsy.

For several years, there was stable, slightly impaired renal function: serum calcium rose gradually from a normal value to 2.89 mmol/liter 3 mo before admission. The patient did not smoke or use alcohol. His medication consisted of bumetanide, isosorbide-5-mono-nitrate and acenocoumarol. His temperature was 36.8°C, blood pressure 140/80 mmHg, pulse 70/min and respiratory rate 35/min. Elevated central venous pressure, grade 2 systolic cardiac

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