CASE REPORT

Intraoperative Hand Held Gamma Probe Detection of a Recurrent Nonfunctional Neuroendocrine Tumor

Robert M Van Haren[1], Timothy L Fitzgerald[2,3]

[1]College of Human Medicine, Michigan State University. Lansing, MI, USA. [2]Department of Surgical Oncology, Richard J Lack Cancer Center at Saint Mary's Mercy Medical Center. Grand Rapids, MI, USA. [3]Division of Surgical Oncology, East Carolina University Brody School of Medicine. Greenville, NC, USA

ABSTRACT

Context The advantage of intraoperative gamma probe detection with ^{111}In-DPTA-octreotide radiotracer has previously been demonstrated in functional neuroendocrine tumors. We report the only known case of a recurrent nonfunctional pancreatic neuroendocrine neoplasm localized intraoperatively using this radiotracer and a hand held gamma probe.

Case report A 51-year-old woman was found to have a recurrence 23 months after laparoscopic distal pancreatectomy, splenectomy and wedge resection of a liver metastasis for a non-functional neuroendocirne neoplasm of the pancreas. CT scan and ^{111}In-DPTA-octreotide scan displayed two lesions in the right lobe of the liver and a third area of increased isotope uptake adjacent to kidney and pancreas. A single liver lesion was seen on CT. There were concerns regarding the ability to localize the lesion in the upper abdomen. In order to facilitate identification the patient was injected with ^{111}In-DPTA-octreotide preoperatively and intraoperatively a gamma probe was used to identify two lymph node posterior to the pancreas, only one of which could be palpated.

Conclusion In this case the technique of preoperative injection with octreotide radiotracer and intraoperative hand held gamma probe successfully localized a nonfunctional neuroendocrine tumor that CT scan and intraoperative exploration failed to identify.

INTRODUCTION

Neuroendocrine tumors can be difficult to localize with conventional imaging such as CT scan, ultrasound (US), or MRI. Single photon emission computed tomography (SPECT) imaging with ^{111}In-DPTA-octreotide radiotracer can be helpful in localization of primary and secondary neuroendocrine tumors. A natural extension of this technique is intraoperative localization with a hand held gamma probe similar to sentinel lymph node biopsy, minimally invasive parathyroid, and radioimmune guided surgery. This approach has been successfully applied to functional pancreatic neuroendocrine tumors. We report the only known case of a nonfunctional pancreatic neuroendocrine tumor localized intraoperatively using ^{111}In-DPTA-octreotide radiotracer and a hand held gamma probe.

CASE REPORT

A 51-year-old woman presented with dull, deep left abdominal pain, and mild fevers. CT scan identified a cystic neoplasm in the tail of the pancreas, measuring 38 mm in diameter. A hepatic lesion most consistent with a

cavernous hemangioma was also visualized on CT scan. Subsequent, endoscopic ultrasound (EUS) demonstrated a solid, round lesion suspicious for a neuroendocrine tumor. The patient underwent a laparoscopic distal pancreatectomy with splenectomy, and intraoperatively she was noted to have one left lateral segment liver lesion that was treated with wedge resection. The surgical pathology revealed a 4.5 cm pancreatic nonfunctional neuroendocrine neoplasm with moderate atypia, 2/9 metastatic lymph nodes, and an isolated hepatic metastasis. The patient tolerated the procedure well and was followed with routine pancreatic polypeptide and chromogranin A.

Twenty three months after initial surgery, multiple metastases were noted. CT scan displayed a vascular lesion with increased size (from 16x10 mm to 21x17 mm) in the right lobe of the liver that was suspicious for metastasis (Figure 1). ^{111}In-DPTA-octreotide scan demonstrated two lesions in the anterior and inferior right lobes of the liver, only one of which was seen on CT, and a third area of increased isotope uptake adjacent to the superior pole of the kidney and posterior to the pancreas. Chromogranin A and pancreatic polypeptide, 26 ng/mL (reference range: 2-18 ng/mL) and 334 pg/mL (reference range: 0-290 pg/mL), respectively, both increased to abnormal range supporting the diagnosis of recurrence.

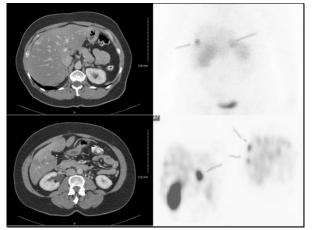Right hepatic resection was planned, however

Figure 1. CT scan and ^{111}In-DPTA single photon emission computed tomography (SPECT) scan. Liver and extrahepatic metastasis are denoted by arrows.

there were concerns regarding the ability to localize the lesion in the upper abdomen. In order to facilitate identification the patient was injected with 3.6 millicuries of ^{111}In-DPTA-octreotide 24 hours preoperatively. Intraoperatively a Navigator probe[TM] (MIPS Technologies, Mountian View, CA, USA) was used to identify regions of increase tracer uptake. Identification was hindered by high background counts, particularly in the kidney. However, an area of clear increased uptake was noted posterior to the pancreas corresponding to SPECT scan images. An additional lymph node was identified medially with increased activity when compared to the background. After excision an *ex vivo* ten second count was performed and compared to the abdominal background counts and both lymph nodes had significantly increased signals. The first lymph node was palpable and enlarged but the second had normal dimensions. Because the patient was high risk for additional celiac lymph node disease a complete celiac artery lymphadenectomy was performed; 19 additional lymph nodes were obtained, none of which had metastatic disease. Of note *ex vivo* counts of this tissue demonstrated no tracer uptake. The final surgical pathology demonstrated 2 right hepatic lesions, and 3/22 lymph nodes involved metastases.

Post-operatively patient was followed with periodic CT, ^{111}In-DPTA-octreotide scan, and laboratory studies (chromogranin A and pancreatic polypeptide). Fifteen months after the second surgery, ^{111}In-DPTA-octreotide with SPECT imaging revealed an abnormal focus of radiotracer uptake within in the central portion of the residual liver that was not visualized on CT scan. MR imaging correlated to the ^{111}In-DPTA-octreotide scan with a small area (10 mm) of enhancement just lateral to the bifurcation of the portal vein and patient underwent complex wedge resection of this segment 4a/b lesion.

DISCUSSION

Neuroendocrine tumors typically arise from the pancreatic islets of Langherans, and are also known as islet cell tumors. They are rare

tumors, with an incidence of 1-2/100,000 cases per year. Pancreatic neuroendocrine tumors are divided into two groups: functional and nonfunctional. Functional tumors are often discovered secondary to symptoms of the active hormone such as: insulin, glucagon, somatostatin, growth hormone releasing factors, adrenocortico-trophic hormone (ACTH), vasoactive intestinal peptide (VIP), or gastrin. Nonfunctional neoplasms are identified by local tumor mass effects, vague abdominal pain, or incidentally on imaging. Increasing use and quality of abdominal imaging has lead to increased identification of asymptomatic neoplasms such as kidney, liver, and pancreatic lesions [1, 2, 3]. There are several reports of pancreatic "incidentalomas" in the literature [4, 5, 6]. Many of these incidentalomas are nonfunctional neuroendocrine neoplasms. Surgery is the mainstay of treatment for neuroendocrine tumors, and the only curative therapy.

A variety of imaging studies can be used for tumor staging and localization of neuroendocrine tumors such as CT scan, MRI, EUS, and myocardial ^{123}I-metaiodo-benzylguanidine (MIBG) [7]. Although, as was evident in our case, imaging techniques such as CT scan, EUS, and MRI can fail to localize neuroendocrine tumors. This failure has also been reported for functional neuroendocrine tumors such as insulinomas where 40% of cases are not visualized by conventional imaging [8].

SPECT ^{111}In-DTPA-octreotide scans utilize tumor receptor binding of radio labeled isotopes to somatostatin receptors to localize these neoplasms. Somatostatin is a natural peptide hormone secreted by the digestive system and many other sites of the body. Five cell membrane receptors (somatostatin receptors 1-5) are responsible for cellular functions including inhibition of cell proliferation (somatostatin receptors 1 and 2), apoptosis (somatostatin receptor 3), and antimitotic effects (somatostatin receptor 5). Octreotide, a somatostatin analog, has been effective in inhibiting hormone secretion by

targeting these somatostatin receptors and thus controlling hormone related symptoms [9].

SPECT ^{111}In-DTPA-octreotide scan is superior to CT, MRI, angiography, and EUS for identifying islet cell neoplasms, carcinoid and their metastases; with a sensitivity of 82-95% [10]. A natural extension of this technique is intraoperative localization with hand held gamma probe. This is currently employed in clinical practice with sentinel lymph node biopsy and minimally invasive parathyroid surgery. Radioimmune guided surgery has been described for localizing primary or metastatic colorectal cancer, medullary thyroid carcinoma, and insulinomas [11, 12]. The superiority of intraoperative gamma probe detection was reported in a study of gastro-entero-pancreatic neuroendocrine (carcinoid) neoplasms. Seventy somatostatin receptor positive lesions were localized by intraoperative gamma probe. Only 74% of these lesions were visualized on preoperative receptor imaging, 44% were localized by surgical palpation, and 43% by other radiological techniques. Additionally, intraoperative gamma probe localized smaller lesions (6 mm) as compared to surgical palpation (10 mm) [12].

In the presented case the modified radioimmune guided surgery technique allowed identification of pathologic lymph nodes that were radiologically but not clinically obvious. One lymph node was palpable and could possibly have been identified with some difficulty by manual exploration; the second would not have been detected in this manner. Identification was somewhat difficult secondary to high background counts, but there was a clear distinction confirmed with *ex vivo* counts.

In conclusion, the use of ^{111}In-DPTA-octreotide radiotracer and intraoperative hand held gamma probe can be used to localize nonfunctional neuroendocrine metastases that are not seen on imaging or that would be difficult to localize with traditional surgical exploration. This tumor localization technique was shown to be superior to CT scan and SPECT imaging in our patient's case.

Correspondence
Timothy L Fitzgerald
Division of Surgical Oncology
Brody School of Medicine
600 Moye Blvd
Greeenville, NC
USA 27834
Phone: +1-252.744.5418
Fax: +1-252.744.5777
E-mail: fitzgerald_timothy@hotmail.com

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