Intraoperative Detection of a Bronchial Carcinoid With a Radiolabeled Somatostatin Analog*

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Carcinoid tumors of the lung are rare neuroendocrine tumors that make up approximately 1 to 2% of all lung neoplasms. These tumors overexpress somatostatin receptors, and somatostatin analog therapy has become standard in the treatment of carcinoid tumors. In addition, radiolabeled somatostatin analogs have been used to diagnose and treat these lesions. We describe the case of a patient with a right lung mass diagnosed as a carcinoid tumor. The patient underwent complete resection of this tumor with the assistance of intraoperative detection with a handheld gamma probe after the administration of the radiolabeled somatostatin analog 111In-pentetreotide. This approach allowed us not only to detect the tumor easily, but to scan the bed of the tumor after resection and to re-excise an area of increased radioisotope uptake that corresponded to the presence of residual tumor. We believe this to be the first reported case of bronchial carcinoid resected with the assistance of intraoperative gamma detection after the administration of a radiolabeled somatostatin analog. This technology allowed us to achieve a complete surgical resection with no residual tumor detected either pathologically or by somatostatin scanning. (CHEST 2002; 121:985–988)

Key words: bronchial carcinoid; indium; 111In-pentetreotide; radiolabeled; somatostatin

*Carcinoid tumors were first described by Labarsch in 1888, when he reported the autopsy findings of two patients with multiple tumors in the distal ileum. In 1907, Oberndorfer introduced the term Karzinoide or resem-

blng carcinoma to describe a midgut tumor that was morphologically different than an intestinal adenocarcinoma. Carcinoid tumors of the lung are rare neuroendocrine tumors that make up approximately 1 to 2% of all lung neoplasms. They are derived predominantly from enterochromaffin or Kulchitsky cells, which are located in the bronchial mucosa.3

Most patients with a bronchial carcinoid tumor present without symptoms in the fifth decade of life. The majority of the tumors are perihilar in location, and patients often present with recurrent pneumonia, cough, hemoptysis, or chest pain. The carcinoid syndrome occurs in 5 to 10% of the cases and clinically develops when the vasoactive substances produced by carcinoid tumor escape hepatic degradation and gain access into the systemic circulation.4 The cardinal feature of the carcinoid syndrome is flushing attacks, occurring in 25 to 70% of patients initially and in 60 to 95% at some time during the course of the disease. The typical flush is the sudden appearance of a deep red or violaceous erythema of the upper part of the body, primarily the face and neck.4 Cardiac involvement by echocardiogram reportedly occurs in roughly two thirds of patients with carcinoid syndrome and reaches hemodynamic significance in a smaller percentage of cases.

Carcinoid tumors also have been shown to overexpress somatostatin receptors, and somatostatin analog therapy for carcinoid disease has become a mainstay of treatment. Because of the short half-life of native somatostatin (approximately 2 min), several somatostatin analogs have been developed, and among these is octreotide acetate (Sandostatin, SMS 201–995; Sandoz; Basel, Switzerland).5 This analog has a half-life of nearly 1 h and is also more potent than native somatostatin.

Based on the effects of somatostatin and its analogs on both in vitro and in vivo carcinoid tumors, Krenning et al6 began using radiolabeled somatostatin analogs and external scintigraphy to image carcinoid and other neuroendocrine tumors in 1987. Currently, the somatostatin analog diethylenetriamine pentaacetic acid (DTPA)-D-Phe6 octreotide (pentetreotide), labeled with 111In (OctreoScan; Mallinkrodt-Tyco; St. Louis, MO) is widely used as a radioligand to identify somatostatin receptor-expressing tumors, especially neuroendocrine tumors.7,8

In addition to external scintigraphy imaging of neuroendocrine tumors after the administration of radiolabeled somatostatin analogs, intraoperative localization of these tumors also has been described. This technique has been used for the detection of occult gastrinomas after the administration of 123I-lanreotide.9 In this study, patients received 100 to 150 μCi of the drug intraoperatively, and a hand-held gamma detector was used to detect tumor binding of the analog. This approach also has been
described for the intraoperative detection of lymph node metastases in women undergoing surgery for primary breast carcinomas.\textsuperscript{10}

We report a case of a bronchial carcinoid resected in a 38-year-old woman with the assistance of intraoperative tumor detection using a hand-held gamma probe after the administration of the radiolabeled somatostatin analog \textsuperscript{111}In-pentetreotide. A review of the literature leads us to believe that this is the first reported case of a bronchial carcinoid tumor resected with the assistance of this technology.

**Case Report**

A 38-year-old white woman presented with a 9-month history of dry, hacking cough, palpitations, chest pain, and shortness of breath. She was treated initially for bronchitis without improvement, and a chest radiograph was obtained, which revealed a 5-cm lung mass (Fig 1). A further workup included a CT scan of the chest, which showed a right lower lobe lung mass (Fig 2), and bronchoscopy, which was nondiagnostic. The patient also underwent a transthoracic echocardiogram, which showed an abnormal mitral valve secondary to a rheumatic process with mild mitral stenosis and severe mitral regurgitation.

The results of laboratory testing included a serotonin level of >2,000 pg (normal, <220 pg) and an elevated 5-hydroxyindolacetic acid level. This prompted the performance of a radionuclide scan with the radiolabeled somatostatin analog \textsuperscript{111}In-pentetreotide (Fig 3), which showed an area of increased activity in the right lung that was consistent with the lesion seen on the chest radiograph, confirming the presence of a somatostatin receptor-expressing tumor. No other sites of increased activity were identified.

Preoperatively, the patient received a 6-mCi dose of \textsuperscript{111}In-pentetreotide. Five days after the administration of the analog, the patient was taken to the operating room and a right thoracotomy was performed. A handheld gamma detector was used to obtain counts of the area of the lesion and surrounding tissues. When used in scanning mode, the detector allows for the squelching of background counts from adjacent reference tissue. When the gamma detector is passed over a tumor with counts greater than the mean reference tissue counts, an alarm is sounded. With the detector in the scan mode, a focus of activity encompassing the known lesion was identified. This was confirmed to be in the right lower lobe, and the patient underwent a wedge resection of the lower lobe. After this resection, the gamma detector again was used to scan the right chest. This revealed a residual focus of increased activity in the bed of the tumor.

**Figure 1.** Chest radiograph revealing a 5-cm mass in the right lung.

**Figure 2.** CT scan of the chest demonstrating a 5-cm mass in the right lower lobe of the lung.

**Figure 3.** Radiolabeled somatostatin analog \textsuperscript{111}In-pentetreotide procedure revealing increased activity in the right lung.
wedge resection and in the adjacent middle lobe. This finding led us to perform a wedge resection of the middle lobe. Following this, the gamma detector again was used to scan the right chest. At this time, no areas of increased activity were identified. Postoperatively, another radionuclide scan with the radiolabeled somatostatin analog 111In-pentetreotide was performed, which showed no evidence of residual disease (Fig 4). The patient was discharged to home without complications on postoperative day 10.

A pathologic analysis of the specimen revealed a carcinoid tumor measuring 6.5 cm in its greatest dimension and infiltrating the lung parenchyma from the hilum to near the pleura. The tumor had involved one surgical margin of the original lower lobe specimen. We were able to clear this margin pathologically after probe-guided wedge resection of the middle lobe.

**Discussion**

Bronchial carcinoid tumors represent one end of a spectrum of malignant tumors of Kulchitsky cell origin. Small cell lung cancers comprise the other end of the spectrum with their predilection for rapid growth as well as early, diffuse dissemination. The biological behavior of typical carcinoid tumors is that of slow growth and rare metastasis. Atypical carcinoid tumors have features intermediate between the two and have a 30 to 70% likelihood of being metastatic at the time of diagnosis, compared with a 5 to 10% incidence for typical carcinoid tumors.11

It is well-known that carcinoid tumors and other neuroendocrine tumors express somatostatin receptors.12 A number of authors6,8 have described the use of radiolabeled somatostatin analogs to detect these tumors using scintigraphic imaging techniques. In this report, we have described the use of intraoperative gamma probe detection of a bronchial carcinoid tumor after injection with 111In-pentetreotide.

This technique has been reported previously for other somatostatin receptor-positive tumors. Woltering et al9 described this technique for the localization of occult gastrinomas after injection with 125I-lanreotide, another radiolabeled somatostatin analog. In that study, two patients with unlocalized gastrinomas were studied with intraoperative gamma detection of an 125I-labeled somatostatin analog (lanreotide) to localize their tumors. In both patients, a 100-mCi dose of the analog was injected during exploration and a hand-held gamma probe was used to scan the abdomen. In one patient, a single source of increased counts was discovered in a retroduodenal lymph node. Histologic analysis of this node did not identify any tumor, but the patient’s gastrin level, which had been elevated preoperatively, was normal 4 months after the operation. In the second patient, five areas of increased activity were discovered and excised. Three of these had visible tumor present on histologic examination, and this patient had a gastrin level that normalized after surgery as well. Cuntz et al10 also described intraoperative gamma detection of axillary lymph nodes in women with primary breast carcinomas after the administration of 125I-lanreotide. In this study, 13 women underwent radio-guided axillary dissection after administration of the isotope preoperatively. This technique predicted the presence of microscopic tumors in 20% of lymph nodes that had received negative results by routine histologic testing but had been confirmed by more sensitive pathologic techniques.

Bronchial carcinoid tumors typically have been treated with the anatomic resection of the tumor.13,14 In this case, the patient underwent such a resection followed by intraoperative scanning of the resection bed. This identified what appeared to be an area of residual disease, despite a gross tumor-free margin, and prompted further resection. When the specimen was analyzed pathologically, this confirmed the presence of a microscopically positive tumor margin at the site of increased probe activity, which we were able to clear by further resection. This technique of radio-guided tumor resection allowed us to achieve a complete resection of the tumor, which we believe would
not have been achieved with conventional surgery. This technique may be useful in localizing smaller somatostatin receptor-expressing tumors at the time of operation. More importantly, it is beneficial in achieving complete resection of the tumor and its nodal basin.

References

Management of an Intrabronchial Rupture of Right Main Pulmonary Artery*

A Case Report

Christophe Pinet, MD; Wojciech Palka, MD; Dominique Metras, MD; Pascal Thomas, MD; Bernard Méric, MD; and Jean-François Dunion, MD, FCCP

We report a case of massive endobronchial hemorrhage following a fistula formation of the right pulmonary artery to the right mainstem bronchus in a 15-year-old girl. The fistula had occurred 39 days after the patient had undergone bilateral lung transplantation for cystic fibrosis. The post-transplantation course was remarkable for bronchial colonization by Aspergillus at the site of right bronchial anastomosis and an episode of spontaneous, self-limited hemoptysis on postoperative day 17. A massive endobronchial hemorrhage during surveillance bronchoscopy occurred 39 days after transplantation. Immediate intervention, including rigid bronchoscopy followed by surgery, was effective in saving the patient. The pathophysiologic hypothesis to explain the fistula of the right pulmonary artery to the right mainstem bronchus probably involves ischemia of the anastomosis with necrosis of the suture zone complicated by endobronchial infection with Aspergillus. Rigid bronchoscopic intervention associated with an excellent medical surgical collaboration was pivotal in successfully rescuing the patient.

Key words: bronchial aspergillosis; cystic fibrosis; massive hemoptysis; surgical treatment

Truly massive hemoptysis fortunately is rare but, most often, is fatal. At this time, the therapeutic alternatives are limited. We report a case of massive hemoptysis following intrabronchial rupture of the right pulmonary artery 6 weeks after the patient underwent bilateral single-lung transplantation. The young patient was saved due to an effective collaboration between the endoscopy and surgery services.

Case Report

The patient was a 15-year-old girl who presented with terminal respiratory insufficiency secondary to cystic fibrosis. She was otherwise stable with no other significant active medical and surgical problems. On August 20, 1999, the patient underwent bilateral lung transplantation. The time of total ischemia of the graft was 7 h and 30 min. Medical treatment involved use of cyclosporine, azathioprine, and methylprednisolone, combined with empirical anti-infectious agents (IV ganciclovir and amphotericin B). The immediate postoperative period was significant for septicemia due to Alcaligenes xylosoxidans, which resolved with therapy with ceftazidime, tobramycin, and ciprofloxacin. Endobronchial Aspergillus colonization, for which therapy with inhaled amphotericin B was added, occurred mainly on the right

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