

Thymic Carcinoid Responds to Neoadjuvant Therapy with Sunitinib and Octreotide: A Case Report

Anu Dham, MD,* Alexander M. Truskinovsky, MD,† and Arkadiusz Z. Dudek, MD, PhD*

Carcinoids are malignant neuroendocrine tumors consisting of a spectrum of neoplasms from low-grade typical carcinoid to high-grade small cell carcinoma. We report a case of atypical thymic carcinoid that responded to neoadjuvant therapy with octreotide and sunitinib, an oral multikinase inhibitor. After 3 weeks of treatment, tumor size significantly decreased to allow for a safe surgical resection with clear margins. We believe that further study of sunitinib and octreotide with the neoadjuvant intent of preparing tumors for resection is warranted as a strategy to improve curative management of neuroendocrine tumors.

Key Words: Carcinoids, Neoadjuvant therapy, Octreotide, Sunitinib, Somatostatin receptor, Vascular endothelial, Growth factor receptor, Platelet-derived growth factor receptor.

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Carcinoids are a rare type of neuroendocrine tumor that are frequently inoperable due to anatomic location or number of metastases. Chemotherapy is associated with limited response rates and significant toxicities.^{1,2} Carcinoids tumors overexpress somatostatin receptor, and somatostatin analogues are commonly used in the diagnosis and treatment of carcinoids, in which they have shown benefit in improving tumor localization and increasing tumor control.³ Similarly, carcinoids may be susceptible to neoadjuvant therapy targeting several other receptors overexpressed in these tumors, including vascular endothelial growth factor receptor (VEGFR)⁴ and platelet-derived growth factor receptor (PDGFR).⁵ Here, we describe the rapid shrinkage of a thymic carcinoid following neoadjuvant therapy with the somatostatin analogue octreotide and the receptor tyrosine kinase inhibitor sunitinib.

CLINICAL SUMMARY

A 40-year-old man presented with a 6-month history of exertional dyspnea and fatigue. His symptoms subsequently

progressed into dysphagia. Past medical history was not significant for weight loss, night sweats, fevers, facial flushing, or diarrhea. The patient reported mild asthma, use of chewing tobacco, and occasional use of alcohol. He had undergone operations on his knee and wrist. His family history revealed paternal diabetes and rheumatoid arthritis. His physical examination revealed no signs of adenopathy or organomegaly.

Chest radiogram revealed a large anterior mediastinal mass. Positron emission tomography and computerized tomography (PET/CT) scan confirmed the location of a lobulated, heterogenous, soft-tissue mass (8.3 × 5.0 cm) with lymphadenopathy extending into the right hilar region and compressing the right mainstem bronchus (Figure 1). The standardized uptake value (SUV) was 12.7. The mass also abutted the right anterior pericardium, and a 1.4 cm right cardiophrenic lymph node (SUV 5.3) was observed. Patchy nodular opacities were also seen in both lungs. The original percutaneous needle biopsy of the mediastinal mass showed solid sheets of small, monotonous neoplastic cells separated by hyalinized fibrous septa. The tumor had prominent areas of crush artifact. The cells contained scant cytoplasm and small, hyperchromatic nuclei with finely dispersed chromatin. No conspicuous mitotic activity was identified (Figure 2). Immunostains performed at the referring institution demonstrated that the tumor had a neuroendocrine immunophenotype. The tumor showed positive immunostaining for CD117 (c-kit), but not for epidermal growth factor receptors. Based on the low mitotic activity, lack of necrosis, and a low Ki67 (proliferative) index of the tumor, a diagnosis of typical carcinoid tumor was rendered.

As part of staging, the patient underwent drainage of the pericardial fluid along with pericardial biopsy to rule out malignant invasion. No malignant cells were seen in the pericardium, pericardial nodule, or pericardial fluid. OctreoScan imaging showed a large focus of increased tracer uptake in the chest corresponding to the mediastinal mass noted on PET/CT. Normal uptake in liver, spleen, gallbladder, and kidneys was observed. No other focus of abnormal tracer uptake was noted.

The tumor was considered unresectable at the time of diagnosis because of extensive invasion into the mediastinum. The patient was started on sunitinib 50 mg per day for 4 weeks with 2 weeks off and 30 mg of depot formulation of octreotide once every 4 weeks. No treatment-related toxicity was observed. The patient reported resolution of chest pain, pressure and dysphagia. Three weeks after initiation of ther-

From the *Division of Hematology, Oncology, and Transplantation, and †Department of Laboratory Medicine and Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

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Address for correspondence: Arkadiusz Dudek, MD, PhD, Division of Hematology, Oncology, and Transplantation, MMC 480, 420 Delaware Street SE, Minneapolis, MN 55455. E-mail: dudek002@umn.edu

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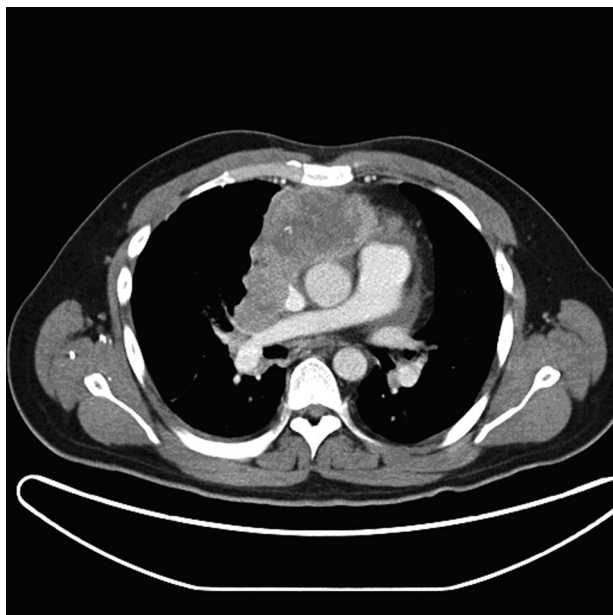


FIGURE 1. Lobulated, heterogenous, mediastinal, soft-tissue mass (8.3×5.0 cm) with right hilar lymphadenopathy. Mass was measured at the level of branching of the main pulmonary artery.

apy, PET/CT scan revealed that the mass had decreased in size to 7.7×4.5 cm (Figure 3). Pericardial thickening adjacent to the mass was observed. The right cardiophrenic lymph node had also decreased in size to 1.3 cm. The patient underwent right pneumonectomy, and the tumor was removed with clean margins. The surgical resection specimen of the right lung showed a firm white tumor measuring $8.5 \times 6.2 \times 3.6$ cm, which was invading the upper lobe of the lung.

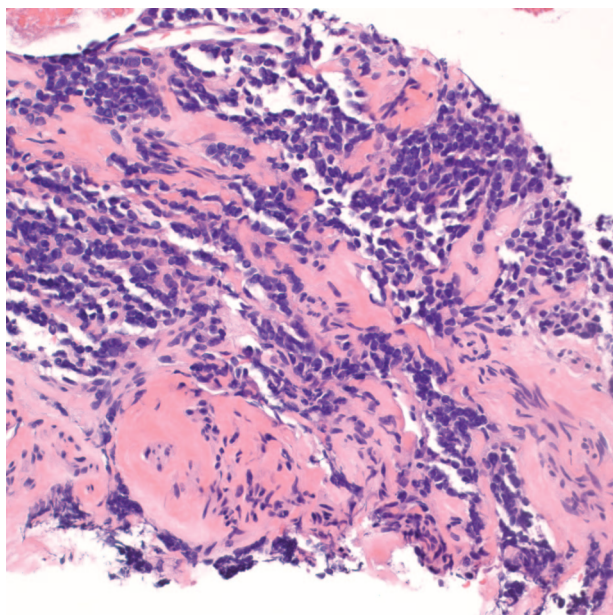


FIGURE 2. Needle biopsy specimen of the mediastinal mass. (Hematoxylin and eosin, original magnification $\times 400$.)



FIGURE 3. Decrease in size of anterior mediastinal mass (7.7×4.5) after 3 weeks of sunitinib and octreotide therapy. Mass was measured at the level of branching of the main pulmonary artery.

The tumor invaded the pericardium, the visceral pleura and the azygous vein. The histopathological findings indicated extensive necrosis and hyalinization of the tumor. Only approximately 30 to 35% of the neoplasm was viable. The viable tumor cells were arranged in nests and solid sheets. They had a moderate amount of cytoplasm, which was more prominent than the cytoplasm of the neoplastic cells in the needle biopsy. The tumor nuclei had finely granular chroma-

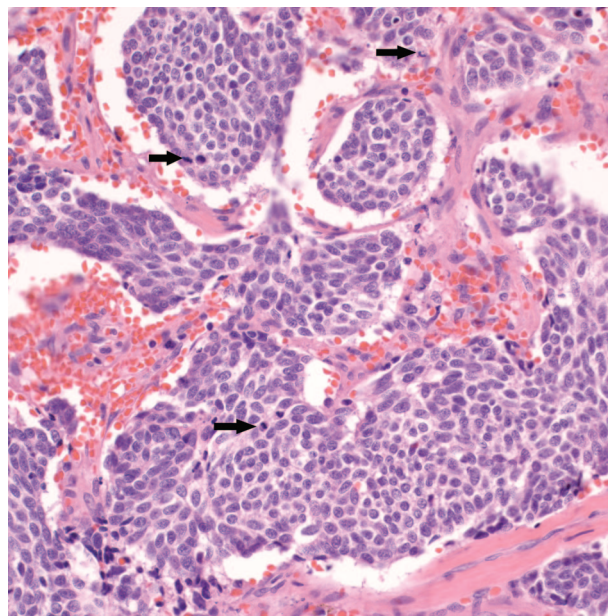


FIGURE 4. Tumor in the resection specimen of the right lung. Arrows mark mitotic figures. (Hematoxylin and eosin, original magnification $\times 400$.)

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