



## Bronchial Carcinoid as a Cause of Hemoptysis

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### Introduction

Carcinoid was first characterized by Lubarsh in 1888.<sup>1</sup> However, Ranson is given credit for the first description of a carcinoid of the ileum in 1890.<sup>2</sup> The term 'karzinoide' was used first by Oberndorfer in 1907 to describe tumors that behaved in a more indolent fashion than typical adenocarcinomas.<sup>3</sup> In 1928, Masson stated that carcinoids should be considered as endocrine tumors since the malignant chromaffin or Kulchitsky cells in this disease exhibit amine uptake and decarboxylation characteristics.<sup>4</sup> In 1930, Kramer grouped carcinoid tumors with cylindromas as bronchial adenomas because of their good prognosis compared with bronchogenic carcinoma.<sup>5</sup> In 1972, Arrigoni and associates<sup>6</sup> designated a subset of carcinoid adenomas that were more aggressive as "atypical".

Bronchial carcinoid is a rare cause of pulmonary neoplasms accounting for about 1-2% of all pulmonary malignancies<sup>7</sup> and unique in the fact that it has neuroendocrine differentiation on histology. The incidence of carcinoid tumors varies with gender, age, and race. The overall incidence in the United States is estimated to be two cases per 100,000 people.<sup>8</sup> Carcinoid tumors often are diagnosed in a person's fifth or sixth decade of life. Except in appendiceal and bronchopulmonary sites, African Americans have a higher incidence than other ethnic groups.<sup>9</sup> It is slightly more common in females (55%

of all cases) than males.<sup>8</sup> Seventy-four percent of carcinoid tumors originated in the gastrointestinal tract; the second most frequent site was in the tracheobronchopulmonary tree with 25%.<sup>8</sup> Bronchial carcinoids have a relatively indolent course and good prognosis if treated, although they do have malignant potential,<sup>10</sup> therefore, it is important to recognize and treat them as soon as possible.

### Case Report

A 46-year-old healthy Caucasian female presented to her primary care physician (PCP) two years prior for an episode of sporadic hemoptysis consisting of 1-2 teaspoons of bright red blood without symptoms of cough, fever, or chills. Laboratory studies and chest x-rays were done at the PCP's office and did not suggest any pathology. No further workup was done.

Two years later, she presented to the PCP's office again with two episodes of hemoptysis about one week apart. The patient did not have any systemic signs of anorexia, weight loss, fever, chills, cough, sputum production, or chest pain. Computed tomography (CT) of the chest showed a 17 x 19 mm nodule in the left perihilar region (Figure 1). She was referred to the pulmonology service because of recurrent episodes of hemoptysis and CT evidence of a nodule.

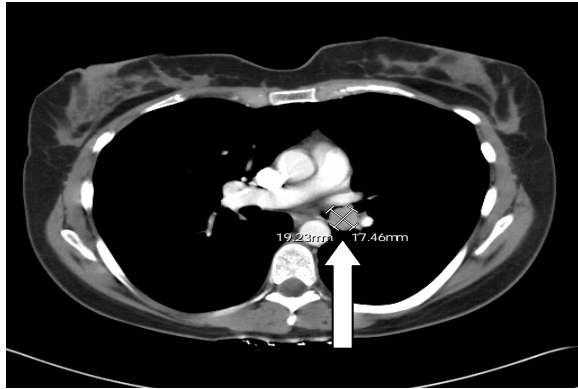


Figure 1. Chest x-ray shows a left perihilar 17 x 19 mass (arrow).

A flexible bronchoscopy was performed electively. During bronchoscopy, an obstructing lesion at the bifurcation of left bronchus was found (Figure 2). Endobronchial brushings and multiple biopsies from the mass showed cells to be consistent with carcinoid features with no pleomorphism (Figure 3) and staining for neuron specific enolase (NSE; Figure 4).

The patient subsequently underwent radiotherapy to decrease the tumor size and the sleeve resection of the tumor. The patient has been doing well since.



Figure 2. Bronchoscopy showed typical finding of a solitary intraluminal mass (arrow).

**Discussion**

Carcinoid tumors are derived from dispersed neuroectodermal cells. They are neoplasms of peptide- and amine-producing

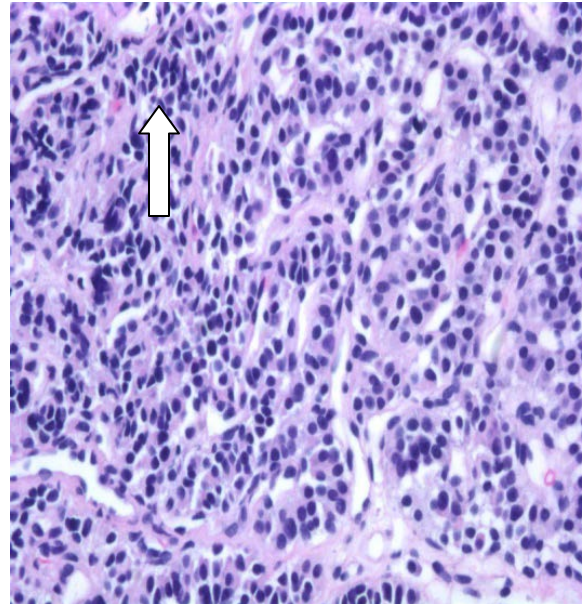


Figure 3. Pathology slide shows the carcinoid cell nests.

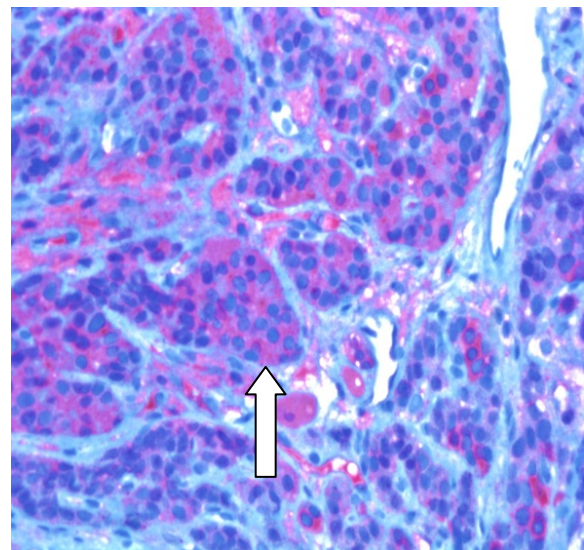


Figure 4. Positive staining is shown for neuron specific enolase.

cells, and their variable hormone profiles are based on the site of origin.<sup>11</sup> Carcinoid tumors can be divided into foregut derived, midgut derived, and hindgut derived.<sup>9</sup> Foregut carcinoids include those derived from the stomach, duodenum, thymus, and bronchus. Carcinoid syndrome is rare in foregut and hindgut derived tumors because the tumor cells of foregut and hindgut origin

do not have enzyme dopa decarboxylase to convert 5-hydroxytryptophan to serotonin. Carcinoid syndrome, if present, is atypical in these tumors. It is mainly the midgut derived which presents with typical carcinoid syndrome.

Bronchopulmonary carcinoid tumors account for approximately 25% to 30% of all carcinoid tumors.<sup>5</sup> The annual incidence rates of bronchial carcinoids are 0.52 and 0.89 per 100,000 population in males and females, respectively (the corresponding values for black males and females are 0.39 and 0.57, respectively).<sup>5</sup>

Pulmonary carcinoid tumors are thought to arise from Kulchitsky cells/neuroectodermal cells disseminated throughout the bronchopulmonary mucosa.<sup>6</sup> Histologically, bronchial neuroendocrine tumors are divided into four distinct histologic types. These include typical bronchial carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma, and small cell neuroendocrine carcinoma.<sup>12</sup> Representing nearly two-thirds of pulmonary carcinoids, well-differentiated neuroendocrine tumors of the lungs and bronchi (typical carcinoids) are composed of cytologically bland cells that exhibit minor cellular atypia and rare mitoses.<sup>12</sup> Based on the 2004 WHO classification, these tumors must demonstrate fewer than two mitoses per 10 high power fields (10 HPF), lack necrosis, and be equal to or greater than 5 mm.<sup>13</sup>

Foregut carcinoids (including those arising in the lung) generally have a low serotonin content. This is because foregut carcinoids often lack aromatic amino acid decarboxylase and cannot make serotonin and its metabolites (including 5-HIAA). Although they can produce a variety of other peptides and hormones within the cell (gastrin releasing peptide, 5-hydroxytryptophan, and chromogranins), bronchial carcinoids only occasionally secrete bioactive amines. As a result, elevated

plasma or urinary hormone levels rarely are detected. Serum levels of chromogranin A are sensitive but a non-specific marker, its levels being lower with bronchial carcinoids than with other neuroendocrine tumors. Measurement of serum CGA levels, however, can be useful to follow disease activity in the setting of advanced or metastatic disease.<sup>14</sup>

Bronchial carcinoids usually present in the fifth decade of life and demonstrate a relatively indolent disease course. Patients may present with recurrent pneumonia, cough, wheezing, hemoptysis, and chest pain.<sup>15</sup> Symptoms are highly variable and often present years before diagnosis. Cushing's syndrome occurs in 2% of patients; moreover, 1% of patients presenting with Cushing's syndrome have a pulmonary carcinoid tumor.<sup>15,16</sup> Acromegaly from ectopic secretion of growth hormone-releasing hormone also has been reported in cases of bronchopulmonary carcinoid. Thus, ectopic secretion of biologically active hormones is not uncommon, as these tumors may secrete corticotrophin and growth hormone with relative frequency. However, carcinoid syndrome occurs in greater than 5% of patients with these tumors because of the relative paucity of serotonin secretion.<sup>17</sup>

Radiologically, most bronchial carcinoids present as abnormal chest x-ray with rounded or ovoid perihilar opacities. A CT scan provides better resolution of the tumor with regard to extent, location, and surrounding lymph nodes.<sup>18</sup> Extensive imaging is important for staging. Endosonography can be used to detect luminal lesions as small as 2-3 mm in size.

Bronchoscopic appearance is a pink or red vascular mass which is endobronchial with intact overlying epithelium.<sup>19</sup> They appear as smooth, cherry red, polypoid endobronchial nodules. Most bronchial carcinoids are in a central location within

reach of a bronchoscope. The histologic diagnosis is made with bronchoscopic biopsy. There may be massive hemorrhage following endoscopic biopsy due to the highly vascular nature of carcinoids.<sup>20</sup>

Surgical resection is the preferred treatment of bronchopulmonary carcinoid tumors in those patients with adequate functional pulmonary reserve. In patients with relatively small (less than 2 cm), localized tumors of the peripheral lung parenchyma, conservative resection via a wedge or segmental resection results in low recurrence rates and excellent long-term survival.<sup>12,21</sup> Tumors with extensive central bronchopulmonary involvement, those with large peripheral parenchymal involvement (> 2 cm), and atypical carcinoids may require more extensive surgical resection with a lobectomy or pneumonectomy.<sup>12</sup> Given the significance of nodal involvement in long-term prognostic models of pulmonary carcinoid disease, systematic radical mediastinal lymphadenectomy provides an advantage to all patients at the time of initial treatment.<sup>22</sup> There is no role for chemotherapy or radiotherapy in treatment of bronchial carcinoid. Palliative radiotherapy prior to surgical resection can be performed to decrease the tumor burden prior to resection.

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Patients with pulmonary carcinoid tumors often have a good prognosis, with 5-year survival rates between 60% and 100% and 10-year survival rates between 40% and 100%.<sup>23</sup> Typical bronchial carcinoid tumors have the best prognoses with 5-year survival of 87 to 100%. Metastases from typical pulmonary carcinoids occur in approximately 12% of cases, and the overall survival rate is greater than 90%.<sup>12</sup>

The optimal post-treatment surveillance strategy is not defined. There is no consensus on what tests should be ordered. Most clinicians perform history and physical examination and chest CT annually for patients with resected typical carcinoid and every six months for resected atypical carcinoids for the first two years, then annually.<sup>24</sup>

## Conclusion

It is important to keep bronchial carcinoid tumor in the differential diagnosis of a patient with hemoptysis who is a non-smoker and has no other risk factors for malignancy or infection and is otherwise healthy. Also, not all lung tumors have poor prognosis. Timely treatment can lead to normal life expectancy in an otherwise healthy patient.

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