

Two cases of endobronchial carcinoid masked by superimposed aspergillosis: a review of the literature of primary lung cancers associated with *Aspergillus*

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ABSTRACT

We describe 2 cases of endobronchial pulmonary carcinoid tumor with superimposed *Aspergillus* colonization. The *Aspergillus* hyphae were associated with fibrin, ulcer debris, and granulomatous inflammation in part masking the carcinoid tumor. Presence of necrotic debris made diagnosis on biopsy difficult, and atypical carcinoid could not be ruled out. The association of carcinoid tumor with aspergillosis is rare and has been reported in 4 other cases thus far. A review of the literature reveals at least 35 cases of lung carcinoma with coexisting *Aspergillus* upon presentation. Most of these carcinomas are either cavitory squamous cell or adenocarcinomas harboring an aspergilloma. The other carcinomas are associated with bronchial obstruction as in carcinoids or are a minor component of a preexisting cavity raising the possibility of “scar carcinoma.” As in aspergillomas not associated with carcinoma, upper lobe involvement predominates. Diagnosis can be challenging with delayed discovery of underlying neoplasm leading to suboptimal treatment.

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1. Introduction

Aspergillus is a genus of mold found worldwide, commonly in soil, decaying vegetation and indoor environments. The genus includes approximately 200 species, but only a few are human pathogens, including *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus terreus*, and *Aspergillus nidulans*. Disease is acquired through inhalation of fungal spores, without person-to-person spread [1]. Aspergillosis is primarily seen in patients with immunocompromise or underlying chronic lung disease. It is also well known to complicate malignant disease, particularly hematologic neoplasms [2]. The fungal infection coexisting with solid cancers is infrequent in the immunocompetent setting [1,3]. However, in 1 small screening study, approximately 25% of patients presenting with bronchogenic carcinoma had a positive culture for *Aspergillus* [4]. There are also scattered case reports of aspergillosis associated with pulmonary carcinomas at the time of primary diagnosis including 4 carcinoid tumors [5–39]. We present here 2 additional cases of pulmonary endobronchial carcinoid tumor with superimposed *Aspergillus* and a review of literature on association of pulmonary carcinoma with aspergillosis.

2. Case reports

2.1. Case 1

A 56-year-old woman with a medical history of recurrent episodes of pneumonia and bronchitis for the last 2 years came to attention due to hemoptysis and shortness of breath. Chest computed tomographic (CT) scan showed a left pulmonary infrahilar soft tissue mass with an endobronchial component extending into the left lower lobe. No fungal organisms or acid fast bacilli were found in sputum cultures. A bronchoscopic examination revealed a friable, white mass nearly completely obstructing her left lower lobar bronchus.

Microscopic examination of sampled biopsy showed 1 larger piece of tissue with nests of bland appearing tumor cells with low mitotic count, covered by a layer of fibrosis, necrotic debris, and fibrin (Fig. 1A and B). In other tissue fragments, small islands of tumor cells were intimately intermingled with the necrotizing granulomatous inflammation (Fig. 2). On immunohistochemistry, the tumor cells stained positive for neuroendocrine markers (CD56 and chromogranin A) and displayed low proliferation rate (<2%) on a Ki-67 stain. A Gomori methenamine-silver stain revealed several acutely branching, septate hyphae in the necrotic debris, consistent with *Aspergillus* (Fig. 3). The tumor nests were thought to represent carcinoid tumor, and the diagnosis of typical carcinoid was favored. However, atypical carcinoid could not be ruled out due to the necrosis. The patient subsequently underwent a left lower lobectomy after completing a course of voriconazole (Fig. 4). Histologic examination of the resection

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specimen revealed a classical typical carcinoid without areas of necrosis. There were neither residual fungal organisms nor granulomatous inflammation to be found. The patient was discharged with no further follow-up to present date.

2.2. Case 2

An 82-year-old woman presented with complaint of progressive shortness of breath. The patient had a history of smoking, chronic obstructive pulmonary disease, chronic heart failure, diabetes, and gastroesophageal reflux disease. On chest CT scan, a right main bronchial mass was found, causing collapse of the right upper lobe (Fig. 5). Further several smaller nodules were seen in the lung parenchyma bilaterally.

Examination of an endobronchial biopsy revealed several fragments of carcinoid in part covered by fibrin, necrotic debris, and fungi, the latter consistent with *Aspergillus* (Fig. 6). In concordance with case 1, typical carcinoid was favored due to low mitotic rate despite the necrosis, although atypical carcinoid could not be ruled out. Sputum culture grew *A. fumigatus*, and she was subsequently treated with itraconazole. The patient was considered to have metastatic spread because the parenchymal nodules were hypermetabolic on positron emission tomography scan. Because of her underlying conditions,

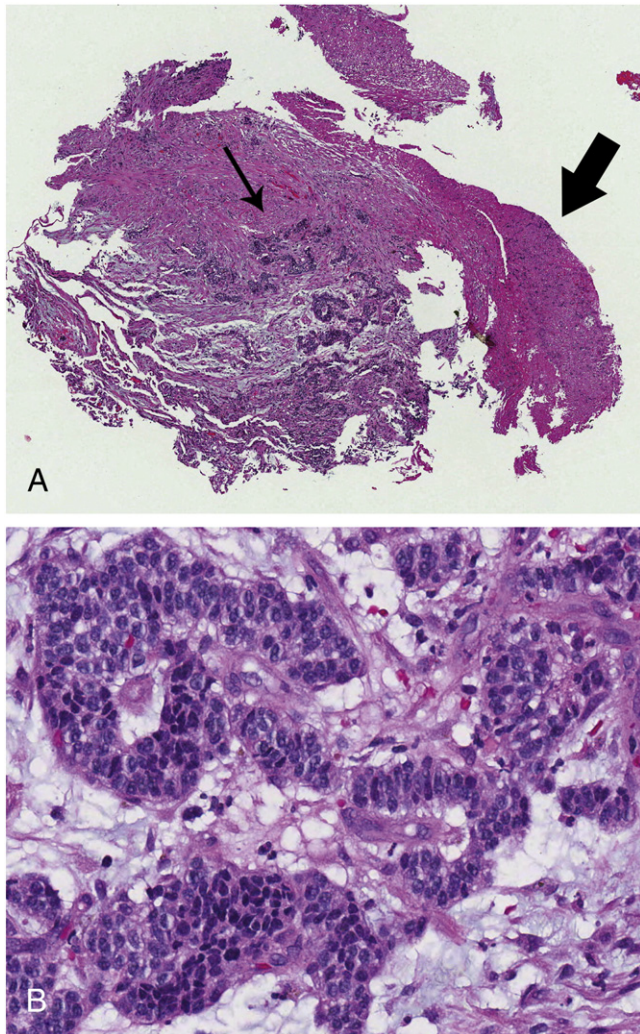


Fig. 1. A, In 1 larger piece of tissue, nests of tumor cells (thin arrow) were seen covered by fibrin, necrotic debris, and fungi (bold arrow) (hematoxylin-eosin). B, In high magnification, nests of bland-appearing tumor cells with low mitotic rate were seen, favoring typical carcinoid (hematoxylin-eosin).

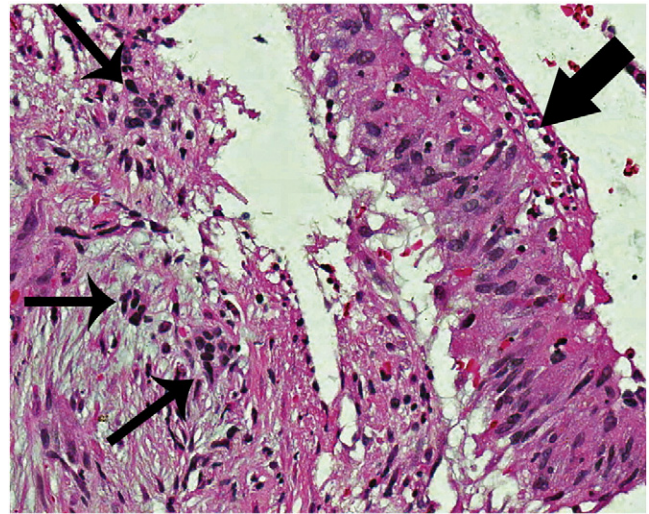


Fig. 2. Other areas displayed fibroblastic proliferation, fibrin, and necrotizing granulomatous inflammation (bold arrow) with intermingled tumor nests (thin arrows) (hematoxylin-eosin).

chemotherapy was withheld. The patient underwent palliative radiation treatment of her main stem lesion and was later lost to follow-up.

3. Discussion

Four previously reported cases of lung carcinoid tumor associated with aspergillosis were found in a review of literature [5–8]. Our 2 cases were received within a period of 6 months. Of these patients (Table 1) [5–8], 4 of the 6 were female. The age span ranged from 11 to 80 years (median, 57 years). In all cases, the tumor was localized centrally in either a main or lobar bronchus and presented itself as an obstructive endobronchial mass without cavity formation. The coexisting *Aspergillus* was considered to represent colonization in our 2 cases. Both patients had an indolent course and were not overtly immunocompromised. Furthermore, there was no fungal invasion of lung parenchyma histologically. Similar findings described in 1 other report were also thought to represent colonization [5]. In 2 other cases, the fungal disease was noninvasive as well, corresponding to an aspergilloma vegetating upon the carcinoid and *Aspergillus* bronchitis,

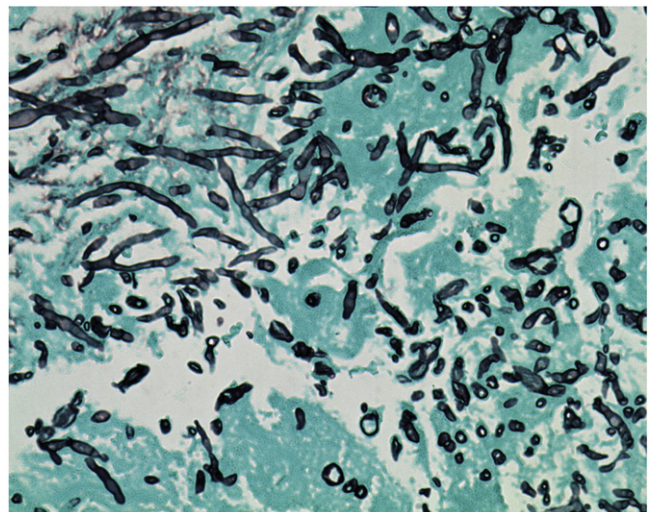


Fig. 3. High-power magnification revealed acutely branching and septate hyphae intermixed with fibrin and necrotic debris (Gomori methenamine-silver).

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