Aspergilloma Within Cavitating Pulmonary Adenocarcinoma

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Pulmonary aspergillosis not infrequently occurs secondary to various malignancies and their associated therapies, but the simultaneous occurrence of Aspergillus and lung cancer is rare. The authors report the case of a 64-year-old male, who presented with a cavitating left upper lobe lesion radiologically, consistent with either fungal infection or carcinoma. Pathologically, the lesion was a thin-walled adenocarcinoma with a large central cavity containing an aspergilloma intermingled with highly necrotic tumor. This represents the fifth such reported case. (Key words: Lung; Carcinoma; Fungus; Aspergillus). Am J Clin Pathol 1989; 91:100-103
PULMONARY ASPERGILLOSIS may present in several forms: Aspergillus hypersensitivity lung diseases (extrinsic asthma, extrinsic allergic alveolitis, and allergic bronchopulmonary aspergillosis); noninvasive pulmonary aspergillosis (aspergilloma and suppurative aspergillosis); and invasive pulmonary aspergillosis.5 The aspergilloma or fungus ball is the most characteristic form of pulmonary aspergillosis and, like other forms of aspergillosis, may occur as primary or secondary disease.4 Secondary pulmonary aspergillosis is usually associated with underlying conditions or treatments that produce debilitative and/or or cavitating pulmonary disease (e.g., tuberculosis, histoplasmosis, bronchiectasis, etc.), impair immune functions (e.g., corticosteroids, antibiotics, or antineoplastic chemotherapy), or alter the indigenous microbiota of the respiratory tract (e.g., antimicrobial chemotherapy). The occurrence of secondary aspergillosis in patients with malignancy is usually attributed to immunosuppressive chemotherapy.2,8,11 We report a case, representing an unusual association between lung cancer and aspergillosis, in which the pulmonary lesion was radiologically consistent with either a fungal infection or carcinoma and pathologic examination revealed a cavitating adenocarcinoma with an aspergilloma in the cavity. This appears to be the fifth reported case in the world literature (Table 1).5,7,12,13

Report of a Case

A 64-year-old white male was admitted to the Kansas City Veterans Administration Medical Center in January 1987 with a four-month history of hemoptysis. A pulmonary lesion was first noted radiologically in November 1986 and progressed over a three-week period from a questionable haziness in the left apex to a nonhomogeneous round density. Computerized tomography of the chest at that time demonstrated a cavitary lesion that involved the apical posterior segment of the left upper lobe and measured 2.5-3 cm in maximum dimension (Fig. 1). Diagnostic considerations included cavitory carcinoma, fungal infection, tuberculosis, and abscess. During the present January 1987 admission, chest roentgenography revealed progression of the cavitary lesion to a size of 4-4.5 cm; the lesion had a thin irregular wall, and there was a suggestion of a nodule in the base of the cavity. Tuberculosis skin test and cultures had negative results, and a histoplasmin skin test had strongly positive results. Physical examination and laboratory data, including fungal cultures, were essentially unremarkable. Bronchoscopic examination revealed a slightly thickened and erythematous mucosa in the apical posterior segment; no distinct endobronchial lesions were identified. Sputum cytologic studies and bronchial washings/brushings demonstrated inflammation, epithelial hyperplasia, atypical squamous metaplasia, and degenerated atypical cells of uncertain type. Bronchial biopsy showed no evidence of malignancy. The patient had a left upper lobe wedge resection and lobectomy, and the postoperative course and follow-up have been uneventful, with no evidence of tumor recurrence.

Pathologic Findings

The wedge resection consisted of a portion of lung measuring 8.2 × 8 × 3 cm and weighing 73 g (Fig. 2). Furthest from the resection margin, the pleural surface had a 3.5-cm-diameter area of firmness and yellowish-gray discoloration. The specimen had previously been partially bisected through this area, revealing a cavity measuring 4 cm in greatest dimension. The lining of the cavity was reddish brown, irregularly granular, and friable. The wall of the cavity was yellowish-gray and moderately firm and measured from 0.7 to 0.2 cm in thickness. A separately submitted specimen, removed at surgery from the above cavity, consisted of a yellowish-pink and focally green portion of friable soft tissue measuring 1.3 × 1.2 × 0.3 cm. Also separately submitted were a 1-cm-diameter left hilar lymph node, and the remainder of the left upper lobe measuring 13.5 × 13 × 3 cm and weighing 160 g. Microscopic examination of the wedge resection (Figs. 3 and 4) revealed the wall of the cavity to be composed of poorly to moderately differentiated adenocarcinoma, with frequent mitotic figures, focal moderate fibrosis, and occasional microfoci of intracytoplasmic mucin. (Electron microscopic examination demonstrated prominent microvillus formation, confirming the diagnosis of adenocarcinoma.) The lining of the cavity consisted of necrotic tumor with scattered purulent exudate and occasional foci of bacterial and fungal proliferation (Fig. 5). (No additional tumor or fungi was identified in this specimen away from the cavity wall or in the subsequent hilar lymph node or lobectomy specimens.) Similarly, the separate specimen removed from the cavity at surgery consisted of highly necrotic tissue with occasional microfoci of viable adenocarcinoma, purulent exudate, bacteria, and prominent fungal proliferation (Fig. 6). The last, particularly toward the periphery, focally had a dense fungus ball-like appearance and was composed of septate hyphae.

### Table 1. Reported Cases of Aspergillus Within Lung Carcinoma

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Carcinoma Type</th>
<th>Aspergillus Species</th>
<th>Author, Year</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>WM</td>
<td>Hemoptysis</td>
<td>LUL</td>
<td>2 × 1</td>
<td>Squamous</td>
<td>Fumigatus</td>
<td>Waremboürg, 1965</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>WM</td>
<td>None</td>
<td>RUL</td>
<td>3.5 × 2.5</td>
<td>Adeno</td>
<td>—</td>
<td>Mays, 1967</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>BM</td>
<td>Dyspnea, hemoptysis</td>
<td>RUL</td>
<td>6.5 × 4.5</td>
<td>Squamous</td>
<td>—</td>
<td>Torpoc, 1976</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>WM</td>
<td>Hemoptysis, shoulder pain</td>
<td>RUL</td>
<td>—</td>
<td>Squamous</td>
<td>Fumigatus</td>
<td>Monie, 1978</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>WM</td>
<td>Hemoptysis</td>
<td>LUL</td>
<td>4.5 × 4</td>
<td>Adeno</td>
<td>Fumigatus</td>
<td>McGregor, 1988</td>
</tr>
</tbody>
</table>

LUL = left upper lobe; RUL = right upper lobe; RLL = right lower lobe.
Fig. 1 (upper, left). Computed tomography scan demonstrating a cavitary density in the apical posterior segment of the left upper lobe.

Fig. 2 (upper, right). Wedge resection specimen from the left upper lobe with a thin-walled cavitary mass. Most of the intracavitary fungus ball had been previously removed at surgery.

Fig. 3 (center, left). Low-power photomicrograph of the cavitating tumor, with the cavity lumen on the right and nonneoplastic lung parenchyma on the left. Hematoxylin and eosin (X25).

Fig. 4 (center, right). Photomicrograph of the cavity wall demonstrating moderately to poorly differentiated adenocarcinoma. Hematoxylin and eosin (X100).

Fig. 5 (lower, left). Photomicrograph of the cavity interior with the lining composed of necrotic carcinoma cell clusters intermingled with fungal hyphae and purulent exudate. Hematoxylin and eosin (X400).

Fig. 6 (lower, right). Photomicrograph of the fungus ball removed at surgery from the tumor cavity, demonstrating branching septate hyphae consistent with Aspergillus. Grocott methenamine silver (X250).
measuring 4–8 μm in diameter and with dichotomous branching. This histologic appearance was interpreted as consistent with Aspergillus.

Fungal cultures, of both the wall of the resected tumor cavity and the specimen removed from the cavity at surgery, grew Aspergillus. The species was determined to be *Aspergillus fumigatus*.

**Discussion**

Pulmonary cavitation is known to predispose individuals to Aspergillus infection and is also a common finding in pulmonary malignancy. Cavitating lung cancer, however, is rarely associated with Aspergillus infection. A literature review revealed four previously reported cases (Table 1). Because our patient did not have an underlying debilitating disease and was not taking drugs (antibiotics, corticosteroids, chemotherapeutic agents, etc.) prone to predispose individuals to Aspergillosis, it is likely that the Aspergillosis infection was secondary to the tumor cavitation itself.

In the present case and in both previously reported cases in which the Aspergillus was speciated, the organism was identified as *A. fumigatus*. This is not unusual, because *A. fumigatus* is the species most frequently recovered from clinical specimens, including respiratory secretions of patients with aspergillosa. Hemoptysis was a presenting complaint in the present case and in three of the four previously reported cases. Although hemoptysis is frequently associated with pulmonary aspergillosis, it also has been shown to have a highly significant association with tumor cavitation and therefore is not helpful in distinguishing carcinoma from fungus ball.

Radiologically, conclusive distinction between neoplasm and fungal infection could not be made. The gross pathologic evaluation also could not distinguish between neoplasm and fungal infection, although the latter was suggested by the relatively thin cyst wall. The surprise of finding carcinoma in the cyst wall on frozen section was compounded by the finding of fungal proliferation on permanent sections, particularly in the specimen removed from the cyst cavity at surgery. As in most of the previously reported cases, the Aspergillus proliferation was intracavitary without evidence of invasion. This finding is consistent with the concept that the Aspergillus infection was secondary to the tumor cavitation itself. Furthermore, although it has been demonstrated that Aspergillus can induce the formation of pulmonary adenocarcinoma, it appears highly unlikely that the Aspergillus infection preceded or induced the formation of the patient’s carcinoma, in view of the tumor-associated fibrosis and the strictly intracavitary aspergillosis with associated purulent exudate.

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**References**