Pulmonary Cryptococcosis within a Pulmonary Carcinoma—Review of Reported Cases

Toshiyuki Harada ¹, Nobuyuki Hakuma ¹, Akira Kamimura ¹, Koji Ito ² and Kenzo Okamoto ³

Abstract

An asymptomatic 71-year-old man was admitted for evaluation of a pulmonary tumor. Chest computed tomography revealed a cavitary tumor in the apical segment of the right lung. Histopathological examination of the resected lung revealed pulmonary cryptococcosis within a papillary adenocarcinoma. Macroscopic and histopathological findings speculated that papillary adenocarcinoma preceded pulmonary cryptococcosis.

Key words: cryptococcosis, lung carcinoma, coexistence, immunocompetent

(DOI: 10.2169/internalmedicine.45.1571)

Introduction

Cryptococcus neoformans is a ubiquitous fungus found worldwide, particularly in soil contaminated by pigeon droppings. Pulmonary cryptococcosis is caused by inhalation of spores from C. neoformans, with effects ranging from primary infectious lesions in the peripheral lung to diffuse pulmonary infiltration following systemic dissemination with cerebral and meningeal involvement. The former are often revealed as solitary nodules which are difficult to distinguish from lung carcinoma. We report herein a rare case of pulmonary cryptococcosis within a pulmonary adenocarcinoma.

Case Report

An asymptomatic 71-year-old man was admitted to Iwamizawa Municipal General Hospital for evaluation of a tumor in the apical segment of the right lung detected on annual screening chest radiography. The patient was a smoker (68 pack years). Physical examination revealed left hemiplegia due to sequelae of cerebral hemorrhage. Routine laboratory investigations, including levels of fungal examination (Candida antigen, Cryptococcus neoformans antigen, and beta-D-glucan) and tumor markers, yielded unremarkable results. Tuberculin reaction was weakly positive (0×0/13×11 mm). Chest radiograph revealed a cavitary tumor in the right upper lung field (Fig. 1). Chest computed tomography also revealed a cavitary tumor, 14 mm in diameter in the apical segment of the right lung (Fig. 2). Neither hilar nor mediastinal lymphadenopathy was noted. No systemic surveys, including brain magnetic resonance imaging, abdominal computed tomography and bone scintigraphy, identified any abnormalities. Bacterial, cytological and pathological examinations of the lesion could not be obtained on bronchofiberscopy to confirm the diagnosis, due to the difficulty inserting the forceps into the lesion. Partial resection was performed based on a suspected diagnosis of pulmonary carcinoma based on radiological findings showing a solitary thin-walled cavitary nodule. Macroscopic examination of the resected lung revealed that the outer part of the lesion comprised poorly demarcated white-gray tumor, with an inner part of caseous necrotic tumor with cavitation (Fig. 3A). Histologically, the outer part of the tumor was identified as well-differentiated papillary adenocarcinoma proliferating along the alveolar walls (Fig. 3B). The inner part of the tumor showed granulomatous inflammation with caseous necrosis. Within the caseous necrosis, isolated cryptococci were identified on staining with hematoxylin and eosin (Fig. 3C), Grocott (Fig. 3D), and mucicarmine staining (Fig. 3E). These findings were consistent with pulmonary cryptococcosis within a pulmonary adenocarcinoma. Pathological staging was T1N0M0 (Stage IA). As of 1 year after resection, the patient remains in good condition without any recurrence of either disease.
Chest radiograph revealed a cavitary tumor in the right upper lung field.

Chest computed tomography revealed a cavitary tumor in the upper lobe of the right lung.

Table 1. Reported Cases of Pulmonary Cryptococcosis Coexisting with Pulmonary Carcinoma

<table>
<thead>
<tr>
<th>Reference number</th>
<th>Age/Sex</th>
<th>Histology of pulmonary carcinoma</th>
<th>Location of pulmonary carcino</th>
<th>Location of pulmonary cryptococcosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>47/M</td>
<td>Ad</td>
<td>R-S</td>
<td>R-S</td>
</tr>
<tr>
<td>4</td>
<td>74/F</td>
<td>Ad</td>
<td>R-S</td>
<td>R-S</td>
</tr>
<tr>
<td>4</td>
<td>43/M</td>
<td>Ad</td>
<td>R-S</td>
<td>R-S</td>
</tr>
<tr>
<td>5</td>
<td>76/M</td>
<td>Ad+Sq</td>
<td>L-S</td>
<td>L-L</td>
</tr>
<tr>
<td>5</td>
<td>74/F</td>
<td>Ad</td>
<td>R-S</td>
<td>R-S</td>
</tr>
<tr>
<td>6</td>
<td>46/F</td>
<td>Ad</td>
<td>L-S</td>
<td>L-L</td>
</tr>
<tr>
<td>7</td>
<td>63/F</td>
<td>Ad</td>
<td>R-S</td>
<td>R-S</td>
</tr>
<tr>
<td>8</td>
<td>74/M</td>
<td>Ad</td>
<td>L-L</td>
<td>L-L</td>
</tr>
<tr>
<td>9</td>
<td>46/F</td>
<td>Ad</td>
<td>L-S</td>
<td>R-S</td>
</tr>
<tr>
<td>10</td>
<td>60/M</td>
<td>Ad</td>
<td>RML</td>
<td>L-L</td>
</tr>
<tr>
<td>11</td>
<td>73/F</td>
<td>Ad</td>
<td>LUL</td>
<td>L-L</td>
</tr>
<tr>
<td>12</td>
<td>77/F</td>
<td>Ad</td>
<td>L-S</td>
<td>L-L</td>
</tr>
<tr>
<td>13</td>
<td>73/F</td>
<td>Ad</td>
<td>L-S</td>
<td>L-L</td>
</tr>
</tbody>
</table>

Diagnosis in the present case was pulmonary cryptococcosis within a pulmonary carcinoma, but the patient was considered immunocompetent as cryptococcosis was in the form of fibrocaseous cryptococcoma.

Discussion

Cryptococcosis is often found in lungs of immunocompromised hosts, but is occasionally found in immunocompetent hosts (1). Histological response to cryptococcal infection depends on the immune status of the host. Pulmonary cryptococcosis displays 6 distinct histological forms: intracapillary cryptococci; mucoid pneumonia; histiocytic pneumonia; granulomatous pneumonia; discrete granuloma; and fibrocaseous cryptococcoma (2). The first 3 types are predominantly found in immunocompromised hosts, while the last 3 types are primarily found in immunocompetent hosts.

Diagnosis in the present case was pulmonary cryptococcosis within a pulmonary carcinoma, but the patient was considered immunocompetent as cryptococcosis was in the form of fibrocaseous cryptococcoma.

Radiographic patterns of pulmonary cryptococcosis include interstitial infiltrates and alveolar infiltrates in immunocompromised hosts, while solitary or multiple nodular shadows are seen in immunocompetent hosts (3). These nodular shadows, particularly in the peripheral lung, can sometimes be confused with lung cancers on computed tomography. Pulmonary cryptococcosis can be difficult to diagnose in immunocompetent hosts displaying negative results for serum cryptococcal antigen, due to nonspecific
Macroscopically, the outer part of the lesion exhibits poorly demarcated white-gray tumor, while the inner part comprises caseous necrotic tumor with cavititation (A). Histological examination demonstrated well-differentiated papillary adenocarcinoma proliferating along alveolar walls (B), and granulomatous inflammation with caseous necrosis (C) (HE stain, ×100). Within caseous necrosis, isolated cryptococci were identified. (D: Grocott stain ×400, E: Mucicarmine stain ×400).

Pulmonary cryptococcosis coexisting with pulmonary carcinoma is rare, and a review of the medical literature revealed 13 reported cases (Table 1) (4-13). The lung cancers were all adenocarcinomas located in the lower lobes, but no reason for this was evident. Since most patients were in an immunocompetent state, coexistence of the 2 lesions was considered coincidental. Coexistence of both lesions in a solitary tumor, as seen in the present case, is extremely rare, and only 3 cases have been reported previously (5, 8, 12).

In the present case, pulmonary adenocarcinoma was speculated to precede pulmonary cryptococcosis for the following reasons: 1) granulomatous inflammation with coagulative necrosis caused by cryptococci was located within the area of papillary adenocarcinoma; and 2) papillary adenocarcinoma showed fibrotic change in the central portion, thought to represent an old lesion. Collapsed alveolar structures with similar fibrotic changes were found in areas of necrosis caused by cryptococci.

The present case thus contains many interesting insights into the differential diagnosis of pulmonary nodules. Under medically permissive conditions, resection of the lesion should be performed to obtain a definitive diagnosis for pulmonary nodules suspected as malignancy.
References