Cavitary Coccidioidomycosis With Fungus Ball Formation*  

Diagnosis by Fiberoptic Bronchoscopy With Coexistence of Hyphae and Spheres

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Pulmonary cavitary coccidioidomycosis with fungus ball formation was observed in two individuals with hemoptysis. The first patient had no overt compromise; the second was an insulin-dependent diabetic. In both, fiberoptic bronchoscopy was performed and cultures yielded *Coccidioides immitis*. The coexistence of spherules and hyphae of *C immitis* was seen histologically on bronchoscopic biopsy specimen of one cavitary lesion.

Infection with the dimorphic fungus, *Coccidioides immitis*, is common in the southwestern United States and other areas of the lower Sonoran life zone.\(^1\) Inhalation of arthrospores results in pulmonary infection that is usually symptomless and recognized only by skin test conversion. A pneumonia, clinically apparent or not, may resolve completely or persist, and sequelae of the infection may be seen roentgenologically as a nodule or cavity.\(^2\) Rarely, a solid nodule can excavate and present as a fungus ball radiographically.\(^3,7\)

The best diagnostic and therapeutic management of pulmonary cavitary coccidioidomycosis is uncertain. Surgical complications in the past have been considerable and recommendations for perioperative use of amphotericin B have been advocated.\(^4,5,11\) Some surgical approaches have emphasized lobectomy as a minimum.\(^8,11\) Others have reported favorable surgical outcomes with more limited resection (segmental or wedge) and without using amphotericin B.\(^12,13\) The presence of diabetes is thought to mandate more aggressive surgery.\(^14\)

Although the natural history of untreated cavitary coccidioidomycosis may result in spontaneous pneumothorax with empyema, the relative risk appears small, and close observation without surgery may be warranted.\(^15\) The role of azole therapy for cavitary coccidioidomycosis is unknown. Percutaneous needle biopsy has been useful in distinguishing *Coccidioides* nodules from malignancy but the rate of pneumothorax may be unacceptably high.\(^16,17\)

Fiberoptic bronchoscopy has been successfully used to elucidate the origin of Coccidioides lesions, primarily through culture of secretions.\(^6\)

We describe two patients with fungus ball formation secondary to cavitary coccidioidomycosis, one of whom was found to have coexistent spherules and hyphae on histologic analysis of bronchoscopic biopsy specimen. No specific antifungal therapy or surgical excision was utilized and both patients have done well for 18 and 29 months, respectively. To our knowledge, this is the first documentation of spherules and hyphae discovered in other than a surgical specimen.

**CASE REPORTS**

**CASE 1**

A 20-year-old woman was transferred to Fitzsimons Army Medical Center for evaluation of hematemesis, possible hemoptysis, and a cavity of the right lung. Over a period of 7 years, she had experienced nausea and abdominal pain with intermittent hematemesis; chest pain and hemoptysis were also described. These symptoms, although intermittent, occurred as frequently as every 1 to 2 weeks. Previously, an upper gastrointestinal barium examination and esophageal duodenoscopy (EGD) had been performed and results were normal (within a year). She also underwent a fiberoptic bronchoscopy that was reported as normal 6 years before hospital admission. Five months prior to transfer, a 2.2 × 2.5-cm right midlung cavity was detected. On repeated chest radiograph during the month of transfer, the cavity measured 2.7 × 3.0 cm (Fig 1). Laboratory examination at the transferring hospital revealed no acid-fast bacilli in sputum; serologic tests were negative for *C neoformans* (latex antigen), *C immitis* (immunodiffusion), and *Histoplasma capsulatum* (complement fixation). Anergy skin test battery was negative for purified protein derivative, mumps, and histoplasmin; however, it was positive for Candida.

In an emergency department in North Dakota, she experienced three episodes of hematemesis/hemoptysis with positive gastric lavage for blood 11 days prior to hospital admission. She denied fever, chills, weight loss, sweats, melena, or bright red blood per rectum. She also denied tuberculosis exposure. She had lived in Arizona until the age of 15 years. Repeated EGD showed cholangiectatic areas along the greater curvature of the stomach.

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The patient had a 2-year history of migraine headaches. She denied alcohol and tobacco use, had no known allergies, used no medications, and had undergone a tonsillectomy.

Laboratory examination showed a leukocyte count of 5,700 mm$^3$ with 13 percent eosinophils; hematocrit was 41 percent. Findings from the remainder of the laboratory analysis were not helpful.

Multiple angiodysplastic lesions in the stomach (20) were visualized and cauterized per EGD during her hospitalization. A coccidioidin skin test (1:100) was negative. Repeated chest radiograph and chest computed tomographic scan (Fig 2) were compatible with a fungus ball; a bronchoscopy with biopsy was performed. Iodine wet mount and subsequent histopathologic study showed mixed hyphal forms and spherules (Fig 3). A pure culture of C immitis was obtained. No further difficulties were encountered and the patient was discharged from the hospital on a regimen of cimetidine and a combination of aluminum hydroxide, magnesium hydroxide, and simethicone (Mylanta). Antifungal therapy was withheld and she continues to do well to date, with no change in the cavity on chest radiograph 18 months later.

CASE 2

A 56-year-old man with a 22-packs/year smoking history presented with a 2-month history of intermittent, weekly hemoptysis of approximately one teaspoonful per episode. He had a history of cardiac disease (two heart attacks), insulin-dependent diabetes mellitus, and hypertension. There were no complaints of fever, chills, night sweats, fatigue, gastrointestinal discomfort, or dyspnea; he had never previously experienced hemoptysis. The previous month he experienced a weight loss of 3.15 kg.

Examination revealed an afebrile man with normal vital signs and findings were noncontributory except for expiratory wheezing. There was no occult blood in the stool.

Laboratory analysis revealed a normal blood cell count, electrolytes, and serum creatinine concentration. The serum glucose level was 367 mg/dl. A chest radiograph showed a peripheral lesion in the right lung. Tomography (Fig 4) demonstrated a fungus ball in an excavated nodule. Otolaryngologic consultation revealed no abnormalities. A bronchoscopy was performed showing normal airways. Cultures of bronchial washings and collected sputa grew C immitis. Organisms were not seen on an initial direct specimen examination. Acid-fast bacilli cultures were negative.

Specific treatment was withheld. The patient experienced no further hemoptysis. Radiographically, the cavity collapsed over time with

![Figure 1](image1.jpg)  
**FIGURE 1.** Left, Chest radiograph demonstrating right lower lung cavity. **Right,** Enlargement of Fig 1 left showing cavity.

![Figure 2](image2.jpg)  
**FIGURE 2.** Chest computed tomographic scan showing "crescent" sign of fungus ball due to coccidioidomycosis.
residual nodule formation. One year after presentation, successful and uneventful cardiac bypass surgery was accomplished. He continues to do well 29 months after his original presentation.

DISCUSSION

Clinically, pulmonary coccidioidomycosis is usually symptomless. Four types of radiographic findings have been described: (1) bronchopneumonia, acute and persistent and chronic fibrocavitary disease; (2) cavities (often thin walled); (3) hilar adenopathy; and (4) nodules (coccidioidomas).18

The majority of cavities are found through serendipity;19 86 percent are single cavities and 14 percent are multiple. The incidence of cavitation has been estimated to be 0.1 percent for symptomatic disease18 and 1.7 to 8 percent for all cases of coccidioidomycosis.19 The typical cavity is thin walled without fluid levels. Symptomatic cavitary coccidioidomycosis presents as fever with hemoptyis.20 Hemoptyis incidence ranges from 23 to 50.6 percent, cough being the most common symptom at 42.7 percent. The majority of cavities resolve spontaneously, 50 percent within 2 years. Winn21 has observed 27 percent of cavities less than 2 cm in size to close within 2 years.

Skin tests to coccidioidin (1:100) are positive in 54 to 70 percent; serologic tests are positive (usually in low titer, less than or equal to 1:4) in 75 to 82 percent, and sputum cultures are positive in 64 percent.18 Skin test positivity may be increased by higher dilutions of coccidioidin (1:10) or spherulin.19

The indications for surgical removal of a cavity are variable and include the following: (1) rapidly expanding cavity (> 4 cm) close to visceral pleura with risk of imminent rupture; (2) serious or persistent hemoptyis; (3) symptomatic fungus ball; (4) bronchopleural fistula; (5) persistence greater than 1 year; and/or (6) culture-positive sputum.11,20,21 Underlying host compromise, including diabetes, has been proposed as mandating surgical removal.19 Surgical removal should not be undertaken lightly, as the complication rate is high (30 percent bronchopleural fistula) and recurrence is not uncommon (18 percent recurrent cavities).4,11,18 Of four deaths in one series, two were related directly to surgery. Smith et al.19 have stated that in the absence of a definite indication, the patient should be left alone with the cavity.19 If surgery is contemplated, amphotericin B has been recommended as the complication rate has been observed to be reduced (4.2 percent vs 20.4 percent).11

Although initially described in 1946 by Forbes and Besterbreutze,22 the presence of hyphae of C immitis in pulmonary cavities remains a rare phenomenon. Hyphae were visualized in only 1 of 95 pathologic specimens analyzed in the series of Forbes and Besterbreutze and no spherules were observed. The coexistence of spherules and hyphae was first described by Bass et al.23 in 1946. Other examples of mixed hyphal/spherule elements have been alluded to without good documentation.19,24,26 The incidence of hyphal forms occurring in pulmonary cavities was found to be 73 percent and in granulomas (coccidioidomas) it was found to be 30 percent when specifically looked for by thin sectioning of tissue blocks and by special staining.24 Overall, hyphae were visualized in 55 percent, but they were rarely encountered in
### Table 1—Demographics of Mixed Hyphae/Spherule Cavitary Coccidioidomycosis

<table>
<thead>
<tr>
<th>Cases</th>
<th>Source</th>
<th>Age/Sex</th>
<th>Race</th>
<th>Underlying Disease</th>
<th>Symptoms</th>
<th>Diagnosis</th>
<th>Serology</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rohatgi and Schmitt\textsuperscript{a}</td>
<td>61/M</td>
<td>Filipino</td>
<td>IDDM</td>
<td>Hemoptysis</td>
<td>Sputum cultures</td>
<td>1.8</td>
<td>AMB, 2 g; lobectomy</td>
<td>Good</td>
</tr>
<tr>
<td>2</td>
<td>Thadepalli et al\textsuperscript{a}</td>
<td>26/M</td>
<td>Black</td>
<td>Disseminated cocci</td>
<td>Meningitis, skin, hemoptysis</td>
<td>Sputum culture</td>
<td>1:1.004</td>
<td>AMB, 4 g; lobectomy</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>Fee et al\textsuperscript{a}</td>
<td>36/M</td>
<td>Black</td>
<td>None</td>
<td>Hemoptysis</td>
<td>Sputum culture</td>
<td>1:16</td>
<td>Lobectomy</td>
<td>Good</td>
</tr>
<tr>
<td>4</td>
<td>Putnam et al\textsuperscript{a}</td>
<td>52/M</td>
<td>White</td>
<td>None</td>
<td>Hemoptysis</td>
<td>Sputum culture</td>
<td>1:8</td>
<td>Lobectomy; AMB</td>
<td>Temporary increase in CF titer: 1:256</td>
</tr>
<tr>
<td>5</td>
<td>Fiese et al\textsuperscript{a}</td>
<td>34/M</td>
<td>White</td>
<td>None</td>
<td>Chronic cough, weight loss, hemoptysis</td>
<td>Sputum culture</td>
<td>1:64</td>
<td>Lobectomy</td>
<td>Good</td>
</tr>
<tr>
<td>6</td>
<td>Fiese et al\textsuperscript{a}</td>
<td>31/M</td>
<td>White</td>
<td>None</td>
<td>None</td>
<td>Sputum culture</td>
<td>Negative</td>
<td>Segmental resection</td>
<td>Good</td>
</tr>
<tr>
<td>7</td>
<td>Fiese et al\textsuperscript{a}</td>
<td>26/M</td>
<td>White</td>
<td>None</td>
<td>Hemoptysis recurrent</td>
<td>Lung culture</td>
<td>1:256</td>
<td>Segmental resection; lobectomy</td>
<td>Good</td>
</tr>
</tbody>
</table>

*IDDM = insulin-dependent diabetes mellitus; AMB = amphotericin B

the same areas as spherules. A second report revealed hyphae in three of eight cavities and three of four granulomas.\textsuperscript{27} Hyphae were seen most frequently on the surface of cavity walls and in necrotic debris within granulomas.

Radiographic evidence of a fungus ball due to *C. immitis* is also unusual, with only six previously published reports.\textsuperscript{3-6} This is usually defined as a mass within a cavity with a crescent of gas surrounding the mass and that is freely mobile with positional change. Both of these cases had radiographically documented fungus balls.

Previously there have been six well-documented case reports of the coexistence of hyphae with spherules in cavitary coccidioidomycosis published in the medical literature (Table 1).\textsuperscript{3,4,27} Three further cases of granulomas were also described by Fiese et al.\textsuperscript{27} No data referable to the individual were given in the report of Puckett.\textsuperscript{24} All patients had undergone limited pulmonary resection, usually due to hemoptysis. Only one patient had disseminated disease.

Chest radiographic data were included in four reports (chest radiograph or tomography) and documented the presence of fungus balls in all four. The present report underlines the utility of chest computed tomographic scanning or tomography in the documentation of the presence of a fungus ball.

All of the published reports have demonstrated the presence of hyphae and spherules from surgically removed specimens. To our knowledge, this is the first report of a pulmonary fungus ball diagnosed by fiberoptic bronchoscopic biopsy specimen. Although both patients described in this report presented with hemoptysis, at the time of initial presentation to Fitzsimons Army Medical Center, the first patient was symptomless with regard to her lung and had no evidence of hemoptysis; therefore surgery and amphotericin B therapy were withheld successfully. In the second case, cautious observation was utilized and resolution of hemoptysis and collapse of the cavity occurred. Although both patients had potential indications for surgery, both have continued to do well without any antifungal therapy or surgical excision of lesions to date, 18 and 29 months after their initial presentation.

Although both patients have done well without surgical excision, close observation continues to be warranted; however, the potential complications and financial expense of surgical procedures\textsuperscript{4,11,16} have been avoided in these patients thus far.

In the absence of controlled information regarding the utility of azole antifungal agents, the potential side effects of amphotericin B, and the potential morbidity of surgical excision of cocci lesions, serious consideration should be given to cautious observation and/or nonsurgical management of cavitary coccidioidomycosis.

**REFERENCES**

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