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Fever, chills, and chest radiographic infiltrates in a middle-aged woman

A 55-YEAR-OLD HOUSEWIFE is referred for evaluation of worsening left lower lobe alveolar infiltrates.

For the past 6 months she has had persistent low-grade fever with temperatures reaching 99.0°F (37.2°C), frequent sweating, nasal congestion, coughing (productive of a minimal amount of clear phlegm and accompanied by wheezing), and shortness of breath. Her shortness of breath has increased over the past few months, forcing her to stop her daily swimming. She has no joint pain.

Medical history

The patient has a history of asthma, hypothyroidism, nephrolithiasis, and loose stools with cramping that suggest the possibility of inflammatory bowel disease.

Eight years ago she was diagnosed with bronchiolitis and bronchiectasis after undergoing an open lung biopsy for right upper and left lower lobe nodules and vague infiltrates. There was no evidence of malignancy or granulomas.

She quit smoking 8 years ago. She occasionally drinks alcohol, uses no recreational drugs, and has had no known exposure to human immunodeficiency virus or tuberculosis.

She has no cats or birds. In the past year, she has traveled extensively in Europe, China, and the Caribbean. For a hobby, she builds English hayracks (hanging plant containers) with wet moss, and plants flowers in them.

Medications

She has been treated with aerosolized bronchodilators and a rotating schedule of azithromycin, doxycycline, and combined

sulfamethoxazole and trimethoprim the first week of every month for the past 4 to 5 years for her bronchiolitis. She takes supplemental antibiotics for acute exacerbations.

She also takes inhaled steroids, tiotropium, thyroxine, and hydrochlorothiazide.

She had her flu shot this year and pneumococcal vaccine 4 years ago.

Physical examination

The patient is thin and in no apparent distress. She is breathing comfortably and has no sinus tenderness, pharyngeal congestion, or lymphadenopathy, and no edema, clubbing, or cyanosis. Her temperature is 99.0°F (37.2°C), her blood pressure is 130/86 mm Hg. Evaluation of the heart, abdomen, extremities, and neurological status is normal. She has no skin lesions.

On auscultation of the chest, there are scant wheezes in the left lower lung fields.

Radiographic tests

A recent chest radiograph shows a spiculated nodule in the left mid-lung field laterally (not seen in a radiograph done 1 year ago) and overlying scarring and fibrotic changes in both lung fields.

Computed tomography shows patchy alveolar infiltrates in the right lung, with stable bronchiectatic changes and new nodules in the left lower lobe and lingula (FIGURE 1).

Laboratory tests

- White blood cell count $7.5 \times 10^9/L$ (normal 4.5–11.0), differential count normal

**For a hobby,
she builds
English hay-
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wet moss**

The patient's CT scan

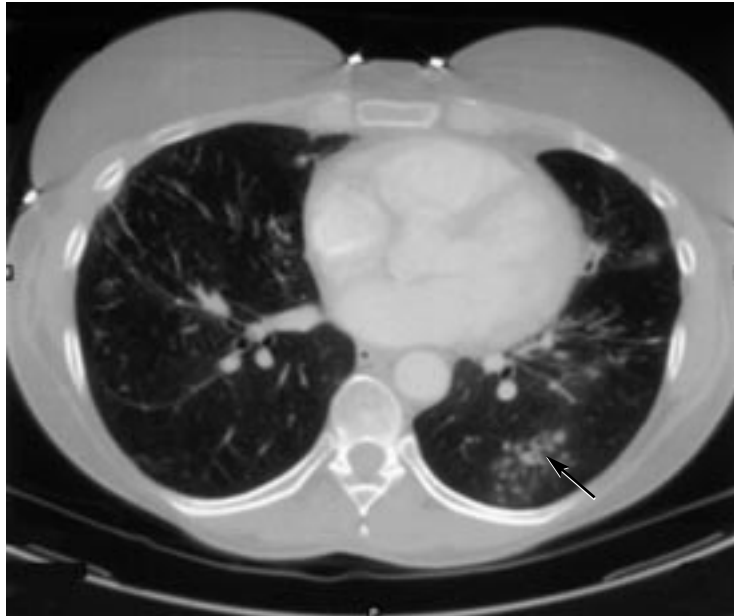


FIGURE 1. Computed tomography reveals left lower lobe infiltrates (arrow).

cANCA is only 60% to 70% sensitive for active limited Wegener granulomatosis

- Eosinophil count $0.1 \times 10^9/L$ (normal 0–0.45); 1.2%
- Hemoglobin concentration 13.2 g/dL (normal 1.4–17.5)
- Platelet count $280 \times 10^9/L$ (normal 150–450).

Other laboratory tests: All of the following are normal: purified protein derivative (tuberculin) test, cytoplasmic antineutrophil cytoplasmic autoantibodies (cANCA), antinuclear antibody, rheumatoid factor, histoplasmosis serology, aspergillus precipitins, immunoglobulin G (IgG) antibodies, and renal, hepatic, and thyroid function tests.

Other diagnostic tests

Pulmonary function test results are consistent with mild obstructive lung disease. A colonoscopy done for inflammatory bowel symptoms was negative.

DIFFERENTIAL DIAGNOSIS

1 On the basis of this information, what is the most likely diagnosis in this patient?

- ☐ Sarcoidosis
- ☐ Wegener granulomatosis
- ☐ Mycobacterial infection

- ☐ Extra-intestinal (pulmonary) manifestation of inflammatory bowel disease
- ☐ Pulmonary mycoses

Sarcoidosis

Sarcoidosis is a multisystem disorder characterized by noncaseating granulomas in the involved organs.

It is most common in young adults and is manifested by hilar lymphadenopathy, pulmonary infiltrates, and skin or eye lesions. Patients usually present with fatigue, anorexia, weight loss, fever, and dyspnea. The respiratory tract becomes involved at some time in nearly all cases. Many asymptomatic cases are discovered when chest radiography is performed during routine screening; however, these cases may not progress and become symptomatic.¹

Clinical features include dry rales, a restrictive pattern of lung disease, and abnormalities in gas exchange.² Radiographic findings vary and can consist of hilar lymphadenopathy or extensive pulmonary infiltrates. Patients with sinonasal tract involvement may present with nasal stuffiness or serious problems such as palatal destruction.^{3,4}

Sarcoidosis is a diagnosis of exclusion.¹ This patient is unlikely to have it, however, because her bronchoscopic biopsy reveals no noncaseating granulomas.

Wegener granulomatosis

Wegener granulomatosis is classically a systemic vasculitis primarily involving the sinuses, respiratory tract, and kidneys and frequently presenting with chronic sinus symptoms, hemoptysis, or glomerulonephritis.

At presentation, almost 25% of cases are limited to the respiratory tract.⁵ Radiographic findings include lung nodules (which may cavitate), alveolar and pleural opacities, and diffuse hazy infiltrates. Patients may have persistent nasal congestion, bloody nasal discharge, oral or nasal ulcers, sinus pain, and nonspecific symptoms such as fever, night sweats, anorexia, weight loss, and malaise.

Although cANCA is the most appropriate



TABLE 1

Important pulmonary mycoses

Endemic infections—occur in restricted geographic areas; organisms are dimorphic soil fungi pathogenic to normal hosts

- Histoplasmosis
- Blastomycosis
- Coccidioidomycosis
- Paracoccidioidomycosis

Opportunistic infections—organisms are ubiquitous in the environment; pathogenic to immunocompromised hosts

- Aspergillosis
- Mucormycosis
- Candidiasis

Cryptococcosis—organism is found worldwide, is encapsulated, is not dimorphic

Sporotrichosis—enters from a skin wound; direct inhalation is rare

ADAPTED FROM DAVIES SF. AN OVERVIEW OF PULMONARY FUNGAL INFECTIONS. CLIN CHEST MED 1987; 8:495–512.

diagnostic test, it is only 60% to 70% sensitive for active limited Wegener granulomatosis.^{6,7}

Wegener granulomatosis is unlikely in this patient: she did not present with hemoptysis or prominent sinus symptoms, and her renal function tests were normal.

Mycobacterial infection

Mycobacterial infection can manifest as primary infection, reactivation, or secondary infection and can be endobronchial or milary. Patients may present with cough, low-grade fever, hemoptysis, chest pain, or weight loss. Radiographic findings vary and may involve hilar lymphadenopathy only, or they may include lung infiltrates, cavities, effusions, and bronchiectasis.⁸

Mycobacterium avium intracellulare infection can present as in this case. One form in healthy (but fastidious) women is termed the “Lady Windermere” syndrome, in which it is postulated that if one habitually suppresses expectoration, a nidus of inflammatory disease at the tip of the lingula or middle lobe may develop that becomes infected by *M avium intracellulare*.⁹ It is difficult to exclude this disease in our patient without a diagnostic culture.

Inflammatory bowel disease

Pulmonary manifestations of inflammatory

bowel disease include airway inflammation at several levels in the tracheobronchial tree, parenchymal disease, and serositis.

The most common patterns of lung involvement are bronchiolitis obliterans with organizing pneumonia (BOOP) and interstitial lung disease. BOOP presents in an acute or subacute form with fever, dyspnea, cough, and pleuritic chest pain. Radiologic studies reveal patchy focal to diffuse infiltrates, which are most likely in the pleura. Interstitial lung disease is usually chronic and presents with dyspnea and interstitial opacities at the lung bases.^{10,11}

Sarcoidosis and ulcerative colitis may also coexist.^{12,13} In addition, pulmonary infiltrates can occur as a complication of sulfasalazine treatment: it is associated with eosinophilia and resolves after discontinuing the drug and steroids.¹⁰

In our patient, a negative colonoscopy makes this diagnosis unlikely.

Pulmonary mycoses

Primary fungal infections can present as in our patient's case.

The important mycoses are listed in TABLE 1. The opportunistic ones are unlikely in a patient who is not immunocompromised. Culture, serology, and antigen testing help to differentiate the remaining four

Many cases of asymptomatic sarcoidosis are found on screening chest radiographs

endemic mycoses, cryptococcosis, and sporotrichosis.

Case continued

The patient undergoes bronchoscopy, trans-bronchial biopsy, and bronchoalveolar lavage, and the specimen is sent for bacterial, mycobacterial, and fungal cultures. The bronchoalveolar lavage specimen grows only one fungus, identified as *Sporothrix schenckii* (FIGURE 2).

■ SPOROTRICHOSIS

Sporotrichosis is caused by the thermally dimorphic fungus *S schenckii*: the yeast form infects human tissues. It is found worldwide in decaying vegetation such as rotting wood, sphagnum moss, rose thorns, and rich humus soil.

Sporotrichosis is an occupational illness of gardeners and forestry workers. Infections occur sporadically from minor trauma from contaminated thorns, branches, and wood splinters.¹⁴

Three forms of sporotrichosis

Lymphocutaneous sporotrichosis, the most common form, is a localized infection of the skin, subcutaneous tissues, and regional lymphatics.¹⁵ It starts as a cutaneous plaque at the site where the spores implant and develops into a nodule that grows and ulcerates. More nodules subsequently develop along the draining lymphatics. It is usually diagnosed clinically and treated with itraconazole.^{15,16}

Pulmonary sporotrichosis is uncommon and is seen most often in middle-aged men with underlying chronic obstructive pulmonary disease and alcoholism. It can occur when conidia are aerosolized from soil or decaying vegetation and are inhaled.¹⁷

It usually presents as chronic cavitory fibronodular disease involving the upper lobes. It is usually diagnosed accidentally when the fungus is cultured from the sputum of a patient suspected of having tuberculosis or chronic cavitory histoplasmosis.¹⁸ The clinical syndrome usually mimics tuberculosis, with cough, dyspnea, low-grade fever, night sweats, and weight loss. There are two radiologic patterns: chronic cavitory disease and involvement of tracheobronchial lymph nodes.¹⁹

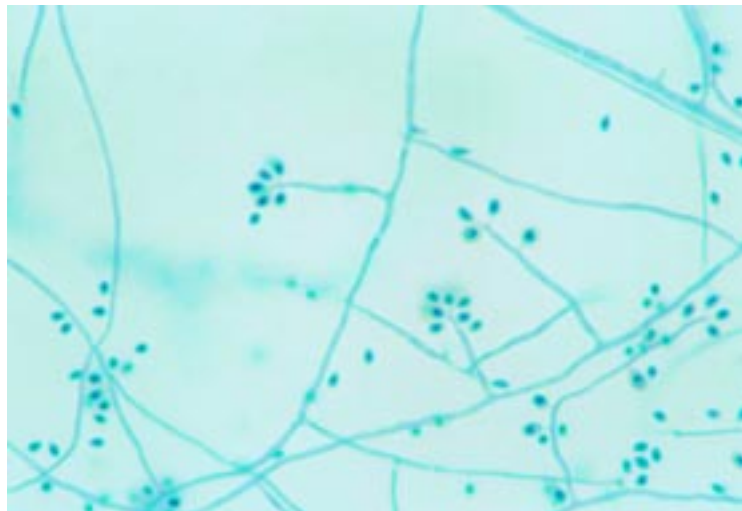


FIGURE 2. Conidia of *Sporothrix schenckii* arranged in a flowerette pattern. Methylene blue stain, 10X magnification.

PHOTOMICROGRAPH COURTESY OF GARY W. PROCOP, MD, HEAD, SECTION OF CLINICAL MICROBIOLOGY, DEPARTMENT OF CLINICAL PATHOLOGY, THE CLEVELAND CLINIC FOUNDATION.

The pulmonary form is diagnosed by sputum culture or bronchoscopic biopsy. Biopsy usually reveals granulomatous pneumonia. A positive complement fixation test might provide a clue to diagnosis but is seldom performed.¹⁵

Itraconazole is the recommended therapy for patients with pulmonary sporotrichosis that is not life-threatening, while amphotericin B is indicated for life-threatening or extensive pulmonary lesions. Surgical removal of the infected tissue along with medications appears to be the most effective therapy.^{16,20}

Osteoarticular, meningeal, and disseminated sporotrichosis are seen in immunocompromised patients, especially in those with alcoholism, diabetes, chronic obstructive pulmonary disease, or human immunodeficiency virus infection.^{15,21}

Case continued

Our patient has an atypical presentation of sporotrichosis. Her exposure to sphagnum moss is probably the source of her infection. This emphasizes the importance of a social history in patients presenting with fever and pulmonary infiltrates.

She is treated with oral itraconazole, and her symptoms improve soon after.

Sporotrichosis is an occupational illness of gardeners and forestry workers



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