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The Clinical Picture
Diffuse reticulonodular infiltrates

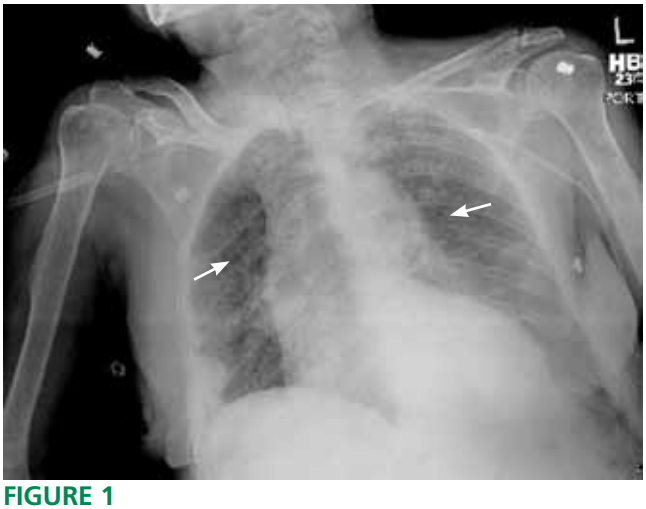

FIGURE 1

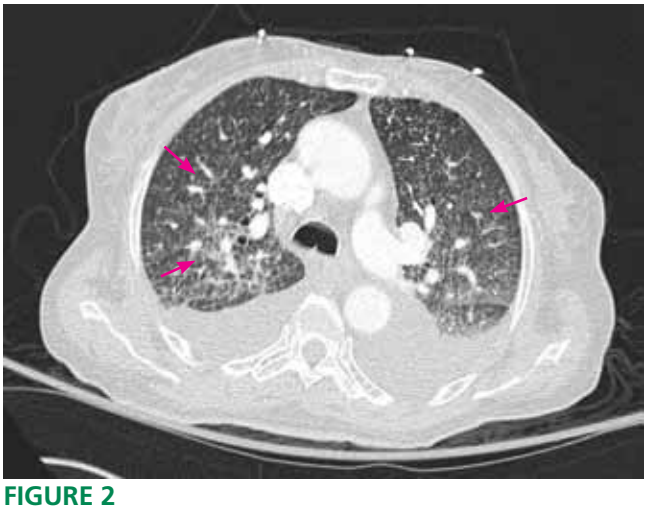

FIGURE 2

Her history of partially treated latent tuberculosis infection raised our clinical suspicion

A 69-year-old woman presented to the hospital with a 3-month history of fever of unknown origin and dyspnea. Her medical history included diabetes mellitus and, many years ago, partially treated latent tuberculosis infection and pancreatic cancer, treated with Whipple surgery and chemotherapy.

Radiography (FIGURE 1) and computed tomography of the chest (FIGURE 2) revealed diffuse reticulonodular infiltrates. Initial cultures of blood and bronchoalveolar lavage fluid were negative for viral, fungal, bacterial, and mycobacterial infection. Transbronchial biopsy specimens showed necrotizing granulomas, which stained negative for acid-fast bacilli and fungus. Study of specimens obtained via open lung biopsy showed granulomatous infiltration with no yeast, fungal elements, or acid-fast bacilli. An interferon-gamma-release assay for *Mycobacterium tuberculosis* and serologic testing for human immunodeficiency virus (HIV) were negative.

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Glucocorticoid treatment was started for presumed sarcoidosis, and a broad-spectrum antibiotic was also started; however, her condition deteriorated, and she developed seizures. Magnetic resonance imaging of the brain showed widespread 2- to 5-mm enhancing lesions (FIGURE 3). Cerebrospinal fluid studies revealed lymphocytic pleocytosis with a low level of glucose (34 mg/dL) and a high level of protein (174 mg/dL). She was subsequently transferred to our tertiary care center.

Q: What is the most likely diagnosis?

- ☐ Sarcoidosis of the lungs and central nervous system
- ☐ Hypersensitivity pneumonitis
- ☐ Miliary tuberculosis
- ☐ Cancer with pulmonary and brain metastases
- ☐ Disseminated fungal infection

A: The correct diagnosis is miliary tuberculosis, ie, progressive and widely disseminated hema-

togenous tuberculosis infection. Granulomas involving multiple organs suggested a broad differential diagnosis. The negative workup for infectious disease initially supported sarcoidosis by exclusion, but her condition failed to respond to steroid treatment. Multiple organ involvement is atypical for hypersensitivity pneumonitis, and antibody panels were negative. The absence of malignant cells in multiple biopsy specimens made metastasis unlikely.

Her remote history of partially treated latent tuberculosis infection raised our clinical suspicion and prompted mycobacterial antibiotic coverage. Three weeks after the initial sample collection, results from an independent laboratory revealed the presence of acid-fast bacilli in cultures of bronchoalveolar lavage fluid, cerebrospinal fluid, and blood, which were confirmed to be M *tuberculosis*. Despite treatment, the patient died of multiple organ failure.

Tuberculosis is rare in the United States, with 11,181 reported cases in 2010.[1] Miliary tuberculosis is associated with malnutrition, HIV infection, AIDS, alcoholism, diabetes, chronic kidney failure, immunosuppressive drugs, and organ transplantation.[2] Acid-fast bacilli smears and cultures confirm the diagnosis but have low sensitivity.[3] Granulomas characterize miliary tuberculosis histopathologically. They may be present in sarcoidosis, hypersensitivity pneumonitis, and fungal infection but are not specific for these conditions. Tuberculin skin testing[2] and interferon-gamma-release assay can be falsely negative in immunosuppressed patients,[4] highlighting the emphasis on clinical suspicion. The estimated death rate is 20%,[3,5] with central nervous system involvement being an independent predictor.[5] Empiric therapy should not be delayed, as culture results may not be available for 6 to 8 weeks.

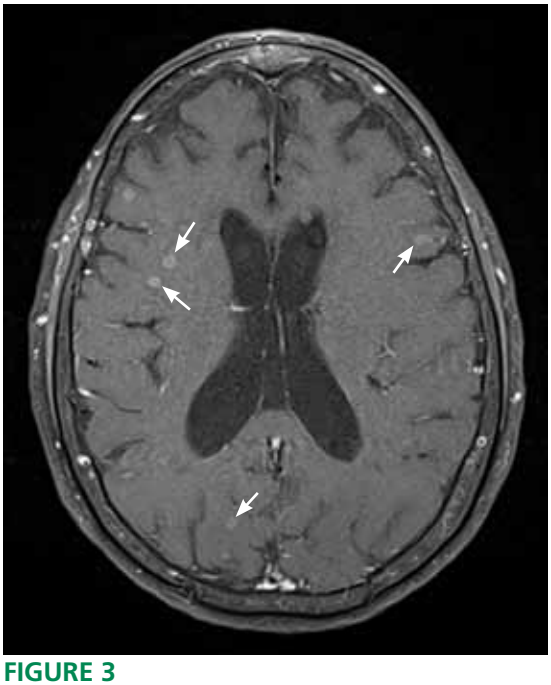

FIGURE 3

Tests for tuberculosis can be falsely negative in immunocompromised patients

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