Clinical Infectious Diseases

PHOTO QUIZ

Anthony Amoroso and Ajit P. Limaye, Section Editors

Cavitary Pulmonary Nodules in an Immunocompromised Patient With Urothelial Carcinoma of the Bladder

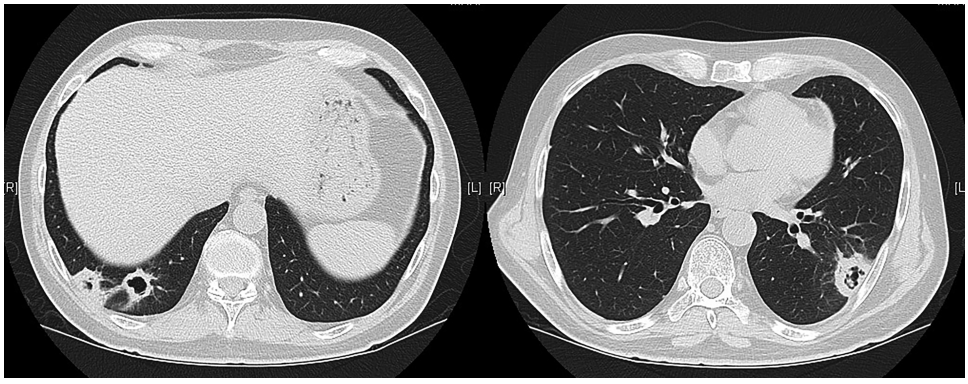

Figure 1. Computed tomographic scan of the chest demonstrating multiple cavitary lung nodules.

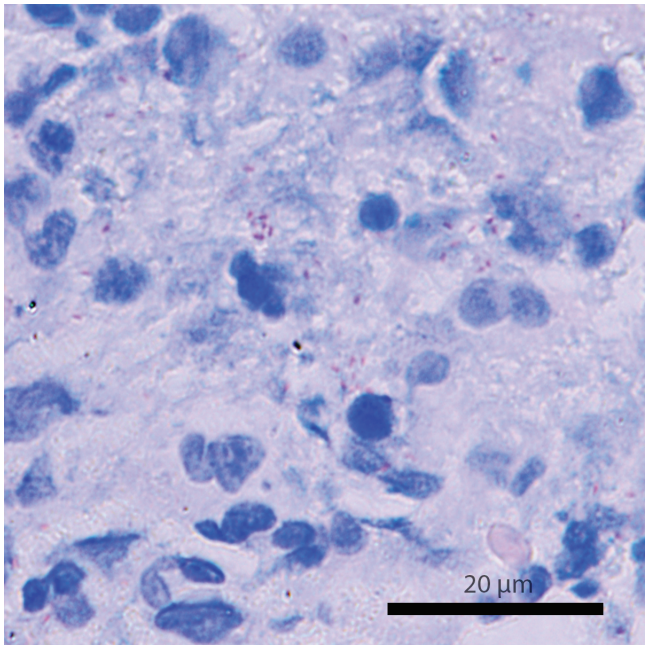

Figure 2. Acid-fast stain of lung core biopsy specimen (Kinyoun stain, original magnification ×1000 [oil immersion]).

A 59-year-old Moroccan man with a history of metastatic urothelial cell carcinoma presented in May 2016 with fever, shortness of breath, and chest pain. Noninvasive urothelial carcinoma had been diagnosed in 2012 and treated with mitomycin. In 2014, the patient had received intravesicular *Mycobacterium bovis* BCG therapy, but invasive bladder carcinoma subsequently developed, requiring 4 cycles of chemotherapy with methotrexate, vinblastine, doxorubicin, and cisplatin. Nine months before the current admission, the patient underwent a radical cystoprostatectomy with creation of a neobladder. Nonetheless, brain metastases developed, for which he received dexamethasone (4 mg orally, twice daily), and underwent neurosurgical resection 3 months before presentation, followed by whole-brain irradiation. He continued receiving intermittent dexamethasone therapy until his admission to our hospital.

A staging computed tomographic scan of his chest and abdomen 2 weeks before admission showed no evidence of metastatic disease. A week before presentation, the patient experienced progressive fatigue and heart palpitations, followed by cough, dyspnea, and pleuritic chest pain. On the day before admission, he experienced acute onset of fever (39°C) with chills. On admission, his temperature was 38.1°C with a pulse rate of 93/min, blood pressure of 101/69 mm Hg, and oxygen saturation of 92% with room air. On physical examination, crackles were auscultated at the right lung base.

The patient's total white blood cell count was 10 400/µL with 93.5% neutrophils; his hemoglobin level, 14.9 g/dL; and his platelet count, 112 000/µL. Chest radiography revealed a left lower lobe opacity. Serial chest computed tomographic scans demonstrated a right lower lobe pulmonary embolus and new bilateral, centrally necrotic nodular opacities that eventually

progressed to cavitation (Figure 1). Blood cultures were negative, as were urinary antigen tests for *Legionella pneumophila* serogroup 1, *Streptococcus pneumoniae*, and *Histoplasma capsulatum*. Results of serum galactomannan and cryptococcal antigen tests were also negative. Induced sputum samples were negative for acid-fast bacilli. On hospital day 5, an interventional radiology–guided biopsy of a lung nodule revealed necrotic material seen on histology and numerous short acid-fast organisms on Kinyoun stain (Figure 2).

What is your diagnosis?

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ANSWER TO THE PHOTO QUIZ

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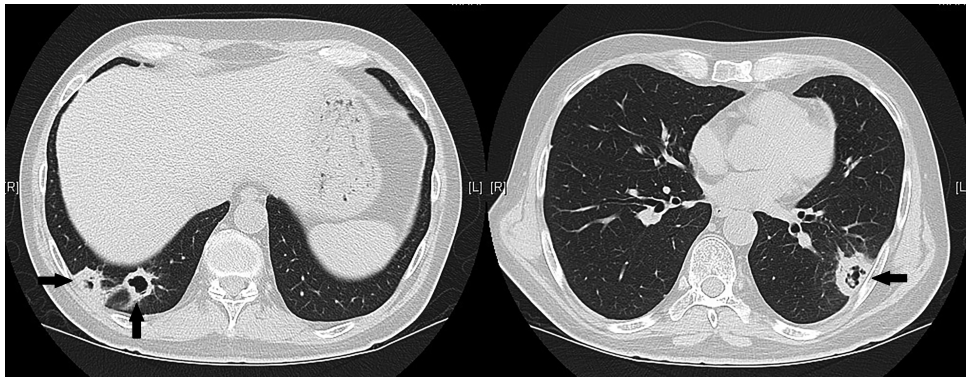

Figure 3. Computed tomographic scan of the chest demonstrating multiple cavitary lung nodules (*arrows*).

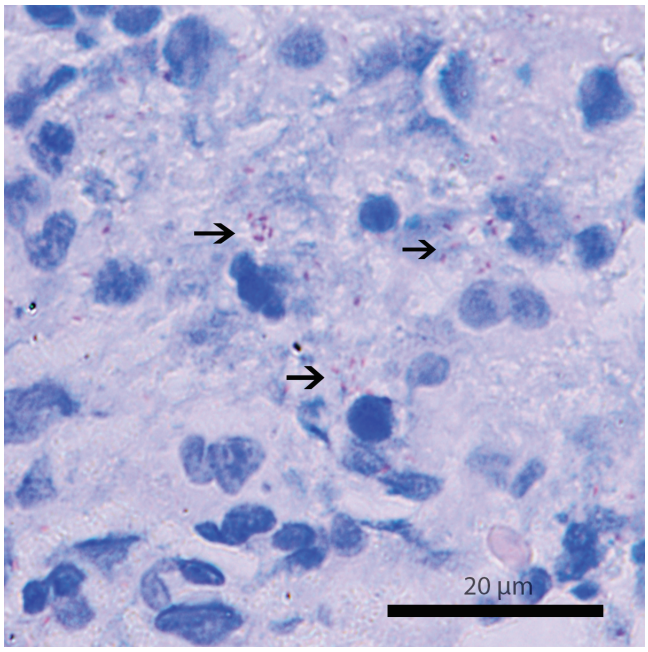

Figure 4. Acid-fast stain of lung core biopsy demonstrating short acid-fast coccobacilli/bacilli (*arrows*) (Kinyoun stain, original magnification ×1000 [oil immersion]).

Diagnosis: *Legionella micdadei* pneumonia with cavitation in an immunosuppressed patient.

The differential diagnosis in this immunocompromised patient is broad; however, given the observation of acid-fast bacilli associated with necrotic tissue and the patient's clinical history, infection due to *Mycobacterium bovis* BCG, used to treat his urothelial carcinoma, or *Mycobacterium tuberculosis* was initially suspected. Other organisms that may stain acid-fast, albeit using a modified acid-fast stain, and have been reported to cause pulmonary infection include *Gordonia*, *Nocardia,* and *Tsukamurella* species and *Rhodococcus equi* [1, 2]. *Nocardia* species and *Rhodococcus equi* seemed less likely based on either lack of exposure history or morphologic appearance and acid-fast staining characteristics. Reports of infection with *Gordonia* and *Tsukamurella* species are so infrequent that there is a paucity of information as to whether they would stain acid-fast (modified or otherwise) in tissue specimens.

Owing to a penicillin allergy, the patient was empirically treated with vancomycin and levofloxacin at presentation. A 4-drug regimen to cover for possible *M. tuberculosis* and disseminated *M. bovis* BCG infection was added when the lung core biopsy revealed acid-fast bacilli.

Results of a plasma QuantiFERON TB Gold test (Qiagen) and an *M. tuberculosis* nucleic acid amplification test (Xpert MTB/RIF; Cepheid) performed on expectorated sputum were negative. Culture for *Nocardia* species was negative, but in a culture of the lung biopsy specimen, *L. micdadei* grew on buffered charcoal yeast extract agar after 6 days. The organism was confirmed as *L. micdadei* by direct fluorescent antibody testing (Monoclonal Technologies) at the New York City Department of Health and Mental Hygiene's Bureau of the Public Health Laboratory.

Antimycobacterial therapy and vancomycin were discontinued after identification of *L. micdadei*. The patient's condition improved clinically, and he was discharged home to complete a 3-week course of levofloxacin (750 mg/d).

L. micdadei is the second most common cause of *Legionella* pneumonia after *Legionella pneumophila,* accounting for 57.8% of non–*L. pneumophila* infections [3], and it typically causes hospital-acquired pneumonia in immunocompromised patients [3, 4]. Extrapulmonary manifestations of *L. micdadei* infection have been described and include brain abscess, prosthetic joint infections, prosthetic valve endocarditis, and skin and soft-tissue infections [5].

Diagnosis of *L. micdadei* infection can be challenging because the *L. pneumophila* urinary antigen test detects only *L. pneumophila* serogroup 1 [6]. Furthermore, *Legionella* species are gram-negative bacilli that stain poorly using Gram stain, especially if safranin is used as the counterstain, and they are difficult to observe in Gram stains of clinical specimens [5]. Therefore, Gram staining of respiratory specimens revealing polymorphonuclear leukocytes in the absence of organisms may suggest infection with *Legionella* species [7, 8].

Because *L. micdadei* stains acid-fast positive in both fresh and formalin-fixed tissue (including modified acid-fast and Kinyoun stains), this organism can be mistaken for mycobacteria. However, unlike in mycobacteria, this acid-fast staining property is lost when *L. micdadei* is isolated in culture [1, 3, 5]. Importantly, *L. micdadei* typically appears as short acid-fast bacilli or coccobacilli [1, 6], whereas mycobacteria are often observed as beaded acid-fast positive bacilli [1]. Thus, the small coccobacillary nature of *Legionella* species, including *L. micdadei* (as observed in our case), should raise suspicion that the acid-fast organism is not a species of *Mycobacterium* [6].

Definitive diagnosis of *L. micdadei* infection relies on isolation of the organism in culture on media designed to recover *Legionella* species, such as buffered charcoal yeast extract agar, followed by identification using immunologic assays (eg, direct fluorescent antibody, as in our case) or molecular methods (eg, polymerase chain reaction or matrix-assisted laser desorption ionization time-of-flight mass spectrometry) [9–11].

Cavitation is not common with *Legionella* pneumonia, but it has been reported, especially in immunocompromised patients receiving glucocorticoid therapy [4]. With respect to treatment, *Legionella* species are facultative intracellular bacteria and require agents with high intracellular activity, such as azithromycin or levofloxacin [12]. In conclusion, physicians should maintain a high suspicion for *L. micdadei* infection in immunocompromised patients with pneumonia to ensure that appropriate diagnostic testing is performed, and they should consider this organism in the differential diagnosis of infection by acid-fast staining organisms.

Note

Potential conflicts of interest. S. J. has served in an advisory capacity to Gilead Sciences unrelated to the current publication. All other authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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