CASE REPORT

Legionella Pneumonia and Use of the Legionella Urinary Antigen Test

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A 33-year-old Caucasian woman presented to an outside hospital with a 10-day history of fever, cough, and progressive dyspnea on exertion. Ten days prior to the onset of symptoms, she had traveled to Calgary, Alberta, Canada. Her niece and nephew had recently suffered upper respiratory symptoms. Additional review of systems was negative for joint pain, rash, diarrhea, or bloody stools. She had a history of ulcerative colitis, primary sclerosing cholangitis, and juvenile rheumatoid arthritis. Her outpatient medications included prednisone 10 mg daily, methotrexate 7.5 mg weekly, and ursodiol 200 mg 3 times daily. She was employed at a local hospital and her annual purified protein derivative (PPD) test had been negative. Computed tomography angiography demonstrated bilateral patchy consolidation. Vancomycin, levofloxacin, piperacillin/tazobactam, and fluconazole were initiated and she was transferred to our hospital for further evaluation.

On arrival, her vital signs were within normal limits. She was breathing comfortably but on auscultation had crackles at the right-mid lung field. A complete blood cell count demonstrated a white blood cell count of 7000/μL with left shift, hemoglobin 10.7 g/dL, and platelet count 156,000/μL. Liver function tests showed albumin 2.6 g/dL, total bilirubin 9.0 mg/dL with conjugated fraction 6.6 mg/dL, alkaline phosphatase 586 U/L, aspartate aminotransferase 104 U/L, and alanine aminotransferase 72 U/L; these were all near her baseline. The basic metabolic panel was within normal limits. A chest X-ray showed dense areas of consolidation in the lingula and left upper lobe. All antibiotics from the outside hospital were discontinued and empiric moxifloxacin was initiated.

On hospital day 1, she underwent bronchoscopy, which yielded cloudy fluid from the bronchoalveolar lavage (BAL). Initial BAL gram stain showed moderate white blood cells but no organisms; fungal smears and stains for acid fast bacilli were negative. Blood cultures and *Legionella* and *Streptococcus* urinary antigen tests were negative. The remainder of her hospital course was uneventful. Her shortness of breath improved and she remained afebrile. She was discharged home on a 10-day course of moxifloxacin with close follow-up. Six days after the BAL specimen

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was collected, the culture grew *Legionella micdadei*. Repeat chest film 2 weeks later demonstrated resolution of the original findings.

DISCUSSION

Legionella is responsible for 8000 to 18,000 hospitalizations for pneumonia annually.[1] It is associated with community-acquired, hospital-acquired, and travel-associated pneumonia. Twenty-five *Legionella* species have been identified and 8 species are associated with pneumonia in humans.[2] Community-acquired and travel-acquired *Legionella* pneumonia is most commonly caused by *Legionella pneumophila*; the second most common cause is *L. micdadei*.[2,3] It was initially identified in 1977 at the University of Pittsburgh in renal transplant patients with acute pneumonitis and is known as the Pittsburgh pneumonia agent. Similar cases were identified in a group of immunocompromised patients in Virginia, all of whom were receiving steroids and cytotoxic chemotherapy. It is unclear why *L. micdadei* predominates in this population, but is likely related to its decreased virulence compared to *L. pneumophila*. The definitive mode of transmission of *L. micdadei* is not known; it may be from contaminated water supplies but infections from inhalation of respiratory secretions have also been documented.[2] While *L. micdadei* is not commonly seen in travel-associated *Legionella pneumonia*, the patient's immunocompromised status secondary to the treatment of her underlying medical conditions made her particularly vulnerable. Given the temporal association with her trip, she was most likely exposed during her travels but her hospital employment should also be considered.

Legionella pneumonia is underdiagnosed because of difficulty distinguishing it from other types of pneumonia, failure to order diagnostic tests, and variable sensitivity of available diagnostic tests.[4] Culture is considered the "gold standard" and is ideally performed from lower respiratory secretions, but variable sensitivity due to interlaboratory variation (range, 10%-80%) limits its use.[3,4] Direct immunofluorescence assay (DFA) testing of respiratory secretions is available but also limited by poor sensitivity. Both culture and DFA have specificities approaching 100%. A newer test, the *Legionella* urinary antigen test, is an immunochromatographic assay. It is less technically difficult and results are available in less than 1 hour. The assay can detect the antigen in the urine starting 1 day after the onset of symptoms, and can remain positive for days or weeks following treatment.[4]

With the introduction and wide availability of the *Legionella* urinary antigen test, it is important to consider its limitations. While the test carries a high specificity, it detects only the soluble antigen of *Legionella pneumophila* serogroup 1. Thus, as in this case, the urinary test can be negative when infection is caused by other species such as *L. micdadei*. In the literature, the urine assay's sensitivity is variously reported at 45% to 100% with lower sensitivities in circumstances such as hospital-acquired disease, where the association with other species is higher than in the community setting.[3,4] For instance, in nosocomial infections, the reported sensitivity is 45%.[3] False-positive results have also been seen in patients with serum sickness.[4]

The *Legionella* urinary antigen test has improved detection of *Legionella* pneumonia. Given its limitations, it is likely to be most accurate in community-acquired and travel-acquired cases.[3] The Centers for Disease Control and Prevention recommend testing for *Legionella* in pneumonia patients requiring admission to the intensive care unit (ICU), immunocompromised patients, patients who traveled within 2 weeks of presentation, and those who have failed treatment with beta-lactams or cephalosporins. A negative test does not rule out *Legionella* infection and additional testing with bronchoscopy may be indicated, especially in immunocompromised hosts.[4]

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