Rhodococcus equi Infection After Lung Transplantation

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***Rhodococcus equi* is an emerging opportunistic pathogen in immunocompromised patients. A lung-transplant recipient developed weight loss, nonproductive cough, dyspnea, and somnolence. Computed tomogram showed a pulmonary nodule and pleural changes in the right allograft that was due to *R. equi* infection. Alteration of cell-mediated immunity is a predisposing risk factor for *R. equi* infection in humans. Our patient developed *R. equi* infection soon after a course of high-dose corticosteroids for acute allograft infection and animal exposure. A course of intravenous vancomycin followed by single-agent long-term therapy with oral ciprofloxacin was successful.** *Key words: Rhodococcus equi; pulmonary nodule; pleural thickening; lung transplantation.* [Respir Care 2011; 56(10):1605–1607. © 2011 Daedalus Enterprises]

Introduction

Rhodococcus equi is a ubiquitous organism found in soil and water, and causes infection in domestic grazing animals via the gastrointestinal and respiratory tracts.[1-3] *R. equi* is a Gram-positive, weakly acid-fast coccobacillus that is related to *Mycobacteriaceae*, *Nocardiaceae*, and *Corynebacteriaciae*, and was initially described in horses.[1,4,5] The first reported case of human *R. equi* infection was published by Golub and colleagues in 1967.[6] Human infections with *R. equi* occur almost exclusively in immunocompromised hosts, including patients infected by human immunodeficiency virus (HIV) and patients receiving immunosuppressive treatment (eg, after solid-organ transplant or hematological malignancy),[1-6] and causes substantial morbidity in those patients.[7]

Case Report

A 62-year-old male who had undergone right single-lung transplantation 3 years earlier for end-stage COPD was taken by family to a community hospital emergency department for progressing somnolence and reduced alertness. The family reported that over the last month he had an obvious decrease in appetite and a weight loss of 5.4 kg, which started soon after attending a horse-race event. He then developed a mild non-productive cough with dyspnea related to ambulation. He became increasingly somnolent the day prior to presentation to the community hospital. In the emergency department, arterial blood gas analysis revealed pH 7.44, P_{aCO_2} 28 mm Hg, and P_{aO_2} 54 mm Hg. That hospital obtained cultures of blood, sputum, and urine. The family refused a lumbar puncture to obtain cerebral spinal fluid. Prior to transfer to our institution, the community hospital also performed computed tomography (CT) of the head, chest, abdomen, and pelvis.

His most recent clinical course, 2 months earlier, was complicated by an acute episode of A2B0 rejection, which was treated with intravenous methylprednisolone sodium succinate 500 mg daily for 3 days, and subsequent oral prednisone taper from 60 mg to 5 mg over 2 weeks. His medical history included episodes of melena, and he was found to have multiple arteriovenous malformations on colonoscopy 2 years earlier, but there were no signs of active bleeding. The patient also had a history of type 2 diabetes, cataract removal, and deep venous thrombosis in the right leg that led to a pulmonary embolism that required placement of an inferior vena cava filter and anticoagulation therapy. His medications included tacrolimus 5 mg twice daily, mycophenolate 750 mg twice daily, prednisone 5 mg daily, coumadin 3 mg daily, omeprazole 20 mg daily, iron 325 mg daily, insulin glargine 12 units at bedtime, regular insulin on a sliding scale, and albuterol and ipratropium inhalers 2 puffs as needed.

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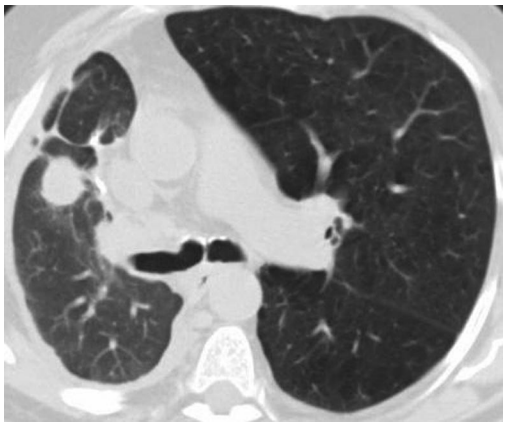

Fig. 1. Computed tomogram shows a 2.7-mm nodule in the anterior right mid-lung zone, and pleural effusion and thickening.

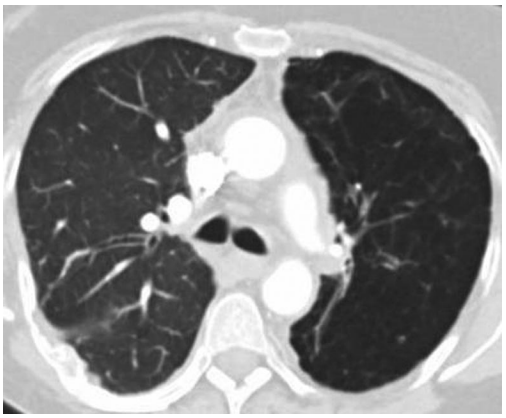

Fig. 2. Computed tomogram after 4 months of oral ciprofloxacin shows resolution of the pulmonary nodule and pleural effusion and thickening, and re-expansion of the allograft.

Physical examination found temperature 38.3°C, blood pressure 130/88 mm Hg, heart rate 98 beats/min, respiratory rate 24 breaths/min, and oxygen saturation 88% on room air. He was oriented but somnolent at times during the examination, with signs of mild dehydration. His respiratory effort was mildly labored and lung examination found reduced air flow in the right base of the allograft. There were a few rhonchi in both the allograft and the native lung. Cardiac examination found no murmur. Abdominal examination was unremarkable; there was no evidence of pain, mass, or hepatosplenomegaly. Stool was negative for blood.

The CTs from the community hospital were unremarkable except for a 2.7-mm pulmonary nodule in the anterior right mid-lung, pleural thickening, and a moderate-size pleural effusion (Fig. 1). Upon admission, blood, sputum, and urine samples were repeated for bacterial, fungal, viral, and acid-fast stains, and cultures and did not isolate an organism. The family again refused a lumbar puncture, but his mental status quickly improved with supplemental oxygen therapy, so his lowered mental status probably resulted from hypoxia from pneumonia. Due to increasing need for more supplemental oxygen over the next 2 days and no isolate of a pathogen, a thoracentesis was performed. While awaiting the culture results, empirical antibiotics included intravenous piperacillin/tazobactam, ciprofloxacin, and vancomycin. The pleural fluid indicated an exudative effusion, based on the ratio of pleural-fluid protein to serum protein (0.9) and the ratio of pleural-fluid lactate dehydrogenase to serum lactate dehydrogenase (0.8). Bacterial, fungal, viral, and acid-fast cultures of pleural fluid found no infecting pathogen. Then, CT-guided fine-needle biopsy of the pulmonary nodule revealed large Gram-positive coccobacillus resembling diphtheroids, which were eventually identified as *R. equi*. Susceptibility testing (E-test, BioMérieux, Marcy-l'Étoile, France) of the *R. equi* isolate indicated a minimum inhibitory concentration of 0.5 μg/mL for vancomycin and 0.75 μg/mL for ciprofloxacin, so these 2 antibiotics were continued, and piperacillin/tazobactam was discontinued. This particular *R. equi* isolate was resistant to imipenem and doripenem (minimum inhibitory concentration $\geq$ 32 μg/mL). Echocardiogram showed normal left-ventricular function and no evidence of heart valve lesions. Cardiothoracic surgery consultation was involved throughout the patient's hospitalization, and the surgeons felt that a chest tube or decortication was not needed. The patient received 7 days of intravenous vancomycin and 4 months of oral ciprofloxacin.

Due to acute onset of dyspnea 4 months later, chest CT (protocol for pulmonary embolus) was performed and found complete resolution of the pulmonary nodule and pleural effusion, re-expansion of the allograft (Fig. 2), and no evidence of pulmonary embolus. Bronchoalveolar fluid culture isolated no pathogens, so there was no recurrence of *R. equi*. The etiology of the dyspnea was deemed completely subjective, related to anxiety from personal stressors.

Discussion

Although the clinical spectrum of infection due to *R. equi* is broad, pulmonary involvement is the predominant feature in most cases.[8] In the literature we found only one case report of a lung-transplant recipient with bacteremia and pneumonia due to *R. equi*.[9] Clinical manifestation of *R. equi* infection typically includes fever, chills, nonproductive cough, dyspnea, weight loss, hemoptysis, and pleuritic pain.[1-11] The infection can be insidious for days to months.[8,10] Necrotizing pneumonia can develop due to *R. equi*, and has a propensity to cavitate in 2–4 weeks after the initial infection.[1,8]

R. equi grows well when incubated aerobically at 37°C on nonselective media routinely used in clinical microbiology laboratories.[12] It typically forms large, irregular, highly mucoid, pale salmon-pink colonies.[12] By 48 hours of incubation on nonselective media, such as Trypticase

soy blood agar, *R. equi* develops its characteristic appearance of irregularly round, smooth, semitransparent, glistening, coalescing, mucoid, teardrop-shaped colonies with entire edges.[12] *R. equi* can be differentiated from morphologically similar pathogens, including diphtheroids, by the mycolic acid staining content and lack of ability to ferment carbohydrates or to liquefy gelatin.[13]

Therapy for *R. equi* is not well established, but successful antimicrobial treatment regimens exist.[2,11] Antimicrobials that concentrate in macrophages are commonly used to treat *R. equi*, which in humans is phagocytosed by alveolar macrophages where they can proliferate.[14] Antimicrobials commonly used include azithromycin, chloramphenicol, clindamycin, fluoroquinolones, rifampin, trimethoprim/sulfamethoxazole,[2,3,8,15] and (recently) linezolid.[16,17] Treatment duration of up to 6 months has been reported.[2,14]

In 2001 the mortality rate of *R. equi* among immunocompetent patients was approximately 11%, compared to 50–55% among HIV-infected patients and 20–25% among non-HIV-infected immunocompromised patients.[18] A more recent review, by Yamshchikov et al,[19] of *R. equi* in transplant recipients found a low overall morbidity and mortality, but the analysis suggested that a longer treatment course is often needed because of protracted immune suppression.

Animal exposure is a risk factor. The surface soil of 50–95% of horse farms has high concentrations of *R. equi*,[20] and dust inhalation is probably the predominant infection route in foals that develop *R. equi* pneumonia.[21]

R. equi is thought to possess several virulence factors that probably contribute to the pathological changes, but the most important virulence determinant for infection is its ability to survive in macrophages.[19] Interestingly, the majority of human *R. equi* infections have occurred in patients with defective cell-mediated immunity,[22] so recent high-dose corticosteroids may have been a risk factor in our patient.

Based on the experience with this patient, clinicians should include *R. equi* in the differential diagnosis of a pulmonary nodule, especially if there are pleural changes, in a transplant recipient after exposure to domestic grazing animals. Furthermore, high-dose corticosteroid therapy probably increases the risk of *R. equi* infection. There is no consensus on the management of *R. equi* infection in transplant recipients, and numerous treatment options have been successful. We successfully treated our patient with 7 days of intravenous vancomycin and a prolonged single-agent course of oral ciprofloxacin.

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