Rhodococcus equi infection

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Rhodococcus equi **is a veterinary pathogen that can cause substantial morbidity in patients that are immunocompromised and are occupationally and recreationally exposed to farming, livestock, and dry soil environments. Although the clinical spectrum of disease associated with *R equi* is broad, pulmonary involvement is a predominant feature in most cases. We present a case of occupationally acquired *R equi* pneumonia and mediastinal lymphadenitis in a patient that has had a renal transplant and is in receipt of a stable immunosuppression regimen. We review the pathogenesis and clinical characteristics of infections with *Rhodococcus* spp, and discuss approaches to treatment of this disease entity in populations of patients who are immunocompromised.**

Introduction

Rhodococcus equi is a zoonotic organism that can cause rare, potentially fatal, disease the predominantly affects immunocompromised patients.

The name *Rhodococcus* was first used by German botanist Wilhelm Friedrich Zopf in 1891 while classifying pigment-producing fungal and bacterial organisms.[1] The genus *Rhodococcus* was redefined in 1977 to include members of the so-called rhodochrous complex that contained organisms resembling nocardiaform and mycobacterial species.[2] The name of the complex derives from the characteristic appearance of colonies of *Rhodococcus* spp after about 4 days of growth on solid media (figure 1): salmon-pink to red coloured and teardrop shaped or coalescent mucoid colonies that vary in size from 2 mm to 4 mm.[3] Rhodococci are generally non-motile Gram-positive rods that look coccoid on solid media and in tissue, but are pleomorphic with long rods or filaments, rudimentary beading, and mycelial branching in liquid media. Isolation and identification of rhodococci in culture is facilitated by selective media, such as colistin-nalidixic agar or phenyl-ethanol agar. Microbiologically, rhodococci can be differentiated from most pathogenic coryneforms by their inability to ferment carbohydrates. The biochemical characteristics of *R equi* include production of catalase, urease, lipase, and phosphatase, but not DNase, elastase, or lecithinase.[3] Although cell walls of *Rhodococcus* spp contain mycolic acids, acid-fast staining of rhodococci needs a modified acid technique with a weaker decolourising step. Development of PCR-based techniques for real-time detection of rhodococci in agricultural and environmental samples is in progress,[4] but has not found widespread application in clinical practice.

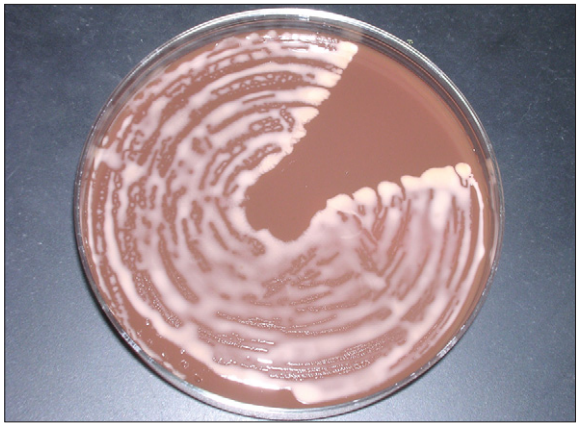

Figure 1: **Coalescent, mucoid, pink-tinged *Rhodococcus equi* colonies on chocolate agar plate**

We report a case of *R equi* pulmonary infection in a patient who received a renal transplant, and we discuss aspects of pathogenesis, clinical presentation, diagnosis, and treatment of this disease entity.

Case presentation

A 69-year-old white man presented with a 4-month history of substernal and right-sided pleuritic chest pain associated with progressive dyspnoea and cough producing yellow sputum 2 years after receiving a renal transplant from a dead unrelated donor. The patient reported subjective fevers, chills, and nightsweats, but no weight loss or other constitutional symptoms. The medical history was indicative of end-stage renal disease secondary to obstructive uropathy.

Additional medical history included hyper-parathyroidism after partial parathyroidectomy in 1999, hypertension, and surgical removal of squamous-cell carcinoma of the skin. The patient did not have any known episodes of rejection after transplantation. On admission, the patient's immune suppression regimen, which had been stable for several months, consisted of tacrolimus (1 mg twice daily), mycophenolate mofetil (1000 mg twice daily), and prednisone (10 mg once daily). The patient was a cattle farmer in rural Georgia, USA, and denied any notable travel history outside of his immediate region. The patient denied the use of alcohol, illicit drugs, and nicotine. Family history included Alzheimer's dementia, coronary artery disease, diabetes mellitus, and hypertension.

On physical examination, the patient had mild respiratory distress with a respiratory rate of 26 breaths per min. His temperature was 36°C, heart rate 77 beats per min, and blood pressure 131/78 mm Hg. His eyes were anicteric and his oropharynx was clear without mucosal lesions. His neck was supple without meningismus or cervical lymphadenopathy. Cardio-vascular examination was unremarkable, and pulmonary

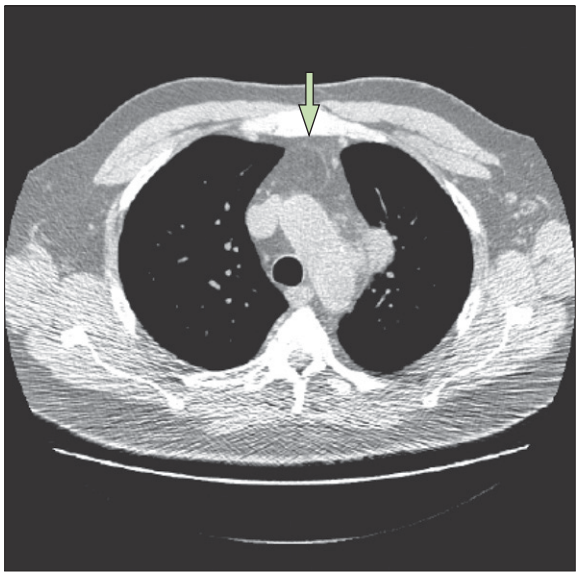

Figure 2: CT of the chest showing lobulated mediastinal mass with matted mediastinal lymph nodes

examination was notable for diminished breath sounds at bilateral bases without asymmetry. Abdominal examination revealed no hepatosplenomegaly or masses with exception of the donor kidney palpable in the right-lower quadrant. The remainder of the physical examination was unremarkable.

Laboratory tests revealed a total leucocyte count of 10 200 cells per µL with 89% segmented neutrophils, 6% lymphocytes, and 4% monocytes, without band forms, eosinophils, or basophils. The patient's red blood cell, platelet, and coagulation indices were within normal ranges. Lactate dehydrogenase, transaminases, and bilirubin concentrations were normal. The patient's electrolyte panel was normal and his creatinine was 1·2 mg/dL, which is consistent with his baseline renal function after transplantation.

Chest radiographs obtained during outpatient workup of the patient's symptoms showed an aortopulmonary window mass in the region of the pulmonary outflow tract, without abnormalities of the cardiac silhouette or pulmonary parenchyma. Follow-up CT of the thorax showed a lobulated mass at the level of the aortic arch, measuring 5·4 cm by 3·9 cm in the largest dimension, and extending inferiorly to the level of the pulmonary artery (figure 2), without evidence of pulmonary consolidation. The lobulated mass was thought to represent matted mediastinal nodes, and multiple additional nodes were noted to be enlarged in the superior mediastinum.

On the basis of the radiographic findings, the patient was electively admitted for exploratory video-assisted thoracoscopy and mediastinoscopy. His blood cultures and urine cultures from admission were negative. In the operating room, thoracoscopy revealed extensive

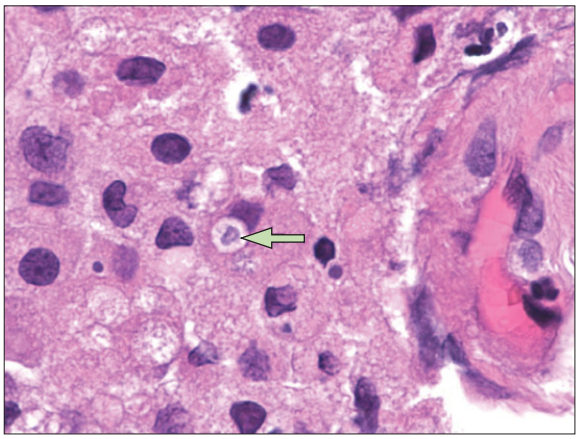

Figure 3: Lung tissue with characteristic targetoid Michaelis-Gutmann body inclusion surrounded by dense infiltrate of foamy histiocytes

inflammation of the lung parenchyma involving the left-upper lobe and the left phrenic nerve. A large amount of purulent material was released on dissection into the mediastinal mass. Multiple matted and necrotic nodes were noted in the superior mediastinum. Pathological tests of biopsy material from the mediastinal lymph nodes and pulmonary parenchyma obtained during the procedure revealed histiocytic infiltration of the lung with intra-alveolar collections of foamy histiocytes and intracellular bacteria that stained with periodic-acid Schiff. Scattered targetoid Michaelis-Gutmann bodies (figure 3) and intracellular coccobacilli on tissue Gram stain (figure 4) were identified, consistent with a diagnosis of pulmonary malakoplakia.

Gram stain of intraoperative biopsies revealed multiple Gram-positive cocci and Gram-variable rods. Intraoperative cultures of necrotic lymph-node material grew Gram-positive coccobacilli with salmon-coloured mucoid colonies on sheep-blood and chocolate agar plates (figure 1). The isolate was confirmed as *R equi* on API NH strip (bioMerieux, Durham, NC, USA), and a modified acid-fast stain of the organism was positive. The patient's symptoms resolved after a 6 week course of intravenous meropenem (1 g every 8 h) and oral azithromycin (250 mg daily), after which the patient received 8 weeks of oral azithromycin consolidation therapy. At present, the patient continues to maintain timely follow-up in the outpatient setting, and is thought to be in good health. A follow-up CT scan revealed complete resolution of pulmonary infiltrates and lymphadenopathy (not shown).

A veterinary and human pathogen

Rhodococcus equi (formerly *Corynebacterium equi*), originally isolated from lungs of young horses with pyogranulomatous pneumonia in 1923,[5] is a well known pathogen in veterinary medicine. Although the organism is present in faeces of many grazing animals, young horses have a unique susceptibility to clinical disease