

Rhodococcus equi pneumonia in a live related renal transplant recipient

Mohammed Yasin Khan,¹ Sajjad Ali,² Shehla Baqi³

Abstract

Rhodococcus equi has emerged as a serious pathogen in immunocompromised patients, including solid organ transplant recipients. Primary pulmonary involvement is the most common presentation. However, this opportunistic pathogen is often not considered in the differential diagnosis of pneumonia in transplant recipients. Furthermore, in cultures, *Rhodococcus* can be misinterpreted by microbiologists in laboratories as a contaminant due to its morphology on gram staining if they have not been provided sufficient clinical information.

We report a case of a young Asian male, 19 months post-live related renal transplantation who presented with a five-day history of productive cough, fever and weight loss. Chest radiography revealed bilateral basal infiltrates. Blood cultures and bronchoalveolar lavage yielded heavy pure growth of unbranched gram-positive rods which were identified as *Rhodococcus equi* (*R. equi*).

Keywords: *Rhodococcus equi*, Immunocompromised host.

Introduction

Rhodococcus equi is a gram-positive coccobacillus that primarily causes zoonotic infections.¹ The most important risk factor for infection in humans with *R. equi* is impaired cell-mediated immunity and it is, therefore, encountered in patients infected with human immunodeficiency virus (HIV), those with haematological malignancies, and in solid organ transplant recipients.²⁻⁶ Since it is a rare infection, even in transplant recipients, *R. equi* is often not considered in vulnerable populations and may be initially discounted by physicians and microbiology laboratories as a contaminant.

We report the first case from Pakistan of a 19-year-old male recipient of a live related renal transplant who developed pneumonia and bacteraemia with *R. equi*.

Case Report

A 19-year-old Asian male was admitted to the transplant

¹Department of Microbiology, ^{2,3}Department of Infectious Diseases, Sindh Institute of Urology and Transplantation (SIUT), Karachi.

Correspondence: Sajjad Ali. Email: sajjad_siut@yahoo.com

ward with a 5-day history of fever, anorexia, weight loss and shortness of breath with productive cough. He had a past history of end-stage renal failure (ESRD) secondary to hypertensive nephropathy and had undergone live related renal transplantation from his brother 19 months prior to the presentation. The patient gave no history of smoking, travel, risk factors for HIV, pets, recent influenza or exposure to tuberculosis, but reported contact with domesticated buffalos and cows.

He had done well post-transplantation, and had not suffered any episodes of acute rejection, opportunistic infections or malignancies. His maintenance immunosuppressive regimen consisted of tacrolimus, cyclosporin, and prednisone. His other medications included atenolol and amlodipine.

At the time of admission, the patient was febrile and in mild respiratory distress. Examination revealed an ill-looking young man with tachycardia and bilateral basal crackles. Laboratory studies revealed the following values: total leukocytes count (TLC), 3.2×10^9 cells/L; neutrophils count 70%; haemoglobin 9.2g/dL; erythrocyte

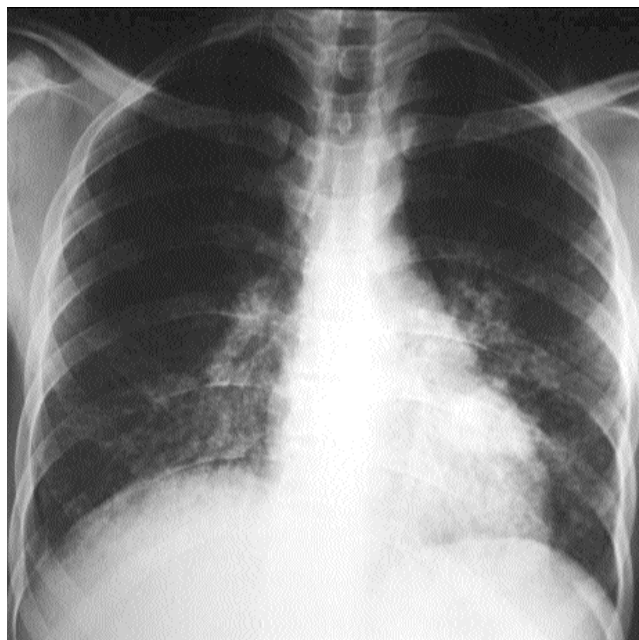


Figure-1: Bilateral basal infiltrates involving both lower lobes and consolidation in the left retrocardiac region.

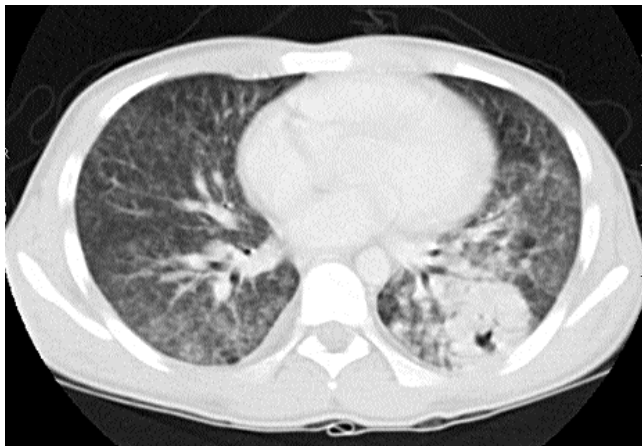


Figure-2: Axial computed tomography scans of the chest showing ground glass haziness with diffuse bilateral alveolar infiltrates with a cavitary mass-like consolidation in left lung base.

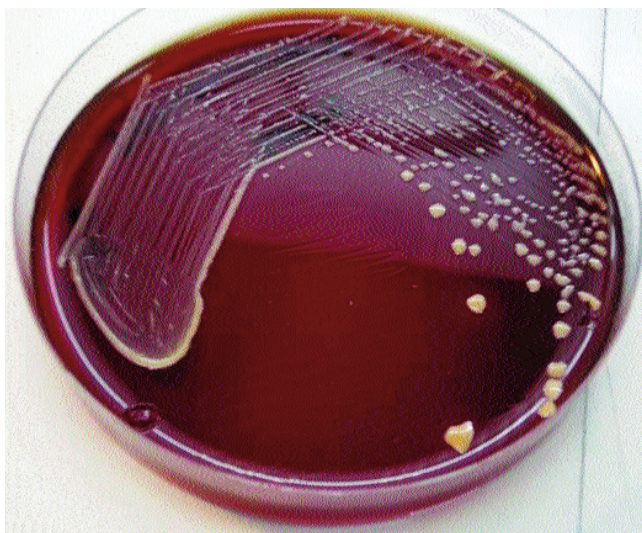


Figure-3: *Rhodococcus equi* on blood agar. Note the characteristic salmon pink pigmentation after prolonged incubation.

sedimentation rate (ESR) 60mm/h; serum albumin, 1.5g/L; total bilirubin 1.1g/L; g-glutamyl transferase 35U/L; aspartate aminotransferase 30U/L; alanine aminotransferase 32U/L; and international normalised ratio (INR) 1.2. His creatinine was elevated at 2.10 mg/dL whereas prior to this illness he had achieved a best serum creatinine of 1.0 mg/dL. Initial chest radiograph revealed bilateral basal infiltrates involving both lower lobes, and consolidation in the left retrocardiac region (Figure-1). Blood and urine cultures were sent and the patient was started on intravenous (IV) ceftriaxone 1gm, 12 hourly. A single blood culture on the second day of admission was reported to be growing gram-positive rods. Though the

culture was thought to represent contamination, in view of the immunocompromised status of the patient, vancomycin was added till further clarification. Subsequently, 5 other blood cultures were reported to be growing gram positive rods. Examination of sputum samples for routine as well as acid-fast bacilli (AFB) smear and culture on 3 consecutive days were reported to have growth of throat commensals only.

Repeat radiograph of the chest revealed progression of pulmonary infiltrates involving both lungs; more marked in the perihilar region. Axial computed tomography (CT) scans of the chest demonstrated ground glass haziness with diffuse bilateral alveolar infiltrates with a cavitary mass-like consolidation in the left lung base (Figure-2). Echocardiography (ECG), both transthoracic as well as transoesophageal, showed no evidence of vegetation.

A bronchoalveolar lavage (BAL) was performed. Gram staining of BAL revealed numerous unbranched gram-positive rods (diphtheroid-like), gram-positive cocci and numerous pus cells. Periodic acid-Schiff (PAS) stain for fungi, cytomegalovirus (CMV) polymerase chain reaction (PCR) and cytology was negative.

Due to clinical deterioration with the worsening of radiographic findings, his empirical anti-microbial therapy was broadened to cover a wider range of potential pathogens and included intravenous vancomycin, imipenem-cilastatin,



Figure-4: Christie, Atkinson, Munch, Petersen (CAMP) test on sheep blood agar. Note the enhanced arrow-head shaped area of β -hemolysis where the streaking of *S. aureus* isolate meets *Rhodococcus equi*.

levofloxacin, trimethoprim/sulfamethoxazole, amphotericin B deoxycholate and gancyclovir. His immunosuppressive therapy with tacrolimus and cyclosporin was discontinued. However, there was no improvement in clinical status despite widened antimicrobial coverage and concomitant reduction of immunosuppression, and the patient expired in the third week of his admission.

All six blood cultures as well as the culture from the BAL specimen yielded a heavy pure growth of unbranched gram-positive rods resembling *Corynebacterium* spp. which was subsequently identified as *R. equi*. Gram staining was reported to show unbranched gram-positive rods with coccobacilli on morphology. The organism was found to be non-motile, catalase-positive and urease-positive. It was positive on modified acid fast stain, and its acid fast property was enhanced when stained from a growth taken from Lowenstein-Jensen media. The colonies showed salmon pink pigmentation on further incubation on the blood agar plates (Figure-3). The organism had a positive CAMP (Christie, Atkinson, Munch, Peterson) test (Figure-4). All these features along with biochemical testing with Coryne alkaline protease inhibitor (API) confirmed the organism to be *R. equi*.

Discussion

The *R. equi* case described did not respond to antimicrobial therapy and resulted in the death of the patient. *Rhodococcus equi* (red pigmented coccus) was first isolated in 1923, and is an important pathogen in veterinary medicine.⁵ *Rhodococcus* was first described in humans in 1967 and is usually seen in immunocompromised hosts such as HIV-infected patients, solid organ transplant recipients, and in those with alcoholism, malignancies, diabetes mellitus and chronic renal failure.²⁻⁶ However, infection in the immunocompetent host has also been described.⁷

R. equi is found in the manure of herbivores and is therefore, present in soil worldwide.⁸ Routes of acquisition of *rhodococcus* in humans include inhalation from the soil, ingestion or inoculation of a wound. Human colonisation and person-to-person transmission have also been described as well as nosocomial spread, and some case reports have suggested transmission from animals to humans via respiratory secretions.⁴⁻⁹ Our patient may have potentially acquired *R. equi* via exposure to domesticated cows and buffalos.

Rhodococcus grows well on non-selective media under aerobic conditions forming large, irregular, smooth, mucoid colonies that turn to a salmon-pink colour with incubation.⁹ It is non-fermentative and modified acid fast positive, non-motile, catalase-positive, urease-positive,

CAMP-positive, and oxidase-negative. Biochemical kits such as API Coryne are available which facilitate identification of *R. equi*.⁵ The negative results of cultures of sputum samples in our patient may have been due to the overgrowth of other organisms reported as throat commensals. This highlighted the importance of obtaining bronchoscopy in immunocompromised patients with undiagnosed pulmonary infiltrates.

The *R. equi* infection has diverse clinical manifestations, with pulmonary involvement and bacteraemia more commonly observed in immunocompromised patients as compared to the immunocompetent. Mean time of presentation after solid organ transplantation has been reported to range from 1 month to 180 months. The most common clinical manifestations of pulmonary *R. equi* infection are fever, rigours or chills, and non-productive cough. The localised infection in the lungs has the propensity to cavitate in 2-4 weeks with necrotising pneumonia as the most common presentation in transplant recipients. Contiguous and haematogenous dissemination of the pathogen can lead to extra-pulmonary disease with metastatic infection to brain, bone, and subcutaneous tissue. Relapses are common and can occur at the initial site of infection or at metastatic sites.⁴

The main differential diagnosis of pulmonary *Rhodococcus* infection in transplant recipients includes viral or bacterial pneumonia, lung abscess, *Pneumocystis jiroveci* pneumonia, nocardiosis, actinomycosis, mycobacterial and fungal infections.⁵

Therapeutic failure, as occurred in our patient, can be attributed to the immunocompromised status of the patient, as well as the ability of the *Rhodococcus* organism to inhibit macrophage phagosome-lysosome fusion and survive within the cell. Therefore, treatment with synergistic antibiotics with high intracellular penetration is recommended with a combination of two or three drugs that may include vancomycin or a carbapenem, rifampicin, fluoroquinolone, an aminoglycoside or a macrolide.⁹⁻¹¹ Intravenous antibiotics should be continued till there is clinical improvement and for a minimum of 2-3 weeks. Oral agents can then be given until cultures are negative and the infection has resolved.⁹ Drainage procedures or surgical debridement may be needed for large abscesses.⁴

Optimal duration of treatment in solid organ transplant patients varies and may require a total of 6-9 months to avoid relapse. In immunocompromised patients, mortality rates are much higher compared to the immunocompetent patients.⁷ Since immunosuppression

in renal transplanted patients is a major predisposing factor for *R. equi* infection, there is a consensus that immunosuppressive therapy should be reduced in patients with life-threatening infection.

Conclusion

R. equi is a serious pathogen in immunocompromised hosts. Patients such as those with organ transplantation or HIV should be counselled regarding exposure to *Rhodococcus* from domestic and farm animals and their waste products. It is imperative that all physicians and laboratory staff consider *R. equi* when an immunocompromised patient develops pneumonia. Gram-positive rods identified in microbiological specimens in such a patient must not be disregarded as contaminants and the samples should be further processed to exclude *Rhodococcus*. Patients should receive a combination of bactericidal and intracellular-active agents for a prolonged period of time to ensure therapeutic success and avoid relapse.

References

1. Scott MA, Graham BS, Verrall R, Dixon R, Schaffner W, Tham KT. *Rhodococcus equi*—an increasingly recognized opportunistic pathogen. Report of 12 cases and review of 65 cases in the literature. *Am J Clin Pathol* 1995; 103: 649-55.
2. Weinstock DM, Brown AE. *Rhodococcus equi*: an emerging pathogen. *Clin Infect Dis* 2002; 34: 1379-85.
3. Cid A, Jarque I, Salavert M, Martin G, Perez-Belles C, Sanz MA. Recurrent bacteremia caused by *Rhodococcus equi* in a non-neutropenic patient with acute myeloid leukemia in complete remission. *Haematologica* 2002; 87: ECR03.
4. Perez MG, Vassilev T, Kemmerly SA. *Rhodococcus equi* infection in transplant recipients: a case of mistaken identity and review of the literature. *Transpl Infect Dis* 2002; 4: 52-6.
5. Speck D, Koneth I, Diethelm M, Binet I. A pulmonary mass caused by *Rhodococcus equi* infection in a renal transplant recipient. *Nat Clin Pract Nephrol* 2008; 4: 398-403.
6. Arya B, Hussian S, Hariharan S. *Rhodococcus equi* pneumonia in a renal transplant patient: a case report and review of literature. *Clin Transplant* 2004; 18: 748-52.
7. Kedlaya I, Ing MB, Wong SS. *Rhodococcus equi* infections in immunocompetent hosts: case report and review. *Clin Infect Dis* 2001; 32: E39-46.
8. Takai S, Ohbushi S, Koike K, Tsubaki S, Oishi H, Kamada M. Prevalence of virulent *Rhodococcus equi* in isolates from soil and feces of horses from horse-breeding farms with and without endemic infections. *J Clin Microbiol* 1991; 29: 2887-9.
9. Meyer DK, Reboli AC. Other Coryneform Bacteria and *Rhodococci*. In: Mandel GL, Bennett JE, Dolin R, eds. *Principle and Practice of Infectious Disease*. 7th ed. Philadelphia: Churchill Livingstone, 2010; 2695-706.
10. El Karoui K, Guillet C, Sekkal N, Lanternier F, Mechai F, Hue K, et al. Synergistic effect of carbapenem-teicoplanin combination during severe *Rhodococcus equi* pneumonia in a kidney transplant recipient. *Transpl Infect Dis* 2009; 11: 359-62.
11. Tse KC, Tang SC, Chan TM, Lai KN. *Rhodococcus* lung abscess complicating kidney transplantation: successful management by combination antibiotic therapy. *Transpl Infect Dis* 2008; 10: 44-7.