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***Case Report:***

# Bacteremia due to *Rhodococcus equi*: a case report and review of the literature*

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**Abstract:** *Rhodococcus equi*, previously known as *Corynebacterium equi*, is one of the most important causes of zoonotic infections in grazing animals. Increased cases of human infection with *R. equi* have been reported, especially in immunocompromised patients, within recent years. We present a case of *R. equi* bacteremia in a 51-year-old man with diabetes and liver cirrhosis, on long-term corticosteroid therapy after skin-grafting surgery. The patient recovered soon after he was treated with vancomycin. This review focuses on the microbiological characteristics of this organism, and the diagnosis and treatment of this infection.

**Key words:** *Rhodococcus equi*, Bacteremia, Opportunistic pathogen
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## INTRODUCTION

Since the advent of the acquired immunodeficiency syndrome (AIDS) epidemic, *Rhodococcus equi* has been emerging as an opportunistic pathogen, especially in immunocompromised patients (Puthucheary *et al*., 2006). Most patients infected with *R. equi* present with a pulmonary syndrome. Other infections include gastrointestinal infections, pericarditis, meningitis, mastoiditis, and abscesses in the liver, kidney, psoas muscles, and cutaneous wounds (Weinstock and Brown, 2002; Roda *et al*., 2009). Only a few cases of isolated bacteremia have been reported.

Here we present a case of *R. equi* bacteremia in a 51 year-old man. The patient was treated with vancomycin and recovered quickly. The diagnosis of *R. equi* is often difficult due to microbiological and clinical similarities with other pathogens such as diphtheroids, mycobacterium species, or *Nocardia*, although it is easily cultured from sputum or blood. The aim of this report is to increase physician awareness about *R. equi* infection in immunocompromised patients.

## CASE REPORT

A 51-year-old man was admitted to our hospital with fever, dizziness, nausea, vomiting, and diarrhea. Eighteen days before admission, he had a fever followed by dizziness. He went to a local hospital where antibiotics (specific type unknown) were prescribed, and his dizziness was eased, while the temperature remained around 38.5 °C. Three days before admission, he developed nausea, vomiting, and diarrhea. He denied headache, seizure, cough, chest, or abdominal pain. The patient could not recall any contact with animals recently. His past medical history included diabetes and cirrhosis secondary to chronic viral hepatitis B. He had a history of a skin-grafting surgery on his left leg one year prior and received prolonged

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treatment with antibiotics and systemic glucocorticoids. He did not travel recently and had no known illness contacts.

On admission, physical examination was only remarkable for fever of 38.9 °C. The results of laboratory examinations were as follows: White blood cell (WBC) count was 11100 cells/μl with 87% neutrophils, C reactive protein (CRP) level was 185.2 mg/L, and erythrocyte sedimentation rate (ESR) level was 91 mm/h. The results of both tuberculin skin testing with purified protein derivative (PPD) and PPD antibodies were negative. Anti-nuclear antibody (ANA), anti-ds-DNA antibody, extractable nuclear antigen (ENA), and serum tumor markers were also negative. Human immunodeficiency virus (HIV) serology was negative. Urine and stool examination revealed no abnormal findings. Liver and renal function tests and a chest X-ray were normal. An ultrasonic cardiography revealed mild pericardial effusion and an electrocardiogram showed low voltages.

After empiric antibiotic treatment with levofloxacin for 4 d, the patient's condition showed no improvement with persistent fever as high as 39 °C, and new symptoms of cough and white sputum appeared. One week after his admission, blood cultures showed large Gram-positive coccobacillus with the microbiologic characteristics shown in Table 1, and this organism was finally identified as *R. equi*. After aggressive treatment with vancomycin for 4 d, the temperature of the patient started to return to normal. The patient finally recovered with a combination of vancomycin and sulbactam/cefoperazone administered for another 5 d. He was discharged on oral rifampin after the two negative blood cultures.

**Table 1 Microbiologic characteristics of the pathogen**

| Test | Result |
|---|---|
| Catalase | + |
| Urease | + |
| CAMP | + |
| Oxidase | − |
| Carbohydrate fermentation | − |
| Mannitol | − |
| Gelatin hydrolysis | − |
| Indole | − |
| Nitrate reduction | − |
| Citric acid | − |

## REVIEW OF THE LITERATURE

*Rhodococcus equi*, previously known as *Corynebacterium equi*, is a Gram-positive pleomorphic coccobacillus. The natural habitat of *R. equi* is soil contaminated with animal manure. It primarily causes zoonotic infections that affect grazing animals, mainly horses and foals. Since the first case of human infection of *R. equi* reported in 1967 (Golub *et al*., 1967), only 12 additional cases were reported by Lipsky *et al*.(1982). However, with the AIDS epidemic, this number has greatly increased. Since then, hundreds of cases of human infection with *R. equi* have been reported (Weinstock and Brown, 2002).

Contact with animals or animal-contaminated soil is thought to initiate infection, but a specific exposure is recalled in less than 50% of cases. The route of infection from animals to humans remains unclear. However, transmission via respiratory secretions was postulated in some case reports (Cronin *et al*., 2008).

*R. equi* mainly affects immunocompromised patients, especially those with HIV infection. Cases have also been reported after solid organ transplantation, hematopoietic stem cell transplantation, splenectomy, corticosteroid use, and in patients with end stage liver disease (Roda *et al*., 2009; Tse *et al*., 2008; Kedlaya *et al*., 2001). Infection in immunocompetent patients is thus extremely rare. The mortality rate among immunocompetent patients is approximately 11%, compared with rates of 50%~55% among HIV-infected patients and 20%~25% among non-HIV-infected immunocompromised patients (Alonso *et al*., 2001). Our patient had a history of diabetes and liver cirrhosis, and also received long-term corticosteroid therapy after skin-grafting surgery.

Most patients initially have a pulmonary syndrome, with findings including infiltrates, empyema, and cavitary lesions (Marchiori *et al*., 2006). It has been concluded that the most common finding in patients with AIDS and pulmonary infection due to *R. equi* was consolidated with cavitation (Kamboj *et al*., 2005). Less frequent manifestations include gastrointestinal infections, pericarditis, meningitis, mastoiditis, and abscesses in the liver, kidney, psoas muscles, and contaminated cutaneous wounds. The disease is commonly chronic and recurrent. Relapse may follow a course of brief antimicrobial therapy, but can also occur during treatment. Malakoplakia is

an uncommon inflammatory disorder associated with immunosuppression. In a rare report, *R. equi* was even isolated from malakoplakia lesions (Wagner *et al*., 2007).

*R. equi* is an intracellular pathogen that can survive inside macrophages. The typical histologic pattern shows a predominance of macrophages having granular cytoplasm that is filled with periodic acid-Schiff (PAS)-positive coccobacilli. Blood and sputum cultures offer the best yield for the diagnosis of this infection. The bacterium grows optimally at 30 °C on solid ordinary non-selective media and forms large, irregular, mucoid colonies that turn to a salmon-pink color within 48 h (Cronin *et al*., 2008). It is a facultative, encapsulated, nonmotile, non-spore forming, Gram-positive coccobacillus, which is partially acid-fast staining and bears a similarity to diphtheroids. *R. equi* can be differentiated from other pathogenic corynebacteria by its mycolic acid staining content and lack of ability to ferment carbohydrates or liquefy gelatin (Perez *et al*., 2002). A particular characteristic of this organism is that it causes synergistic hemolytic reaction with sphingomyelinase-producing bacteria such as *Staphylococcus aureus* and *Listeria ivanovii*, based on Christie Atkins Munch-Petersen (CAMP) test (Puthucheary *et al*., 2006). Characteristics used in routine clinical microbiology laboratories to identify *R. equi* are catalase (+), oxidase (−), carbohydrate fermentation (−), alcohol fermentation (−), gelatin hydrolysis (−), indole (−), urease (+), hippurate hydrolysis (−), esculin hydrolysis (−), nitrate reduction (+), equi factors (+), lipase (+), and phosphatase (+) (Prescott, 1991). *R. equi* may be misidentified as diphtheroids, *Mycobacterium* species, or *Nocardia*. The isolation of difficult-to-identify, Gram-positive rods from the patients with decreased cell-mediated immunity should raise the possibility of *R. equi*. Additionally, *R. equi*-specific polymerase chain reaction (PCR), which is based on the amplification of a fragment of the *choE* gene, can be a useful confirmatory test in human infection (Ladrón *et al*., 2003).

The organism has generally shown in vitro susceptibility to erythromycin, rifampin, vancomycin, fluoroquinolones, aminoglycosides, and imipenem/cilastatin, and resistance to penicillins, although this can vary in specific geographic areas or from previous antibiotic therapy (Torres-Tortosa *et al*., 2003). This organism can inhibit macrophage phagosome-lysosome fusion and survives intracellularly. Although there is no consensus on the optimal duration and regimen of antibiotic treatment, combination antimicrobial therapy using bactericidal and intracellularly active agents should be considered (Torres-Tortosa *et al*., 2003). A carbapenem and a glycopeptide, such as meropenem and vancomycin, are good choices (Tse *et al*., 2008). The use of combination therapy may decrease the risk of developing resistance during therapy, which has been described with penicillin and other beta-lactam antibiotics. The combination of macrolides and rifampin can also be considered (Prescott, 1991). After initial improvement, the patient can be treated with an oral regimen that could include combinations of quinolones, tetracycline, macrolides, and rifampin. The optimal duration of treatment is unknown. Based on similar experiences with difficult-to-treat organisms like *Mycobacterium tuberculosis*, and on the fact that distant relapses of *Rhodococcus* infection are common, prolonged therapy is recommended (e.g., 9 months) (Kedlaya *et al*., 2001). Torres-Tortosa *et al*. (2003) reported that highly active antiretroviral therapy can improve prognosis of patients with HIV infected by *R. equi*.

In conclusion, *R. equi* mainly affects immunocompromised patients, especially those with HIV infection. The isolation of Gram-positive rods from immunosuppressed patients should raise the possibility of *R. equi* and ongoing communication with the microbiology laboratory can help identify this difficult-to-treat organism.

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