

Rare case of *Rhodococcus hoagii* bacteremia in an HIV late-presenter with NTM pulmonary disease: A case report and review of the literature

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Abstract. The present study describes the case of a 33-year-old male patient, who was diagnosed with concurrent infections of *Rhodococcus hoagii* (*R. hoagii*), *Mycobacterium intracellulare* (*M. intracellulare*), human immunodeficiency virus (HIV) and syphilis. This patient, a homeless farm laborer with no prior medical treatments, exhibited symptoms including persistent fever and cough, and was admitted to hospital. Treatment was initiated with a combination of anti-retroviral therapy with emtricitabine/tenofovir alafenamide/dolutegravir, and antibiotics (azithromycin, rifampicin, amikacin and ethambutol) targeted at both *R. hoagii* and *M. intracellulare*, alongside adjustments for drug-drug interactions due to rifampicin administration. Despite initial improvements and discharge after 21 days with scheduled outpatient follow-ups, the patient did not return for further treatment monitoring. The case presented herein underscores the challenges in managing complex infections in severely immunocompromised patients and highlights the need for integrated treatment approaches, careful drug management, and robust follow-up systems to ensure adherence and prevent relapse. In addition, the present case report contributes to the limited literature available on *R. hoagii* infections in HIV-infected individuals and highlights the need for early intervention and comprehensive management in similar clinical scenarios

Introduction

Rhodococcus hoagii (*R. hoagii*; formerly *Rhodococcus equi*), a pathogen originally identified as a cause of zoonotic infections in domestic animals, has emerged as a significant opportunistic bacterium affecting immunocompromised hosts, particularly those with human immunodeficiency virus (HIV)/AIDS (1,2). *R. hoagii* infections exhibit variable geographic distribution, being more common in regions with extensive horse breeding activities. The prevalence among animal populations, particularly young foals, can exceed 10% in some intensive breeding farms. Additionally, seasonal variations are observed, with an increase in incidence during warmer months when contact with contaminated soil is more frequent (3).

Known for its ability to cause severe pulmonary infections, bacteremia, and occasionally, disseminated disease, *R. hoagii* presents unique clinical and therapeutic challenges. In patients with HIV, the incidence of *R. hoagii* infection, although less common than other opportunistic infections, represents a critical intersection between an impaired immune response and the aggressive nature of the pathogen (4,5).

On the other hand, non-tuberculous mycobacteria (NTM) diseases significantly affect patients with HIV, particularly those with advanced immunodeficiency, due to their severe symptoms and complex treatment requirements (6,7). Despite advancements being made in antiretroviral therapy, NTM diseases remain a major cause of morbidity (8). These infections are challenging to manage, often requiring long-term, multidrug regimens that must be carefully coordinated with HIV treatment to avoid drug interactions. The presence of NTM at the initiation of anti-retroviral therapy (ART) can hinder CD4⁺ T-cell count recovery, complicating the overall treatment and prognosis (9-12).

The present study reports a case with a rare instance where *R. hoagii* bacteremia presents in tandem with HIV infection and NTM pulmonary disease. The concurrence of these conditions in a single patient highlights the complexities encountered in diagnosing and managing cumbersome

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infections in severely immunocompromised individuals. The case described herein underscores the necessity for high clinical suspicion for *R. hoagii* in patients with HIV, particularly when presenting with respiratory symptoms or unexplained bacteremia, given its propensity for rapid progression and potential for significant morbidity and mortality.

Case report

A 33-year-old male patient, from Eastern Europe, was admitted to ARNAS Garibaldi Hospital (Catania, Italy) due to 2 weeks of persistent fever and cough. He reported having been homeless and working as a farm laborer. He denied having any comorbidities or receiving any pharmacological therapies. He smoked 15 cigarettes/day for 15 years.

Upon admission, he was febrile (temperature, 38°C), with a blood pressure of 140/80 mmHg, a heartbeat of 90 bpm and 95% oxygen saturation in room air. A clinical examination revealed decreased breath sounds over the left upper pulmonary lobe together with crackles.

Blood tests revealed a hemoglobin level of 10.23 g/dl, a red blood cell count of 3.06×10^6 /mmc, a white blood cell (WBC) count of 5,050 cells/mmc (Ne 58%, Ly 24.6%), a platelet count of 208,000/mmc and a C reactive protein (CRP) level of 8.16 mg/dl (normal value, <0.5 mg/dl); procalcitonin levels were within the normal range (<0.5 ng/ml), as well as the transaminase (AST/ALT) levels (ALT <35 U/l; AST <45 U/l); the creatinine level was 0.81 mg/dl (estimated glomerular filtration rate with CKD-EPI, 117 ml/min). Blood culture and urine culture were performed.

Screening for sexually transmitted diseases yielded positive results for HIV (ELISA) and syphilis (positive VDRL and TPHA) (performed by the hospital laboratory). HIV infection was confirmed with western blot analysis (performed by the hospital laboratory). The CD4⁺ T-lymphocyte count was 29 cells/mmc (2%), CD4⁺/CD8⁺ ratio 0.02, HIV RNA 400,000 copies/ml. ART was commenced with emtricitabine/tenofovir alafenamide/dolutegravir (200/25/50 mg) and benzathine penicillin (2,400,000 U/week for 3 consecutive weeks) to treat the syphilis. HCV and HBV serology tested negative.

A brain, abdomen and chest computed tomography scan was performed, which revealed a consolidative lesion with central cavitation localized to the upper-dorsal segment of the left upper lobe, and two sub centimetric nodules in the left lower lobe in a context of diffuse distal airway inflammation (Fig. 1). No other lesions were detected.

A sputum examination was performed to rule out tuberculosis. The nucleic acid amplification test for tuberculosis (GeneXpert MTB/RIF assay-Xpert® MTB/RIF Ultra) yielded negative results; however, a microscopic examination revealed acid-fast bacillus. PCR analysis of the culture growth yielded positive findings for *Mycobacterium intracellulare* (*M. intracellulare*).

Blood culture analysis revealed positive results for *Rhodococcus hoagii*, identified by matrix-assisted laser desorption ionization-time of flight mass spectrometry. A urine culture yielded negative results.

Due to these findings, therapy with azithromycin 500 mg/die *per os*, IV amikacin 1 gr/die, rifampicin 600 mg/die *per os*, ethambutol 1,000 mg/die *per os* was commenced. Due to rifampicin, the dolutegravir dose was augmented (every 12 h).

Within 48 h, the fever disappeared along with a marked improvement in the general clinical condition of the patient. Blood cultures performed after 48 h yielded negative results. A transthoracic echocardiogram revealed no vegetations (no images available).

The patient was discharged after 21 days with an indication for the continuation of antibiotic therapy *per os* and the administration of intravenous amikacin three times a week at the outpatient clinic of the hospital and follow-up.

At the time of discharge, the patient had a HIV RNA count of 21 copies/ml, a CD4⁺ T-lymphocyte count of 148 cells/mmc (2%), a CD4⁺/CD8⁺ ratio of 0.02, a CRP level of 1.11 mg/dl and a WBC count of 10,000 cells/mmc (Ne 55%, Ly 27.5%). The patient did not appear for further follow-up and therapeutic outpatient visits.

Discussion

R. hoagii, formerly known as *Corynebacterium equi*, is a Gram-positive coccobacillus, naturally found in soil contaminated with animal manure. Zoonotic infections (horses and foals) are the primarily problems caused by *R. hoagii*: It is recognized as the causative agent of severe pyogranulomatous pneumonia in young foals and it is occasionally isolated from granulomatous lesions, joint and skin infections in several other animals (13).

R. hoagii is normally acquired by inhalation from contaminated soil, by inoculation from a continuous solution, such as a wound, or through the mucous membranes of the gastro-intestinal tract, by ingestion of contaminated food. Exposure to farm animals, such as horses and pigs, appears to play a role in some cases of infection (2).

Microbiologically, *Rhodococci* belong to the family Nocardioform, order Actinomycetes, which includes the *Corynebacterium*, *Mycobacterium*, *Nocardia* and *Gordonia* species. *R. hoagii* is a facultative intracellular, asporogenous, non-motile, Gram-positive, obligate aerobe capable of metabolizing a wide variety of organic compounds (1,2).

R. hoagii optimally grows at 30°C but can grow at temperatures from 10 to 40°C. Colonies form on solid media in ≤48 h and appear irregularly round, smooth, semitransparent, glistening and mucoid. The characteristic salmon-pink colour may not appear until days 4-7 (1,2).

The *R. hoagii* cell wall includes mycolic acids. The results of acid-fast staining are highly variable. Given these morphological characteristics, *R. hoagii* can easily be mistaken for a diphtheroid contaminant, or it can be mistaken for *Mycobacterium* due to acid-fast staining results (5).

The first case humans was reported in 1967 when *R. hoagii* was isolated in cultures from a farmer with cavitary pneumonia on immunosuppressive treatment due to autoimmune hepatitis (14). The cultures revealed pleomorphic, Gram-positive coccobacilli, identified as *R. hoagii*. All symptoms cleared up after 8 weeks of treatment with erythromycin. After a period of 6 weeks, the patient developed a subcutaneous abscess, exhibiting *R. hoagii* in cultures samples. The patient was treated with erythromycin for an additional 6 weeks and had no more recurrences (14).

Although *R. hoagii* is considered an uncommon pathogen for humans, currently, the number of cases reported in the literature has significantly increased due to the increasing

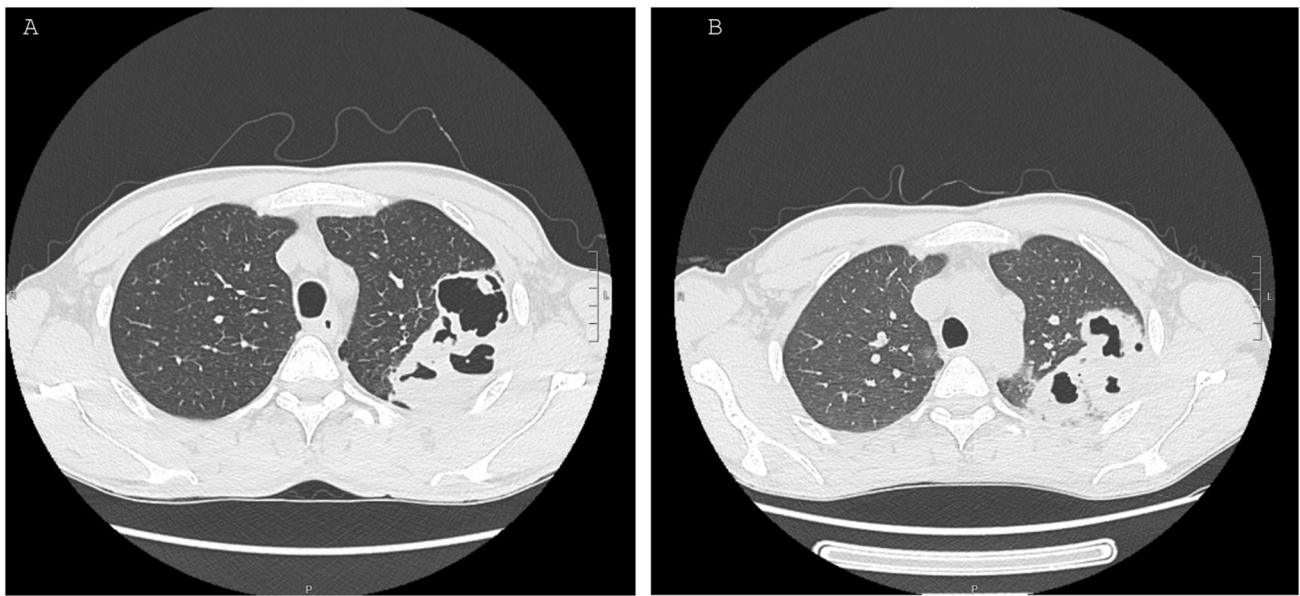


Figure 1. (A and B) Thoracic computed tomography scans showing consolidative lesion with central cavitation localized to the upper-dorsal segment of the left upper lobe.

presence of immunocompromised individuals, even though infection has also been described less commonly in immunocompetent hosts (15-18). Deficiencies in cell-mediated immunity constitute the main predisposing factor for infection by this intracellular germ (19).

Considering that two thirds of patients with *R. hoagii* infection are HIV-positive, HIV infection is considered the main favoring condition, particularly when considering patients who are late presenters, those with AIDS and co-infections (21,22). The patient in the present study was a late presenter with a very low CD4 count.

Other risk factors include solid organ and stem cell transplant patients, leukemia, lymphoma, lung cancer and, following chemotherapy, monoclonal antibodies, or the prolonged use of steroids (23).

The mortality rate among immunocompetent patients is ~11%, compared with rates of 50-55% among HIV-infected patients and 20-25% among non-HIV-infected immunocompromised patients (18,24).

Pulmonary manifestations are typical, with infiltrates and cavitary lesions (25). Bacteremia may give rise to localizations in other organs, such as gastrointestinal infections, pericarditis, meningitis, mastoiditis, liver and kidney abscesses and skin infections. The disease is commonly chronic and recurrent. Relapse may follow an inadequately short course of antimicrobial therapy (26). Although the patient reported herein had pulmonary manifestations, these were caused by NTM rather than *R. hoagii*.

To the best of our knowledge, to date, no standardized therapy has yet been established for the treatment of *R. hoagii* infections, and there are no defined susceptibility interpretation criteria for *R. hoagii* in the guidelines provided by the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (27). Consequently, susceptibility assessments for *R. hoagii* are frequently based on extrapolations from other species and pathogens, such as *Staphylococcus aureus* (28).

Numerous anti-microbials exhibit activity against *R. hoagii* when tested *in vitro*; however, their effectiveness in clinical settings is often undermined due to various factors. These include poor penetration into cells, diminished oral bioavailability, suboptimal pharmacokinetics in the lungs, adverse effects on foals, or the absence of randomized controlled trials (29). Additionally, both intrinsic and acquired resistance, further exacerbated by a mycolic acid-rich cell envelope, such as those found in *Mycobacterium* and other actinomycetes, can lead to erratic drug susceptibility. This has been observed with drugs such as chloramphenicol, β -lactams, and quinolones (30,31).

R. hoagii is usually susceptible *in vitro* to macrolides, rifampicin, fluoroquinolones, aminoglycosides, glycopeptides and imipenem. Susceptibility to cotrimoxazole, tetracycline, chloramphenicol, clindamycin and cephalosporins is variable. Isolates are typically resistant to penicillin, and the use of penicillin is not recommended (32). A combination of antibiotics may be used: One with intracellular activity (e.g., macrolides) and one with much bactericidal activity (e.g., rifampicin or vancomycin) (32). In the case described herein, NTM therapy included *R. hoagii* treatment to avoid the use of too many drugs, opting for a combination of azithromycin plus rifampicin.

Regimens that include >2 drugs have been successful for some patients; however, to date, to the best of our knowledge, no data are available to indicate that they are superior (32). Patients with CNS infection should receive agents with good penetration of the blood-brain barrier.

The duration of therapy is dependent on the site and extent of infection. A minimum of 6 months of antibiotic therapy is typically required for immunocompromised patients with pulmonary, bone and joint, or CNS infections. Intravenous therapy could be replaced with oral therapy when the patient's condition is suitable, and cultures are negative (5).

In HIV-infected individuals, the lack of antiretroviral therapy was an important predictor of mortality from *R. hoagii* infection. In fact, non-compliance with antiretroviral therapy

has been shown to be associated with a worse performance of cell-mediated immunity predisposing to severe infections and cancer (33).

It has been reported that the risk of mortality from *R. hoagii* infection is 53-fold higher among untreated HIV-infected individuals than that among HIV-infected individuals receiving appropriate antiretroviral therapy (34). Effective ART is crucial in reducing mortality rates associated with *R. hoagii* infection in HIV-infected individuals. Non-compliance with ART significantly impairs immune recovery, predisposing patients to severe and recurrent infections (35).

Preventive measures to reduce the risk of *R. hoagii* infection should focus on biosecurity practices on farms, such as regular disinfection and proper management of animal waste to minimize soil contamination. For humans, particularly those in contact with farm animals, proper wound care and hygiene practices are crucial. Public health interventions may include educational campaigns to raise awareness about the risks and transmission routes of *R. hoagii* and promoting the use of protective equipment for farm workers (27,36).

Future research is required to focus on establishing standardized treatment guidelines and susceptibility testing criteria for *R. hoagii*. Additionally, studies on the efficacy of combination therapies and the impact of ART adherence on infection outcomes are required.

In conclusion, the present case report elucidates the clinical complexities and therapeutic management of a HIV late presenter patient, presenting with concurrent infections of *R. hoagii*, *M. intracellulare* and syphilis. His socioeconomic status as a homeless farm laborer underscores the necessity for clinicians to consider environmental and social factors when assessing symptomatic, immunocompromised patients. Key insights from this case include the critical need for comprehensive pathogen screening, the importance of an integrated treatment regimen combining antiretroviral therapy with targeted antibiotics, and the careful management of drug-drug interactions, particularly the adjustment of HIV treatment in response to rifampicin-induced enzyme induction. Furthermore, the failure of the patient to attend follow-up visits highlights the challenges of ensuring continued care and adherence to treatment among transient populations. The present case report emphasizes a multidisciplinary approach to care, proactive pharmacological planning, and robust follow-up strategies to improve long-term outcomes in similar clinical scenarios.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors' contributions

All authors (SP, AM, SSt, MG, VM, CG, SSp, BMC, BC and GN) contributed to the conception and design of the study. SP and AM conceptualized the study. SSt was involved in the diagnostic methodology. MG, VM, CG and SS were involved in the treatment/examination of the patient. SP and AM were involved in the writing and preparation of the original draft of the manuscript. BMC was involved in the writing, reviewing and editing of the manuscript. BC and GN supervised the study. All authors have read and agreed to the published version of the manuscript. BC and GN confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for his participation in the present study.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of his data and any related images.

Competing interests

The authors declare that they have no competing interests.

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