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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Rhodococcus equi infections in HIV late presenters – a case series and therapeutic challenges

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SUMMARY

Introduction *Rhodococcus equi* is a rare but clinically relevant opportunistic pathogen, primarily affecting individuals with compromised cellular immunity. In people living with HIV/AIDS, it typically manifests as severe pulmonary disease. The objective of this case series is to describe the clinical features, management, and outcomes of *Rhodococcus equi* infection in three men with advanced HIV/AIDS.

Outlines of cases We retrospectively analyzed three cases of *Rhodococcus equi* infection treated between 2004 and 2011 at the Clinic for Infectious and Tropical Diseases, University Clinical Center of Serbia, in Belgrade. All patients were men with CD4 counts below 50 cells/mL at the time of presentation. Clinical symptoms included prolonged fever, productive cough, weight loss, and malaise. Pulmonary involvement was universal, with radiological findings of necrotizing pneumonia or cavitary lung abscess. One patient developed cerebritis as an extrapulmonary manifestation. *Rhodococcus equi* was isolated from sputum in all three cases and from blood cultures in two cases. All patients required prolonged hospitalization and combination antibiotic therapy, including macrolides, carbapenems, rifampicin, and trimethoprim-sulfamethoxazole, with antiretroviral therapy introduction. Two patients achieved long-term clinical stability, while one had persistently low CD4 count and detectable viral load due to adherence issues.

Conclusion *Rhodococcus equi* in patients with advanced HIV/AIDS may cause severe pulmonary or disseminated disease. Early recognition, tailored antimicrobial regimens, and careful timing of antiretroviral therapy initiation are critical to improve outcomes in this population.

Keywords: *Rhodococcus equi*; HIV; AIDS; opportunistic infections; pulmonary infection; antimicrobial therapy

INTRODUCTION

Rhodococcus equi is an aerobic, Gram-positive, partially acid-fast, non-spore-forming, facultatively intracellular, pleomorphic coccobacillus which was previously classified within the genus *Corynebacterium* [1]. Originally described as a veterinary pathogen in foals in the 1920s, *Rhodococcus equi* has since been identified in a variety of environmental reservoirs and has been implicated in zoonotic transmission [2]. Human infections are rare but have been increasingly reported among immunocompromised individuals with the capacity of causing life-threatening conditions [1]. This pathogen was reported in human for the first time in 1967, but since then has gained wider recognition during HIV/AIDS epidemics in 1980s, primarily due to its pulmonary manifestations in patients with advanced immunosuppression [3]. In people living with HIV/AIDS, *Rhodococcus equi* typically presents as a subacute or chronic pulmonary infection, often mimicking tuberculosis (TB) or *Nocardia spp*, with radiological findings that include cavitary lesions, consolidations, and abscess formation [3]. In immunocompromised hosts, pulmonary involvement occurs in up to 95% of cases, while extrapulmonary dissemination – including central nervous system (CNS) and soft tissue involvement – can occur via hematogenous spread [4]. The organism's ability to survive and replicate within macrophages contributes to its pathogenicity and complicates treatment, often requiring prolonged multidrug regimens [2]. The diagnosis is frequently delayed due to the slow growth of the organism in cultures and resemblance to diphteroids on Gram stain which is sometimes dismissed as commensal flora and leads to misidentification, contributing to underdiagnosis [3]. Moreover, treatment guidelines were developed in the pre-ART era and still pose challenges due to intrinsic resistance to many antibiotics, lack of standard regimens, and complex interactions with antiretroviral therapy (ART) [3].

CASE REPORTS

In this case series, we describe three male individuals living with HIV and advanced immunodeficiency who developed *Rhodococcus equi* infections between 2004 and 2011. We highlight their clinical presentations, microbiological findings, therapeutic management, and complications – including immune reconstitution inflammatory syndrome (IRIS) and neurologic involvement – as well as long-term outcomes. These cases emphasize the importance

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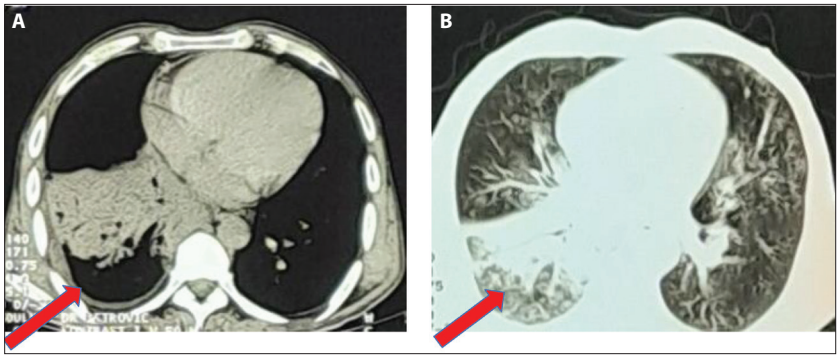

Figure 1. Case 1;
thoracic computed tomography scan: (A, B) – approximately 3 cm below the tracheal bifurcation, posteriorly on the right, involving the posterior half of the right hemithorax – an irregular, infiltrative mass with heterogeneous structure and central necrosis; in the posterior caudal supradiaphragmatic region, the pleural space is filled with fluid

Table 1. Antibiotic susceptibility testing results

Antibiotic	Case 1 Sputum	Case 1 Blood (sterile)	Case 2 Sputum	Case 2 Blood	Case 3 Sputum	Case 3 Blood
Penicillin G	R	-	R	R	R	R
Ampicillin	R	-	-	-	R	R
Amoxicillin	R	-	-	-	R	R
Amox + β-lactamase inhibitor	R	-	-	-	-	-
Piperacillin	R	-	-	R	R	R
Piperacillin-tazobactam	-	-	-	-	-	R
Cefotaxime	R	-	R	R	R	R
Ceftazidime	R	-	R	-	R	R
Cefepime	R	-	-	-	-	R
Ceftriaxone	R	-	S	S	R	R
Cefuroxime	-	-	-	R	-	-
Cefaclor	-	-	-	-	R	R
Meropenem	S	-	S	S	S	S
Imipenem	S	-	S	S	S	S
Erythromycin	S	-	S	S	S	S
Azithromycin	R	-	-	-	-	-
Clindamycin	-	-	S	R	R	R
Chloramphenicol	S	-	-	-	S	S
Vancomycin	S	-	S	S	S	S
Ciprofloxacin	S	-	S	S	S	S
Gentamicin	-	-	-	-	S	S
Amikacin	R	-	S	R	S	S
Trimethoprim-Sulfamethoxazole	R	-	S	R	S	S
Rifampicin	R	-	S	R	S	S

S – susceptible; R – resistant; - – not tested or not reported; sample types: sputum – respiratory sample; blood – blood culture result

of early recognition, tailored antimicrobial strategies, and careful timing of ART initiation in the management of *Rhodococcus equi* infections in people living with HIV.

Case 1

A 40-year-old male was diagnosed with HIV in 1994 but did not seek medical care or initiate ART until 2004, when he presented with advanced immunosuppression: CD4 cell count was cells/mm^3, viral load unavailable), reporting 12-week-long symptoms of progressive weight loss, dysphagia, productive cough, and malaise. Physical examination revealed oropharyngeal candidiasis, generalized lymphadenopathy, bilateral basal crackles, splenomegaly, seborrheic dermatitis, and hairy leukoplakia. Thoracic computed tomography (CT) scan demonstrated necrotizing pneumonia in the posterior right hemithorax (Figure 1). *Rhodococcus equi* was isolated from sputum (growth at 4–6 days) while blood cultures remained sterile (Table 1). The patient was hospitalized twice. During the first hospitalization (21 days), he received erythromycin, ciprofloxacin, trimethoprim-sulfamethoxazole, and terbinafine, resulting in partial pneumonia resolution. He was discharged afebrile and clinically stable, but ART was not initiated due to unresolved insurance status. Twenty days later, ART was started. After 15 days, the patient developed fever, respiratory symptoms, and fatigue, requiring a second hospitalization. He received dual macrolide–fluoroquinolone therapy for 53 days, with gradual improvement. Pulmonary TB was excluded, ART was temporarily interrupted and later resumed, and IRIS was suspected but not confirmed. The patient was discharged in good clinical condition. At follow-up, he remained alive, with CD4 count of 190 and suppressed viral load at the most recent check-up in 2024. The patient resided in an urban area and reported no known occupational or environmental exposure risks, nor any contact with domestic or farm animals.

Case 2

A 43-year-old male was diagnosed with HIV and *Rhodococcus equi infection* concurrently in 2004. At presentation, he was ART-naïve with profound immunosuppression (CD4: 4 cells/mm^3, viral load not available). He reported 12-week-long history of fever higher than 38°C, hemoptysis, weight loss, and malaise. Clinical examination revealed hepatomegaly and tachycardia. Imaging revealed right-sided pulmonary infiltrates. *Rhodococcus equi* was isolated both from blood cultures and sputum (Table 1). During hospitalization, the patient developed sudden-onset right-sided hemiparesis.

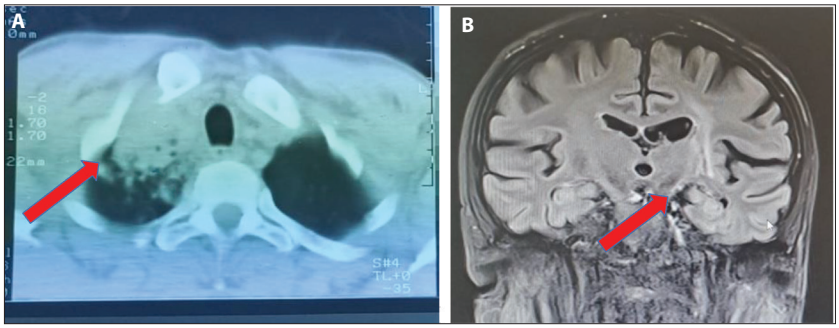

Figure 2. Case 2;
A – thoracic computed tomography: right-sided pulmonary infiltrates; B – brain magnetic resonance imaging (MRI): coronal T2-weighted fluid-attenuated inversion recovery MRI showing a hyperintense lesion in the left basal ganglia, consistent with cerebritis

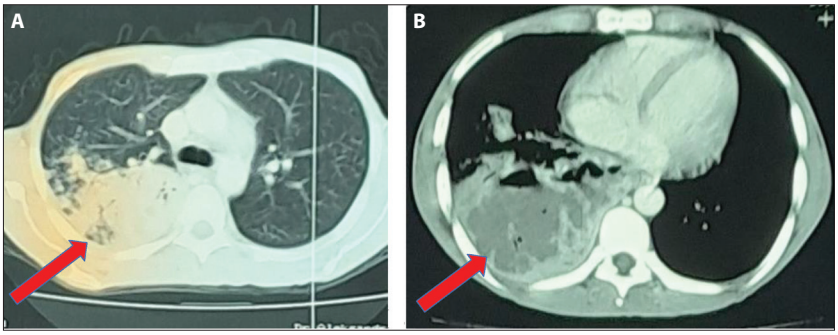

Figure 3. Case 3;
thoracic computed tomography: (A, B) – the entire lower lobe of the right lung is occupied by a large liquefied lesion containing air, measuring approximately 10 × 20 cm in cross-section – a lung abscess; a small pleural effusion is visible in the right basal pleura

Brain magnetic resonance imaging (MRI) revealed a T2-weighted imaging with a fluid-attenuated inversion recovery hyperintense lesion in the left basal ganglia, without mass effect, restricted diffusion, or contrast enhancement, findings consistent with cerebritis, presumed to result from septic embolic dissemination of *Rhodococcus equi*. Initial antimicrobial therapy consisted of erythromycin, rifampicin, and trimethoprim-sulfamethoxazole for 30 days, with modifications according to clinical response and susceptibility. ART was initiated during hospitalization. Lumbar puncture revealed normal cerebrospinal fluid (CSF) findings, and *Rhodococcus equi* was not isolated from CSF. A follow-up brain MRI was not performed, as the patient achieved complete neurological recovery without sequelae**.** At follow-up, viral load remains undetectable, and the latest CD4 count was 348 cells/mm^3. Considering socio-epidemiological data, patient resided in an urban area and reported no occupational or environmental exposure risks, although had regular contact with domestic animals (poultry, swine, cats, dogs).

Case 3

A 32-year-old male was diagnosed with HIV in 2003 and initiated ART which he discontinued in 2008. In 2011, he was presented at our Clinic due to eight weeks of progressive cough, dyspnea, diarrhea, weight loss, and fever up to 39°C. At that moment, CD4 count was 5 cells/mm^3, and HIV viral load was 138,531 copies/mL. Examination revealed tachycardia, hepatosplenomegaly, and crepitations in the right thorax. Chest CT revealed complete involvement of the lower lobe of the right lung with a massive cavitating abscess (10 × 20 cm), consistent with necrotizing infection, with air-fluid levels and associated right pleural effusion. Bilateral zones of consolidation were noted in the middle right lobe and left lingula. Both sputum and blood cultures yielded *Rhodococcus equi* (Table 1). Time to culture positivity was three days from sputum and six days from blood. Initial empiric antibiotics were escalated over time due to lack of response and complications, ultimately including meropenem, imipenem, rifampicin, trimethoprim-sulfamethoxazole, amikacin, tigecycline, and metronidazole, alongside intravenous immunoglobulins. ART was reinitiated during hospitalization, and the total duration of antibiotic therapy was 85 days. The patient required pleural drainage for two months. A pleural pneumothorax and subcutaneous emphysema developed following active drainage, complicated by secondary infection with *Pseudomonas aeruginosa* and *Klebsiella spp.* Despite multiple complications, the patient fully recovered after three months of hospitalization. The latest follow-up in 2024 showed CD4 51 cells/mm^3 and viral load was 15,500 copies/mL, emphasizing adherence issues. Similar to Case 1, the patient denied any contact with animals or known environmental exposure associated with *Rhodococcus equi* infection.

Ethics: This study was performed in line with the principles of the Declaration of Helsinki and good clinical practice. Approval was granted by the patients who signed an informed consent for participation in this case report series. Signed form available upon request.

DISCUSSION

Here we present three cases of *Rhodococcus equi* infection in people living with HIV/AIDS with severe immunosuppression, treated at the Clinic for Infectious and Tropical Diseases, University Clinical Centre of Serbia in Belgrade, between 2004 and 2011. All three are men; the youngest is 33 and the oldest is 43, all Caucasian from Serbia. Without other significant comorbidities, they have in common that they had terminal immunodeficiency caused by HIV at the time of clinical presentation in our clinic. Other data in the literature also show that *Rhodococcus equi* manifests in the stage of advanced immunodeficiency in people

living with HIV/AIDS and that it is most common in men [5]. Several case series, including an extensive review by Yamshchikov et al. [6], have shown a higher incidence of *Rhodococcus equi* infections in males, especially in people living with HIV and transplant recipients. To our knowledge, no study has systematically examined the potential behavioral, biological, or healthcare-related factors that could impact this sex distribution. Epidemiological data are significant because they relate to contact with animals that serve as the natural reservoir for *Rhodococcus equi* [7, 8]. Except for one, the other two of our patients did not have a clear epidemiological risk when it comes to contact with domestic/wild animals, occupational risk, or living in a rural environment. Regarding the clinical presentation, in addition to AIDS-indicative conditions such as oral candidiasis, seborrheic dermatitis, and oral hairy leucoplakia, our patients exhibited severe pulmonary involvement: one developed necrotizing pneumonia with pleural effusion, another presented with a lung abscess, and one patient experienced an extrapulmonary neurological manifestation of *Rhodococcus equi* infection. The most common manifestations of *Rhodococcus equi* in patients with AIDS, as described in the literature, are pulmonary [5]. Radiographic findings in our three patients – necrotizing pneumonia with pleural effusion, with/or cavitation and abscess – are consistent with common radiological features of *Rhodococcus equi* pulmonary infection in people living with HIV, as reported in the literature [5]. Although rare, extrapulmonary manifestations of *Rhodococcus equi* in humans can be very divergent, and various organ and tissue involvement has been reported in the literature, such as osteomyelitis, pericarditis, brain abscesses, spleen, kidney and liver abscesses, mesenteric lymphadenitis and colitis, among others [4, 5]. One of the patients presented in our paper had cerebritis as an extrapulmonary manifestation of *Rhodococcus equi* infection. As far as neurological manifestations of *Rhodococcus equi* infection are concerned, they are rare, with only a few cases described in the literature to date, including purulent meningitis and brain abscess [4]. The differential diagnosis in such cases is broad, covering cerebral toxoplasmosis, tuberculous or pyogenic abscess, cryptococcal or cytomegalovirus encephalitis, progressive multifocal leukoencephalopathy (PML), primary CNS lymphoma, neurosyphilis, and bacterial cerebritis. A prospective study by Sawardekar et al. [9] with 150 HIV-positive patients demonstrating CNS space-occupying lesions demonstrated that the most prevalent etiologies were tuberculomas (29.3%), toxoplasmosis (22.7%), PML (17.3%), primary CNS lymphoma (15.3%), and brain abscess (10%). The findings correspond with broader clinical experience and are supported by a review by Sheybani et al. [10], emphasizing the necessity of timely imaging and empirical therapy due to the overlapping presentations of CNS infections among people living with HIV. In such situations, empiric antimicrobial and antiparasitic therapy with adequate CNS penetration is typically necessary until a definitive diagnosis is confirmed.

IRIS can be unmasking and paradoxical and can develop during the initial period of antiretroviral treatment more often in deeply immunosuppressed individuals. Typical IRIS diagnoses include TB, cryptococcosis, and PML but practically any opportunistic infection can manifest in the context of IRIS. To the best of our knowledge, there have been no reports of *Rhodococcus* infection in the context of IRIS, as described in one of our patients.

Isolation of *Rhodococcus equi* in our three patients was predominantly based on sputum samples and blood cultures. Depending on the clinical manifestations, cultivation of samples from bronchoscopy, CSF, pleural punctate, ascitic fluid, as well as abscess aspirates, is also considered [11].

The antibiotic treatment for the patients presented in this paper consisted of trimethoprim-sulfamethoxazole, macrolides, rifampicin and carbapenems, following initial use of antimicrobial agents from other antibiotic classes. The reason for polypharmacy in these cases was mainly the use of initial empiric antibiotic therapy for patients with severe pulmonary manifestations of AIDS, which was subsequently adjusted based on culture and susceptibility results (antibiogram). *Rhodococcus equi* can show resistance to various antibiotics and can develop resistance during treatment with only one drug [2]. To date, multiple case reports and case series of *Rhodococcus equi* infection in people living with HIV/AIDS have been published, describing various antibiotic regimens used in the therapeutic approach [11].

The optimal drug regimen and duration of treatment for *Rhodococcus equi* pneumonia have not been clearly defined. For now, recommendations are usually based on two-drug regimens, according to susceptibility testing. Recommended choices usually include vancomycin, meropenem, imipenem, macrolides, rifampicin, and levofloxacin [11]. Ranganath et al. [3] reported over 95% susceptibility of *Rhodococcus equi* to imipenem, vancomycin, linezolid, rifampin, and clarithromycin. The majority of patients described in their paper received two- or three-drug combination therapy for 2–6 months with favorable clinical response, and they concluded that imipenem and vancomycin remain appropriate empiric treatment options for *Rhodococcus equi*. [3]. Torres-Tortosa et al. [12] reported susceptibility rates of *Rhodococcus equi* as high as 100% for vancomycin and amikacin, followed by 97.9% and 97.6% for rifampicin and imipenem, respectively. Less than half of isolates of *Rhodococcus equi* in the same study (44.7%) were susceptible to trimethoprim-sulfamethoxasole (co-trimoxazole) [12]. Considering the small number of cases globally and the different geographic and clinical settings in which diagnosis and treatment are carried out, it is not surprising that a standard therapy for *Rhodococcus equi* has not yet been established. Judging by the data from the literature, a clearly defined consensus has not yet been reached regarding the recommended antibiotic therapy for *Rhodococcus equi* infection, nor its duration. Prolonged use of combination antibiotic therapy, particularly regimens containing macrolides, fluoroquinolones, and rifampicin, has been associated with hepatotoxicity, QT interval prolongation, and gastrointestinal complications [13]. Among these, *Clostridioides difficile* infection (CDI) represents a

significant concern, especially in immunocompromised patients. A recent systematic review noted antibiotic exposure as the primary risk factor for CDI in diverse populations [14]. This potential complication requires awareness during extended treatment, particularly in immunocompromised individuals. In addition, rifampicin is a potent inducer of cytochrome P450 enzymes and can reduce plasma levels of several antiretroviral agents, including non-nucleoside reverse transcriptase and integrase inhibitors [15]. Adjustments to ART may therefore be necessary during concomitant use.

Rhodococcus equi is an emerging human pathogen, especially in immunocompromised individuals. Our cases complement existing literature data on *Rhodococcus equi* infections in people living with HIV, highlighting the importance of early recognition, tailored antimicrobial strategies, careful timing of ART initiation, as well as the need for standardized antibiotic therapy guidelines. Clinicians should take precautions regarding the diagnosis and treatment of *Rhodococcus equi* in people living with HIV, considering it can be clinically similar to other opportunistic infections and can be susceptible to some antimicrobial agents that are often used as first-line options in those with AIDS but often for a shorter course than what is required for successful treatment of *Rhodococcus equi*.

Conflict of interest: None declared.

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Инфекције изазване *Rhodococcus equi* код касних презентера са ХИВ инфекцијом – прикази болесникâ и терапијски изазови

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САЖЕТАК

Увод *Rhodococcus equi* је редак али клинички значајан опортунистички патоген који се првенствено јавља код особа са компромитованим ћелијским имунитетом. Код особа које живе са ХИВ-ом/сидом, *Rhodococcus equi* обично изазива тешке инфекције плућа. Циљ овог рада је да прикаже клиничке карактеристике, терапијске приступе и исходе инфекције изазване *Rhodococcus equi* код тројице мушкараца са узнапредовалом ХИВ инфекцијом.

Приказ болесникâ Ретроспективно су анализирана три случаја инфекције *Rhodococcus equi*, лечена у периоду од 2004. до 2011. године на Клиници за инфективне и тропске болести Универзитетског клиничког центра Србије у Београду. Сви пацијенти били су мушкарци, са бројем *CD4* ћелија испод 50/*μL* у тренутку пријема. Доминантне клиничке манифестације укључивале су продужену фебрилност, продуктиван кашаљ, губитак телесне масе и изражену малаксалост. Код свих је инфекција имала тешку плућну презентацију, уз радиолошке налазе типичне за некротизујућу пнеумонију или кавитационе апсцесе. Код једног пацијента регистрована је и екстрапулмонална манифестација у виду церебритиса. *Rhodococcus equi* је изолован из спутума код сва три пацијента, а из хемокултуре код два. Лечење је захтевало продужену хоспитализацију и комбиновану антимикробну терапију, укључујући макролиде, карбапенеме, рифампицин и триметоприм-сулфаметоксазол, уз антиретровирусну терапију. Два пацијента су постигла дугорочну клиничку и имунолошку стабилност, док је код једног забележен трајан пад *CD4* ћелија и перзистентна виремија услед лоше адхеренције на антиретровирусну терапију.

Закључак Инфекција изазвана *Rhodococcus equi* код особа са узнапредовалом ХИВ инфекцијом може довести до тешке плућне и дисеминоване болести. Рано препознавање, адекватна антимикробна терапија и правовремено започињање антиретровирусне терапије кључни су за повољан исход.

Кључне речи: *Rhodococcus equi*; ХИВ; сида; опортунистичке инфекције; плућна инфекција; антимикробна терапија