

A Rare Case of Coinfection of *Rhodococcus equi* and *Nocardia abscessus* in an Immunocompetent Human Host

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Background: *Rhodococcus* and *Nocardia spp.* are aerobic, gram-positive bacteria distributed extensively in the sediment of various environments globally. They usually manifest as opportunistic infections in immunocompromised hosts. Here, we report a coinfection case of *Rhodococcus* and *Nocardia spp.* in a patient with normal immune system.

Case Presentation: We present a case of a 52-year-old healthy man who sustained right hand injury at work. The patient exhibited post-traumatic infection. The skin of the right palm was swollen with acute pain, and active flexion and extension of his fingers were limited. Ultrasound scanning of the dorsolateral aspect of the right hand showed an uneven echogenic area of about 3.5 cm × 1.3 cm × 0.9 cm in the deep surface of the extensor muscles between the 4th and 5th metacarpals. The patient underwent right hand debridement and negative pressure suction under brachial plexus anesthesia. After bacterial cultures of the pus and necrotic tissues, *Rhodococcus equi* and *Nocardia abscessus* were determined using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF/MS) (Zybio, China). Treatment with a combination of levofloxacin and sulfamethoxazole led to a favorable clinical outcome.

Conclusion: This report highlights the necessity and urgency of precise species identification, providing a critical guide for physicians in the choice of targeted treatment.

Keywords: *Rhodococcus equi*, *Nocardia abscessus*, abscess, immunocompetent, mixed infection

Introduction

Rhodococcus equi, previously known as *Corynebacterium equi*, is a gram-positive, aerobic, intracellular, nonmotile, and weakly acid-fast coccobacillus that belongs to the genus *Rhodococcus* within the *Nocardiaceae* family.¹ *R. equi*, an emerging zoonotic pathogen, was first reported in 1967 as a human pathogen.² It mainly presents with pulmonary diseases, such as necrotizing pneumonia and lung abscesses,³ but can also involve extrapulmonary organs, such as brain abscesses.⁴ *R. equi* can cause rare, potentially fatal diseases, predominantly affecting patients who are immunocompromised⁵ and has been reported in patients with competent immune systems as well.⁶

Nocardia spp. are aerobic, branched, gram-positive bacteria with partial acid tolerance that are frequently isolated from soil and typically cause opportunistic infections in immunocompromised hosts. However, multiple case reports have demonstrated that *Nocardia spp.* cause various forms of disease in immunocompetent patients as well, such as pulmonary,⁷ lymphocutaneous,⁸ pyomyositis,⁹ and brain abscesses.¹⁰ Thirteen species of *Nocardia*, including *Nocardia abscessus*, *Nocardia farcinica*, *Nocardia brasiliensis*, *Nocardia asteroides*, and *Nocardia otitidiscaviarum* are the most common causes of human infections.¹¹

Here, a coinfection of *R. equi* and *N. abscessus* is described in a Chinese man who presented immunocompetence as well as the treatment therapy used. This report is rare of its kind.

Case Presentation

Clinical Features

A 52-year-old man was presented to our hospital due to trauma with pain and swelling of the right hand and that symptoms got worse over the past 10 days. The patient accidentally injured his hand using a hydraulic press at work 10 days ago. He experienced sharp pain, and a small amount of hydraulic oil was squeezed from his right palm. Without any special treatment, the skin of the right palm was swollen with acute pain, and active flexion and extension of his fingers were limited. When the patient arrived, physical examination and medical history examination were performed, with no history of hypertension, diabetes mellitus, food and drug allergies, and the abdomen was soft. The patient's temperature was 37.2°C. A sinus was observed between the 4th and 5th metacarpal bones of the right palm, and the skin of the right hand showed obvious swelling with a high temperature. Pressure pain around the sinus opening was apparent, the 3–5 fingers of the right hand were limited in active flexion and extension due to pain, and the distal end of the affected limb had good peripheral blood flow but was slightly numb (Figure 1A).

Abnormal elevation of white blood cell (WBC) count (15.73×10^9 cells/L) with 78% neutrophils and C-reactive protein (CRP) (52.78 mg/L) was indicated by blood routine examination. The clinical and laboratory findings are summarized in Table 1.

Imaging Examination

Ultrasound scanning of the dorsolateral aspect of the right hand showed an uneven echogenic area of about 3.5 cm × 1.3 cm × 0.9 cm in the deep surface of the extensor muscles between the 4th and 5th metacarpals, with blurred borders, speckles of strong echoes and small patches of fluid echoes and the pressurized probe could be flowed, indicating that it was abscess (Figure 1B).

Debridement

The patient underwent right hand debridement and negative pressure suction under brachial plexus anesthesia. A longitudinal incision was made between the 4th and 5th metacarpals on the back of the right hand, and the skin and subcutaneous tissues were incised sequentially. A large amount of purulent discharge and necrotic tissue was detected, and the interosseous muscles were involved. The dorsal purulent secretion and necrotic tissue were completely removed.



Figure 1 (A) A sinus was observed between the 4th and 5th metacarpal bones of the right palm. (B) Imaging examination. Ultrasound scanning of the dorsolateral aspect of the right hand showed an uneven echogenic area of about 3.5 cm × 1.3 cm × 0.9 cm in the deep surface of the extensor muscles between the 4th and 5th metacarpals.

Table 1 Clinical and Laboratory Variables of the Patient

Laboratory Indicators	Measurements	Normal Value	Clinical Indicators	Measurements
WBC ($10^9/L$)	15.73	4-10	Temperature ($^{\circ}C$)	37.2
NEU# ($10^9/L$)	12.28	2-7.5	Blood pressure (mmHg)	150/90
LYM# ($10^9/L$)	2.04	0.80–4.00	Heart rate	104
MON# ($10^9/L$)	1.32	0.1-1	Respiratory rate	18
RBC ($10^{12}/L$)	4.91	4-5.5		
HGB (g/L)	146	120-160		
PLT ($10^9/L$)	221	100-300		
CRP (mg/L)	34.66	0-10		
ESR (mm/h)	7	≤ 20		
PT (sec)	10.8	10-14		
APTT (sec)	28.1	25-43		
D-Dimer	2.0	0-15		
HIVAg (S/CO)	0.212	0-1		
HIVAb (S/CO)	0.349	0-1		
ALT (U/L)	19	0-41		
AST (U/L)	16	0-40		
TP (g/L)	66.0	60-83		
UREA (mmol/L)	5.21	2.14–8.07		
CREA ($\mu\text{mol/L}$)	71	21-106		

A serrated incision was made between the 4th and 5th metacarpal bones of the right palm, and the skin and subcutaneous tissue were incised sequentially. A large amount of purulent discharge and necrotic tissue was detected, and the tendon sheath of the flexor tendon of the ring finger was involved. Thoroughly remove the purulent and necrotic tissue on the palmar side. Repeatedly flush the wound with large amounts of saline and dilute iodophor, thoroughly stop bleeding and then cover the wound with VAC dressing, external negative pressure suction and sterile dressing. Bacterial cultures of the purulent discharge and necrotic tissue were performed.

Etiological Examination

Specimens were handled and identified according to standard laboratory protocols. After the pus and necrotic tissues were cultured on the Columbia blood agar plate (BAP) at $37^{\circ}C$ for 3 days under aerobic conditions, two different forms of colonies could be seen (Figure 2A). Gram staining and acid-fast staining were performed on the creamy white, irregular, and wrinkled colonies, and the observation under the oil microscope showed that it was gram-positive rod and partially acid-fast, suggesting that it was likely to belong to *Nocardia spp.* (Figure 2B and C). The other yellowish and mucoid colonies were characterized as gram-positive cocci or coccobacillus (Figure 2D). The two forms of colonies were identified by Matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF MS) (Zybio, China) as *Nocardia abscessus* with a reliable score value of 2.26 (Figure 2E) and as *Rhodococcus equi* with a reliable score value of 2.08 (Figure 2F). The germ identification results were confirmed by 16S rRNA gene sequencing (Tsingke Co., Ltd., Beijing, China).

The minimal inhibitory concentration (MIC) of the isolated *N. abscessus* strain against amikacin, cefotaxime, and ceftriaxone was used in the Epsilonometer test (E-test) method, and the maximum zone of inhibition against amoxicillin-clavulanic acid, trimethoprim/sulfamethoxazole and minocycline were performed by Kirby–Bauer method (KB). Antibiotic susceptibility results of the *N. abscessus* were judged by the Clinical and Laboratory Standards Institute (CLSI) interpretive breakpoints. The isolated strain *N. abscessus* was sensitive to amikacin (Table 2). *R. equi* is a rare bacterium that lacks a standardized drug-sensitive breakpoint. Therefore, no antimicrobial susceptibility testing was performed.

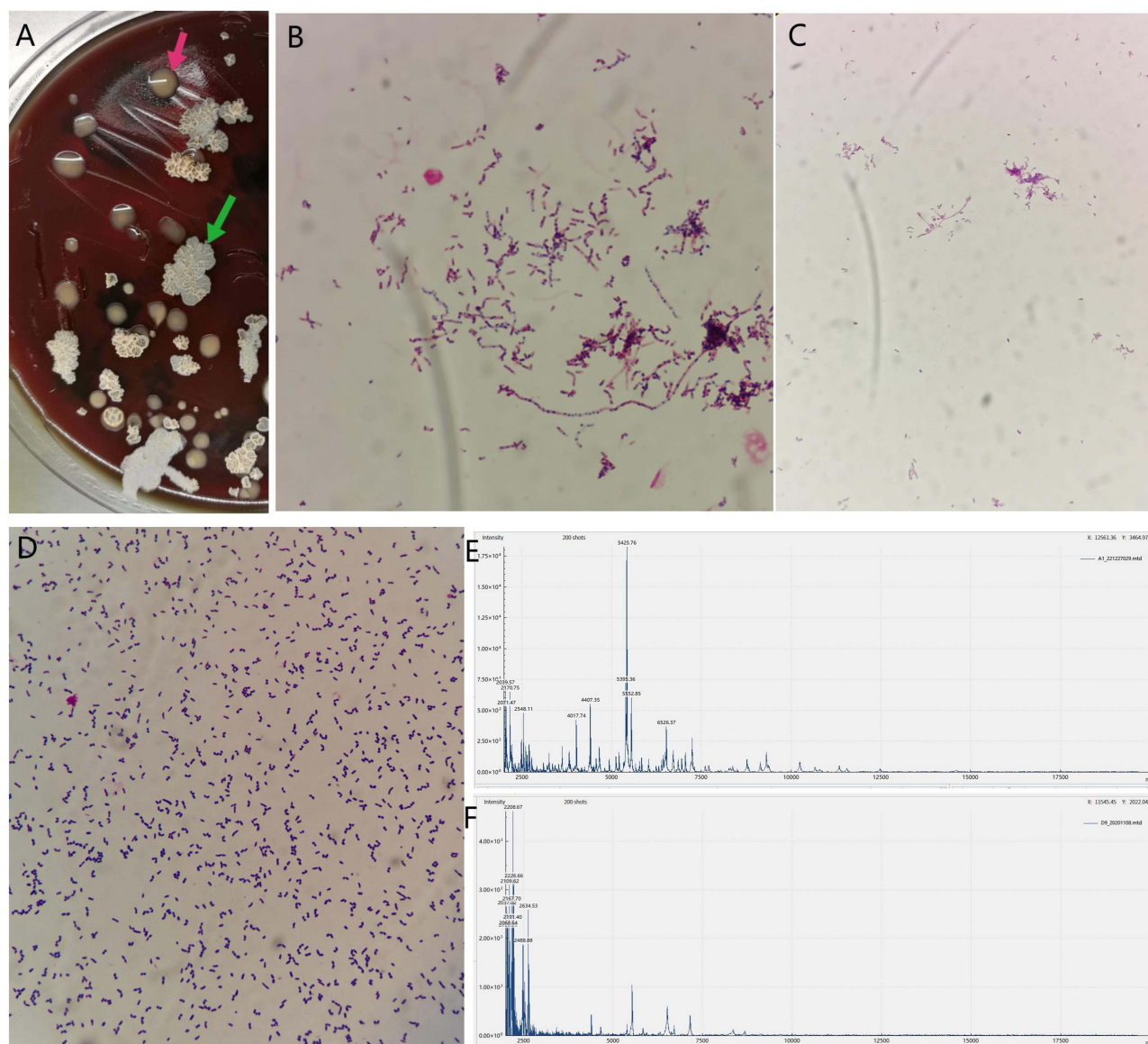


Figure 2 Pathogenic examination. (A) Two different forms of colonies were observed by culture on the blood plate. (B) The creamy white, irregular colonies indicated by the green arrow in Figure 2A showed gram-positive rod-shaped bacterium under oil mirror ($\times 1000$ magnification). (C) Acid fast staining showed weak positive mycelia, which proved that it was probably *Nocardia* spp. (D) The yellowish, mucoid colonies indicated by the red arrow in Figure 2A showed gram-positive cocci or coccobacillus bacterium under oil mirror ($\times 1000$ magnification). (E) Matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF MS) confirm the colony indicated by the green arrow in Figure 2A was *Nocardia abscessus*. (F) Matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF MS) confirm the colony indicated by the red arrow in Figure 2A was *Rhodococcus equi*.

Medication and Prognosis

When the patient arrived at our hospital, he was treated empirically with piperacillin/tazobactam sodium to prevent infection. Antibiotic use was adjusted after 4 days based on secretion culture results and antibiotic sensitivity, piperacillin/tazobactam sodium was discontinued, and levofloxacin (300 mg/day) and sulfamethoxazole (2 tablets q12h) were initiated. Approximately two weeks after the initiation of this treatment regimen, the patient's clinical symptoms improved significantly. The patient was discharged for oral sulfamethoxazole therapy and routine follow-up. Two weeks after discharge, the patient completed the medication regimen and was stable at outpatient follow-up with no evidence of infection.

Table 2 Antimicrobial Susceptibility of the *Nocardia abscessus* by Kirby–Bauer Method and Epsilometer Test

Antibiotics	Method	Result	Unit	Breakpoint	Interpretation
Amikacin	E-test	0.75	µg/mL	8-16	S
Cefotaxime	E-test	32	µg/mL	8-32	R
Ceftriaxone	E-test	32	µg/mL	8-32	R
Amoxicillin-clavulanic acid	KB	20	mm	-	-
Trimethoprim/sulfamethoxazole	KB	19	mm	-	-
Minocycline	KB	16	mm	-	-

Discussion

Rhodococcus and *Nocardia spp.* are aerobic, gram-positive bacteria that are found globally in soil, dust, and marine sediments. They usually manifest as opportunistic infections in immunocompromised hosts, especially those infected with HIV.¹ Our patient was deemed immunocompetent after a workup including HIV screening as well as testing for immunoglobulins and complement resulted as normal. The case presented here is the first report describing a rare *R. equi* and *N. abscessus* coinfection in a patient with normal immune system in China.

In humans, *R. equi* primarily invades the lungs, causing pneumonia and suppurative lesions. In addition, *R. equi* can also occur in extrapulmonary organs, such as the kidneys and brain, resulting in bronchitis, meningitis, bacteremia, and other diseases.¹² It is acquired through inhalation, ingestion, or inoculation of wounds.¹³ Currently, there is no standardized drug-sensitive breakpoint for *R. equi*. Because *R. equi* resides in cells, at least one antibiotic with good intracellular penetration is recommended.⁵ Rifampin, imipenem, vancomycin, ciprofloxacin, and erythromycin exhibit good antibiotic activity against *R. equi*.¹⁴

An increasing number of infections are caused by *Nocardia spp.*, but infections caused by *N. abscessus* are rare in humans. *N. abscessus*, previously known as *Nocardia asteroides* type 1, was first classified in 2000.¹⁵ *Nocardia cyriacigeorgica* and *Nocardia farcinica* are considered the main pathogenic species worldwide, while in China, *Nocardia asteroides* is commonly found.¹⁶ *Nocardia* is typically found in the environment, especially in the soil, decaying plants, and standing water. *Nocardia* can enter the human body through the respiratory tract or skin wounds, causing local infections and spreading to other organs through blood circulation.^{17,18} Our patient was likely exposed to a high burden of bacteria after injuring his hand by a hydraulic press, while a large number of bacteria entered the wound along with the hydraulic oil. Direct inoculation being is the source of bacteria entry. It is important to tailor the antibiotic therapy by identifying the species level of *Nocardia*, as the resistance profile can differ significantly across strains. *Nocardia* can be identified accurately using MALDI-TOF MS or 16S rRNA sequencing.^{19,20} MALDI-TOF MS is more commonly used than 16S rRNA sequencing because of its short time and ease of use. In this case, filamentous shapes were observed on gram staining and partially positive on modified acid-fast staining, which aided in the identification of *Nocardia*. Eventually, *Nocardia* species were identified accurately using MALDI-TOF MS. The results were confirmed using 16S rRNA gene sequencing. *N. abscessus* is generally susceptible to multiple antibiotics, including trimethoprim/sulfamethoxazole, ceftriaxone, amikacin, amoxicillin-clavulanic acid, and tigecycline. It demonstrates variable susceptibility to imipenem, minocycline, ciprofloxacin, moxifloxacin, and clarithromycin/azithromycin.²¹

The patient was treated with levofloxacin, which has excellent intracellular penetration, and sulfamethoxazole, which ultimately proved to be effective. The patient showed good results and recovered from the disease.

Conclusion

In conclusion, this is the first report of *R. equi* and *N. abscessus* coinfection in a patient with normal immune system in China. The *R. equi* and *N. abscessus* isolates were successfully identified by MALDI-TOF MS, which provided a new option for the identification of *R. equi* and *Nocardia*. After timely and appropriate anti-infection treatment, the patient's condition improved and was discharged. This case shows that precise species identity provides a critical guide for physicians in the choice of targeted treatment.

Ethics Approval and Consent to Participate

This case report was approved by the ethical review committee of Liaocheng Second People's Hospital. The patient's written informed consent was obtained for publications of all the images and case details. No institutional approval was required to publish the case details.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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