

Nocardia pseudobrasiliensis infection in a patient with arthritis

Journal of International Medical Research

2023, Vol. 51(12) 1–7

© The Author(s) 2023


Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/03000605231206959

journals.sagepub.com/home/imr



Youqi Ji^{1,2,*}, Mengyuan Chen^{1,3,*},
Xin Hong^{1,4,*}, Liya Pan⁵, Dongqing Cheng² and
Yumei Ge^{1,2,3,4,5,6} 

Abstract

Nocardia pseudobrasiliensis is a new taxon constituting an emerging species of human pathogenic *Nocardia*, which shares morphological features with *N. brasiliensis*. However, *N. pseudobrasiliensis* is more invasive and more easily disseminated, and it exhibits distinctive antibiotic susceptibility. Few clinical cases related to *N. pseudobrasiliensis* infection have been reported, and *N. pseudobrasiliensis* hydrarthrosis has not been described. Here, we analyzed the case information, diagnostic process, treatment, and prognosis of a patient with *N. pseudobrasiliensis* hydrarthrosis who received treatment in Zhejiang Provincial People's Hospital. Magnetic resonance imaging showed joint cavity effusion and soft tissue swelling with high signal on proton density-fat saturated images and low signal on T1-weighted images. Oil microscopy revealed abundant acid-fast-positive filaments in hydrarthrosis puncture fluid. The pathogen was identified as *N. pseudobrasiliensis* by matrix-assisted laser desorption ionization–time of flight mass spectrometry. In contrast to the 100% ciprofloxacin resistance displayed by *N. brasiliensis*, this clinical isolate of *N. pseudobrasiliensis* was completely susceptible. In summary, this is the first report of *N. pseudobrasiliensis* in joint effusion from a patient with arthritis.

¹Laboratory Medicine Center, Department of Clinical Laboratory, Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou Medical College, Hangzhou, Zhejiang, China

²School of Medical Technology and Information Engineering, Zhejiang Chinese Medical University, Hangzhou, Zhejiang, China

³The Second Clinical Medical College, Zhejiang Chinese Medical University, Hangzhou, Zhejiang, China

⁴Department of Green Pharmaceutical Collaborative Innovation Center, School of Pharmacy, Zhejiang University of Technology, Hangzhou, Zhejiang, China

⁵Center for Rehabilitation Medicine, Department of Radiology, Zhejiang Provincial People's Hospital (Affiliated People's Hospital, Hangzhou Medical College), Hangzhou, Zhejiang, China

⁶Key Laboratory of Biomarkers and In Vitro Diagnosis Translation of Zhejiang Province, Hangzhou, Zhejiang, China

*These authors contributed equally to this work.

Corresponding author:

Yumei Ge, Laboratory Medicine Center, Department of Clinical Laboratory, Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou Medical College, Hangzhou, Zhejiang 310014, China.
Email: 11218070@zju.edu.cn



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative

Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

Keywords

Nocardia pseudobrasiliensis, hydrarthrosis, arthritis, matrix-assisted laser desorption ionization–time of flight mass spectrometry, ciprofloxacin, anti-bacterial agent, joint effusion, prognosis, acid fast staining

Date received: 20 June 2023; accepted: 25 September 2023

Introduction

Nocardiosis, occurring primarily in immunocompromised patients, is a local or disseminated infection caused by obligate aerobic actinomycetes in the genus *Nocardia*.¹ This genus has undergone rapid taxonomic expansion, such that more than 100 subtypes and approximately 30 human pathogens have been identified thus far.^{2,3} *Nocardia pseudobrasiliensis* is a new taxon constituting an emerging species of human pathogenic *Nocardia*; it was genotypically characterized by Ruimy et al and previously considered a member of *Nocardia brasiliensis* based on its phenotype.⁴ Although *N. pseudobrasiliensis* shares morphological features with *N. brasiliensis*, it has nitrate reductase and adenine decomposition activities, which enable greater invasiveness and dissemination, along with distinctive antibiotic susceptibility.⁵ Thus far, fewer than 10 clinical cases related to *N. pseudobrasiliensis* infection have been reported; most reports have described *Nocardia* pneumonia, cutaneous nocardiosis, and disseminated nocardiosis.⁶ To our knowledge, there have been no reports of *N. pseudobrasiliensis* hydrarthrosis. Here, we describe a man in his 70s who presented with *N. pseudobrasiliensis*-induced left hydrarthrosis and a 7-year history of systemic lupus erythematosus (SLE).

Case presentation

Clinical features

This report was written in accordance with the CARE guidelines.⁷ A man in his early

70s experienced left hip pain without an apparent cause, numbness, or skin redness. Nearly 5 months later, he presented to a local hospital for redness and swelling in the left knee; he received injections of the antibiotics piperacillin sodium and tazobactam sodium, as well as oral treatment with the antiviral entecavir. One month later, the redness and pain in his knee had not improved. For further assessment, the patient was referred to Zhejiang Provincial People's Hospital. He reported a 7-year history of SLE characterized by abnormally low lymphocyte counts; he had taken prednisone 15 mg daily for more than 6 months, but he had not received other treatments. The patient's laboratory results suggested that he was a carrier of hepatitis B virus, and he had a history of recurrent oral ulcers. Otherwise, he had no other infectious diseases and no histories of surgery, trauma, allergies, or clinically significant family genetics. The patient had normal body temperature (37.1°C), normal respiration (18 breaths/minute), good mental status, soft abdomen, rough breath sounds in both lungs, no rales, no tenderness, and no rebound pain. Laboratory analysis showed increases in white blood cells ($12.68 \times 10^9/L$) and neutrophils (95.6%), along with decreases in lymphocytes (2.0%), monocytes (2.2%), hemoglobin (105 g/L), red blood cells ($3.43 \times 10^{12}/L$), and C-reactive protein (52.4 mg/L). Biochemical function tests revealed an increased ratio of urea nitrogen to creatinine (31.52), and routine urinalysis indicated the presence of urine protein (Table 1). Magnetic resonance imaging showed joint

Table 1. Clinical assessments and laboratory results.

Laboratory results	Measurements	Reference interval	Clinical assessments	Measurements
WBC	$12.68 \times 10^9/L$	$3.5-9.5 \times 10^9/L$	Blood pressure	157/87 mmHg
Lymphocytes	2.0%	20%–50%	Respiratory rate	18 breaths/min
Monocytes	2.2%	3%–10%	Heart rate	87 beats/min
Neutrophils	95.6%	40%–75%	Temperature	37.1°C
Eosinophils	$0.03 \times 10^9/L$	$0.02-0.52 \times 10^9/L$		
Basophils	$0 \times 10^9/L$	$0-0.06 \times 10^9/L$		
RBC	$3.43 \times 10^{12}/L$	$3.8-5.1 \times 10^{12}/L$		
Hemoglobin	105 g/L	115–150 g/L		
Platelets	$252 \times 10^9/L$	$125-350 \times 10^9/L$		
CRP	52.4 mg/L	<10 mg/L		
ESR	34 mm/h	<26 mm/h		
Urea nitrogen: creatinine	31.52	7.50–27.50		
Urine protein	+	–		
HBsAg	+	–		

WBC, white blood cell count; RBC, red blood cell count; C-reactive protein, CRP; ESR, erythrocyte sedimentation rate; HBsAg, hepatitis B surface antigen.

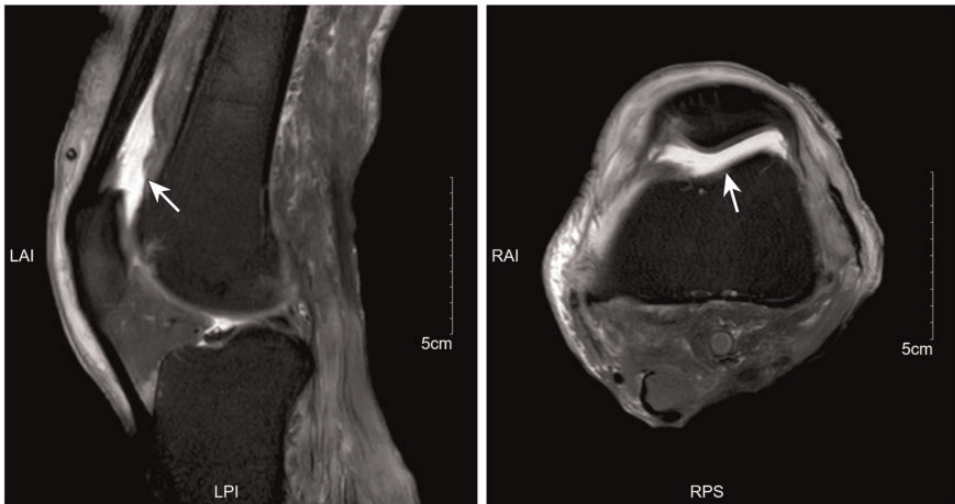


Figure 1. Magnetic resonance imaging showed joint cavity effusion and soft tissue swelling with low signal on T1-weighted images and high signal on proton density-fat saturated images (arrows). LAI, left anterior inferior; LPI, left posterior inferior; RAI, right anterior inferior; RPS, right posterior superior.

cavity effusion and soft tissue swelling with low signal on T1-weighted images and high signal on proton density-fat saturated images (Figure 1).

Etiological investigation

Acid-fast staining of hydrarthrosis puncture fluid was performed, and oil microscopy revealed red acid-fast-positive

filaments (Figure 2a). The pathogen was identified as *N. pseudobrasiliensis* via matrix-assisted laser desorption ionization–time of flight mass spectrometry (bioMérieux, France) (Figure 2b). The maximum zone of inhibition of the *N. pseudobrasiliensis* isolate, upon exposure to trimethoprim/sulfamethoxazole, was determined by the Kirby–Bauer method. The minimum inhibitory concentrations of amoxicillin/clavulanic acid, clindamycin, ciprofloxacin, imipenem, amikacin, linezolid, and levofloxacin against *N. pseudobrasiliensis* were determined by the Epsilon meter

test. The isolate was sensitive to all tested antibiotics, according to standard drug susceptibility assays.⁸ (Table 2)

Treatment and prognosis

The patient underwent debridement and drainage of the knee joint. A 1-cm incision was made at the front of the left knee. The inner side of the incision was repeatedly washed with normal saline using a 50-mL syringe; yellow pus was expelled, and two drainage tubes were placed. The wound was washed again with normal saline, the drainage tubes were sutured and fixed, and the

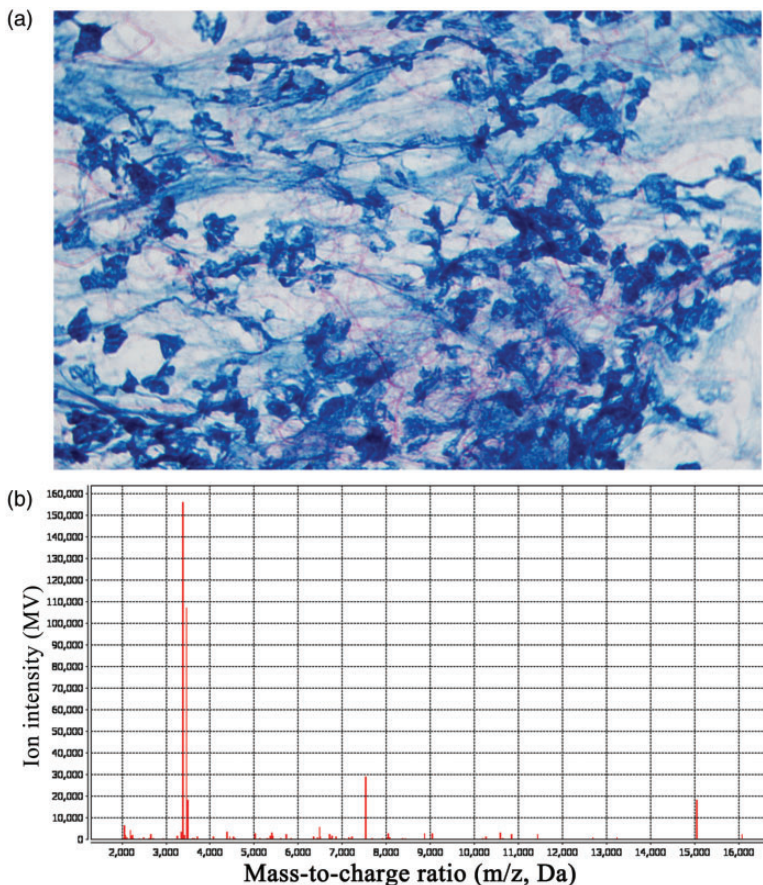


Figure 2. Pathology findings. (a) Oil microscopy revealed acid-fast–positive filaments in hydrarthrosis puncture fluid ($\times 1000$ magnification). (b) Matrix-assisted laser desorption ionization–time of flight mass spectrometry confirmed the presence of *Nocardia pseudobrasiliensis*. Da, Daltons; MV, megavolts.

Table 2. *Nocardia pseudobrasiliensis* antimicrobial susceptibility according to Kirby–Bauer method and Epsilon meter test.

Antibiotics	Method	Result	Breakpoint	Unit	Interpretation
Amoxicillin/clavulanic acid	E-test	4	8–32	µg/mL	S
Amikacin	E-test	1.5	16–64	µg/mL	S
Clindamycin	E-test	4	–	µg/mL	–
Ciprofloxacin	E-test	0.25	0.25–1	µg/mL	S
Imipenem	E-test	1	1–4	µg/mL	S
Linezolid	E-test	1	4–8	µg/mL	S
Levofloxacin	E-test	0.25	–	µg/mL	–
TMP-SMZ	KB	15	–	mm	–

E-test, Epsilon meter test; KB, Kirby–Bauer method; TMP-SMZ, trimethoprim/sulfamethoxazole.

wound was bandaged with compression. Antibiotic treatment was administered by intravenous infusion of amoxicillin sodium/clavulanate potassium (1.2 g, every 8 hours) and levofloxacin (100 mL, twice daily). The patient's symptoms were alleviated and he returned to the local hospital for subsequent treatment.

Discussion

Studies have shown that more than half of apparent *N. brasiliensis* isolates associated with pulmonary or disseminated infections belong to a new taxon known as *N. pseudobrasiliensis*^{4,9}; however, cases of *N. pseudobrasiliensis* infection are rare. *N. brasiliensis* is a common cause of opportunistic infection in immunocompromised patients, and its clinical presentation typically comprises cutaneous nocardiosis.^{10–13} However, according to published reports,^{14–21} *N. pseudobrasiliensis* has nitrate reductase and adenine decomposition activities, which lead to greater invasiveness and dissemination, as well as distinctive antibiotic susceptibility, compared with *N. brasiliensis*. *N. pseudobrasiliensis* can be distinguished from *N. brasiliensis* by 16S rRNA gene sequencing, adenine hydrolysis, and nitrate reductase analysis; however, these methods can be time-consuming, expensive, and inconvenient. Here, we obtained

accurate results by conducting aseptic culture of the patient's hydrarthrosis puncture fluid and subjecting colonies to matrix-assisted laser desorption ionization–time of flight mass spectrometry identification. Although this method has been used to identify *N. brasiliensis*, a more complete commercial database is needed for the identification of rare *Nocardia* spp.²² The *N. pseudobrasiliensis* isolate obtained in this case was susceptible to trimethoprim/sulfamethoxazole, amikacin, ciprofloxacin, clindamycin, imipenem, amoxicillin/clavulanic acid, linezolid, and levofloxacin. *N. brasiliensis* is resistant to ciprofloxacin^{3,5}; thus, ciprofloxacin can be used to control *N. pseudobrasiliensis* but not *N. brasiliensis*. Our patient had a 7-year history of SLE, and long-term use of the glucocorticoid prednisone presumably had increased the risk of *Nocardia* infection. Furthermore, the patient's arthritis symptoms indicated immunosuppression. Therefore, opportunistic pathogen monitoring should be performed in patients with immune disorders.

Currently, there are strict criteria for the diagnosis of SLE. The patient in this case had been diagnosed with SLE 7 years prior to his visit to our hospital, but he did not show characteristic symptoms of SLE during the course of *N. pseudobrasiliensis* infection; his symptoms solely comprised immune dysfunction. Therefore, we inferred

that the patient had previously met the criteria for a diagnosis of SLE. Nevertheless, *Nocardia* prevention and treatment efforts should be extended to all immunocompromised patients, rather than solely focusing on patients with SLE.

In conclusion, we have reported the first case of *N. pseudobrasiliensis* hydrarthrosis in a Chinese patient with arthritis. The *N. pseudobrasiliensis* isolate obtained in this case was susceptible to ciprofloxacin, whereas previous reports have shown that *N. brasiliensis* is resistant to ciprofloxacin. There is a need to emphasize awareness of *N. pseudobrasiliensis* as an emerging human pathogen in immunocompromised patients. Antibiotic use should be guided by drug sensitivity results to prevent further clinical deterioration.

Acknowledgements

We thank our colleagues and mentors for their support.

Author contributions

YJ, MC, XH, LP, and DC collected the patient's clinical information and analyzed the data. YG wrote the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

All relevant data are provided in this article.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.


Ethics statement

This study was approved by the Ethics Committee of Zhejiang People's Hospital (Approval No.: 2022JS008) and was conducted in accordance with the ethical standards of the Declaration of Helsinki. This case report and all images were published with written informed consent from the patient. All identifying information has been anonymized in the report.

Funding

This study was supported by the New Project of Zhejiang Provincial People's Hospital, entitled "Construction of Rapid Nucleic Acid Detection Platform for Invasive Fungi" (20211214).

ORCID iD

Yumei Ge  <https://orcid.org/0000-0003-3321-2176>

References

1. Wang H, Zhu Y, Cui Q, et al. Epidemiology and antimicrobial resistance profiles of the *Nocardia* species in China, 2009 to 2021. *Microbiol Spectr* 2022; 10: e0156021.
2. Brown-Elliott BA, Brown JM, Conville PS, et al. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. *Clin Microbiol Rev* 2006; 19: 259–282.
3. Schlaberg R, Fisher MA and Hanson KE. Susceptibility profiles of *Nocardia* isolates based on current taxonomy. *Antimicrob Agents Chemother* 2014; 58: 795–800.
4. Ruimy R, Riegel P, Carlotti A, et al. *Nocardia pseudobrasiliensis* sp. nov., a new species of *Nocardia* which groups bacterial strains previously identified as *Nocardia brasiliensis* and associated with invasive diseases. *Int J Syst Bacteriol* 1996; 46: 259–264.
5. Ruimy R, Riegel P, Carlotti A, et al. Multidrug-resistant *Nocardia pseudobrasiliensis* presenting as multiple muscle abscesses. *BMJ Case Rep* 2015; 2015: bcr2014205262.
6. Makadia S, Patel I, Soosaipillai I, et al. First case of *Nocardia pseudobrasiliensis* causing primary cutaneous nocardiosis in an immunocompetent patient. *J Investig Med High Impact Case Rep* 2020; 8: 2324709620938228.
7. Gagnier JJ, Kienle G, Altman DG, et al; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.
8. Barry M, AlShehri S, Alguhani A, et al. A fatal case of disseminated nocardiosis due to *Nocardia otitidiscaviarum* resistant

- to trimethoprim-sulfamethoxazole: case report and literature review. *Ann Clin Microbiol Antimicrob* 2022; 21: 17.
9. Wallace RJ Jr, Brown BA, Blacklock Z, et al. New *Nocardia* taxon among isolates of *Nocardia brasiliensis* associated with invasive disease. *J Clin Microbiol* 1995; 33: 1528–1533.
 10. Chen B, Tang J, Lu Z, et al. Primary cutaneous nocardiosis in a patient with nephrotic syndrome: a case report and review of the literature. *Medicine (Baltimore)* 2016; 95: e2490.
 11. Mangieri NA, Guevara Nuñez D, Echavarría G, et al. Sporotrichoid nocardiosis by *Nocardia brasiliensis*. *Rev Argent Microbiol* 2021; 53: 43–47.
 12. Al-Obaydi S and DeMaio J. Two cases of cutaneous nocardiosis after a natural disaster. *Cureus* 2019; 11: e6278.
 13. Wilson JW. Nocardiosis: updates and clinical overview. *Mayo Clin Proc* 2012; 87: 403–407.
 14. Sekar A, Gupta A, Rawat A, et al. Persistent pneumonia in an infant. *Indian Pediatr* 2021; 58: 1067–1073.
 15. Seol CA, Sung H, Kim DH, et al. The first Korean case of disseminated mycetoma caused by *Nocardia pseudobrasiliensis* in a patient on long-term corticosteroid therapy for the treatment of microscopic polyangiitis. *Ann Lab Med* 2013; 33: 203–207.
 16. Mongkolrattanothai K, Ramakrishnan S, Zagardo M, et al. Ventriculitis and choroid plexitis caused by multidrug-resistant *Nocardia pseudobrasiliensis*. *Pediatr Infect Dis J* 2008; 27: 666–668.
 17. Kageyama A, Sato H, Nagata M, et al. First human case of nocardiosis caused by *Nocardia pseudobrasiliensis* in Japan. *Mycopathologia* 2003; 156: 187–192.
 18. Lebeaux D, Lanternier F, Degand N, et al. *Nocardia pseudobrasiliensis* as an emerging cause of opportunistic infection after allogeneic hematopoietic stem cell transplantation. *J Clin Microbiol* 2010; 48: 656–659.
 19. Brown BA, Lopes JO, Wilson RW, et al. Disseminated *Nocardia pseudobrasiliensis* infection in a patient with AIDS in Brazil. *Clin Infect Dis* 1999; 28: 144–145.
 20. Harent S, Vuotto F, Wallet F, et al. *Nocardia pseudobrasiliensis* pneumonia in a heart transplant recipient. *Med Mal Infect* 2013; 43: 85–87.
 21. Javaid W, Rawling R and Granato P. *Nocardia pseudobrasiliensis* systemic infection in an immunocompetent patient. *Clin Microbiol Newsl* 2012; 34: 72–73.
 22. Conville PS, Brown-Elliott BA, Smith T, et al. The complexities of *Nocardia* taxonomy and identification. *J Clin Microbiol* 2017; 56: e01419–17.