Clin. Lab. 2024;70:XXX-XXX

CASE REPORT

A Rare Case Report of Skin Infection Caused by Nocardia brasiliensis in an HIV Patient

Yun Xing, Shilu Li

Department of Laboratory Medicine, Daping Hospital, Army Medical Center of The PLA, Chongqing, China

SUMMARY

Background: **In October 2023, our hospital confirmed a case of a patient with HIV with concurrent infection with *Nocardia brasiliensis*. A patient with HIV developed a lump on the surface of the dorsum of his left hand without any obvious cause. He used a nail clipper to trim it. Due to improper disinfection and treatment methods, the condition worsened, and he subsequently sought medical attention at our hospital. A series of clinical laboratory tests were conducted based on the patient's medical history, symptoms, and signs. Based on the test results, a reasonable clinical treatment plan was adopted, ultimately achieving satisfactory treatment outcomes for the patient.**
Methods: **Clinical implementation of pus bacterial culture and identification (matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry, MALDI-TOF MS), serum anti HIV detection, and Treponema pallidum antibody detection. Additional related auxiliary examinations: blood routine, liver function, kidney function, CRP, electrolytes.**
Results: **Blood routine and CRP (venous blood): White blood cell count 16.00 x 10^9/L, total number of lymphocytes 3.73 x 10^9/L, total monocyte count 1.66 x 10^9/L, total number of neutrophils 10.37 x 10^9/L, total number of basophils 0.10 x 10^9/L, average platelet volume 8.8 fL, whole blood high-sensitivity C-reactive protein 46.44 mg/L, urine routine: protein+-. Liver function test: Albumin 37.7 g/L, aspartate aminotransferase 55.5 U/L, alanine aminotransferase 63.7 U/L, blood lipid test: triglycerides 2.22 mmol/L, high-density lipoprotein cholesterol 0.77 mmol/L, coagulation function test: fibrinogen test 5.69 g/L, lymphocyte subgroup analysis: T4/T8 cell ratio 0.78, total mature T cell count 2.501 x 10^9/L, T8 cell count 1.351 x 10^9/L, B cell count 0.574 x 10^9/L. Serum pathogen test: anti HIV positive, Treponema pallidum antibody 214.70 IU/mL, unheated serum reactive hormone test positive (1:8). Gram staining of pus: a large number of Gram positive bacteria were found, arrange in a branching form, weak acid-fast staining: positive, pus culture and bacteria identified (MALDI-TOF MS): *Nocardia brasiliensis*. Clinical treatment includes trimethoprim/sulfamethoxazole 800 mg/160 mg po q12 hours, local wet compress with Baiduobang ointment, and abscess incised and drained. Seven days later, the patient had a circular ulcer on the left back without any new pustules. Slightly elevated skin temperature, no tenderness, and no purulent or bloody secretions. His condition had improved and he was discharged. Follow up infectious disease specialist hospitals treat HIV, syphilis, and other related diseases.**
Conclusions: **Patients with HIV are prone to various types of infections, even rare bacteria, as their immune function decreases. At present, there are few reports about a patient with HIV with concurrent infection with *Nocardia brasiliensis*. This case can provide reference for clinical diagnosis and treatment of related diseases in the future. In addition, with the popularity of new identification methods such as mass spectrometry, laboratories should pay attention to traditional staining methods and use microscopes to detect pathogens.**
(Clin. Lab. 2024;70:xx-xx. DOI: 10.7754/Clin.Lab.2024.240528)

Correspondence:
Shilu Li
Department of Clinical Laboratory
Daping Hospital
Army Medical Center of The PLA
Chongqing, 400042
China
Phone/Fax: +86 023 68746995
Email: 15009788182@163.com

Case Report accepted May 29, 2024

KEYWORDS

Nocardia brasiliensis, HIV, MALDI-TOF MS

CASE PRESENTATION

A 46-year-old patient had a lump (0.5 cm x 0.5 cm) on his left hand for no obvious reason. After self-trimming with a nail clipper, there is a small amount of bleeding that has not been disinfected, resulting in local redness, swelling, fever, and pain. The purulent secretion on the local skin gradually increases. The patient received disinfection, debridement, and intravenous infusion (cefazolin) treatment at the clinic, but the symptoms did not improve. The patient came to our hospital for further treatment. The patient went to the private clinic to inject penicillin five years ago because of a cold and fever. The use of dirty needles led to HIV infection (viral load: 4.24E+05 copies/mL) and received long-term oral medication (tenofovir, po qd; ribavirin, po qd) for antiretroviral treatment (ART). Surgical history (cholecystectomy performed in our hospital in 2021), no history of blood transfusion, drug contact, medical history, or other chronic diseases. Specialized examination: A pustule was seen on the back of the left hand, with a size of 3 cm x 4 cm, a brown scab about the size of a mung bean could be seen in the center, with redness and swelling around it, increased skin temperature, and tenderness. A linear erythema could be seen on the left forearm and upper arm, which could fade when pressed, with tenderness and no itching. The left axillary and supraclavicular lymph nodes were swollen and tender. Auxiliary examination: Blood routine and CRP (venous blood): White blood cell count 16.00 x 10^9/L, percentage of monocytes 10.4%, total number of lymphocytes 3.73 x 10^9/L, total monocyte count 1.66 x 10^9/L, total number of neutrophils 10.37 x 10^9/L, total number of basophils 0.10 x 10^9/L, average platelet volume 8.8 fL, whole blood high-sensitivity C-reactive protein 46.44 mg/L, urine routine: protein+-. Liver function test: Albumin 37.7 g/L, aspartate aminotransferase 55.5 U/L, alanine aminotransferase 63.7 U/L, L-γ-Glutamatyltransferase 120.3 U/L, blood lipid test: triglycerides 2.22 mmol/L, high-density lipoprotein cholesterol 0.77 mmol/L, coagulation function test: fibrinogen test 5.69 g/L, lymphocyte subgroup analysis: T4/T8 cell ratio 0.78, total mature T cell count 2.501 x 10^9/L, T8 cell count 1.351 x 10^9/L, B cell count 0.574 x 10^9/L. Serum pathogen test: anti HIV positive, Treponema pallidum antibody 214.70 IU/mL, unheated serum reactive hormone test positive (1:8). The abscess was incised and drained, and the pus was sent to the laboratory for a pathogen examination. Gram staining of pus: a large number of Gram positive bacteria were found, arranged in a branching form (Figure A), weak acid-fast staining: positive, pus culture and bacteria identified (MALDI-TOF MS): *Nocardia brasiliensis* (Figure B, C). Clinical diagnosis: 1. *Nocardia brasiliensis* infection in the dorsum of the left hand, 2. Positive for human immunodeficiency virus. Clinical treatment includes trimethoprim/sulfamethoxazole 800 mg/160 mg oral administration twice a day, local wet compress with Baiduobang ointment, and abscess incised and drained. Seven days later, the patient had a circular ulcer on the left back without any new pustules. Slightly elevated skin temperature, no tenderness, no purulent or bloody secretions, visible quail egg sized erythema on the left forearm, which could fade under pressure without tenderness. Patient condition had improved and he was discharged. Follow up infectious disease specialist hospitals treat HIV, syphilis, and other related diseases.

DISCUSSION

The human immunodeficiency virus, without proper treatment, can attack and gradually damage the human immune system [1]. Nocardia is a class of aerobic opportunistic pathogenic bacteria that are widely present in the natural environment [2]. Nocardia can easily cause infection in patients with chronic wasting diseases, immune dysfunction, and the use of immunosuppressants [3]. This bacterium can invade various tissue parts of the body, causing corresponding clinical symptoms. For example, pulmonary infections may cause fever, cough, and sputum production, while skin infections may cause skin swelling, affecting subcutaneous tissue, fascia, and bones. Some may have sinus tract formation, while brain infections may cause symptoms such as headaches and consciousness disorders [4]. Due to the slow growth of Nocardia, traditional cultivation methods are prone to misdiagnosis [5]. This article reports a case of an HIV patient with concurrent skin infection caused by *Nocardia brasiliensis*. The diagnosis was confirmed based on the patient's medical history, symptoms and signs, auxiliary examinations, bacterial culture, Gram staining, weak acid-fast staining and mass spectrometry identification. We hope that this report can draw high attention to patients with HIV, especially those in advanced stages, in clinical practice. With the weakened immune function of the body, various types of infections, and even some rare bacteria, are more likely to occur. In addition, with the popularity of new identification methods such as mass spectrometry, laboratories should pay attention to traditional staining methods and use microscopes to detect pathogens.

Patients with HIV are a high-risk group for opportunistic bacterial infections, especially for late-stage patients [6]. As the body's immune function decreases and CD4+T cell levels decrease, it is more likely to be associated with exogenous infections [7]. Previously, there have been few reports of patients with HIV being infected with *Nocardia brasiliensis*. The patient in this case was HIV positive, Treponema pallidum positive, and had a low T4/T8 ratio. Therefore, facing the invasion of exogenous pathogenic bacteria, the patient's immune defense ability is greatly challenged. Blood rou-

Figure A. Gram staining of pus: a large number of Gram positive bacteria were found, arranged in a branching form x 1,000.
Figure B. Growth of *Nocardia brasiliensis* on Chocolate agar plate at 35°C, 5 days.

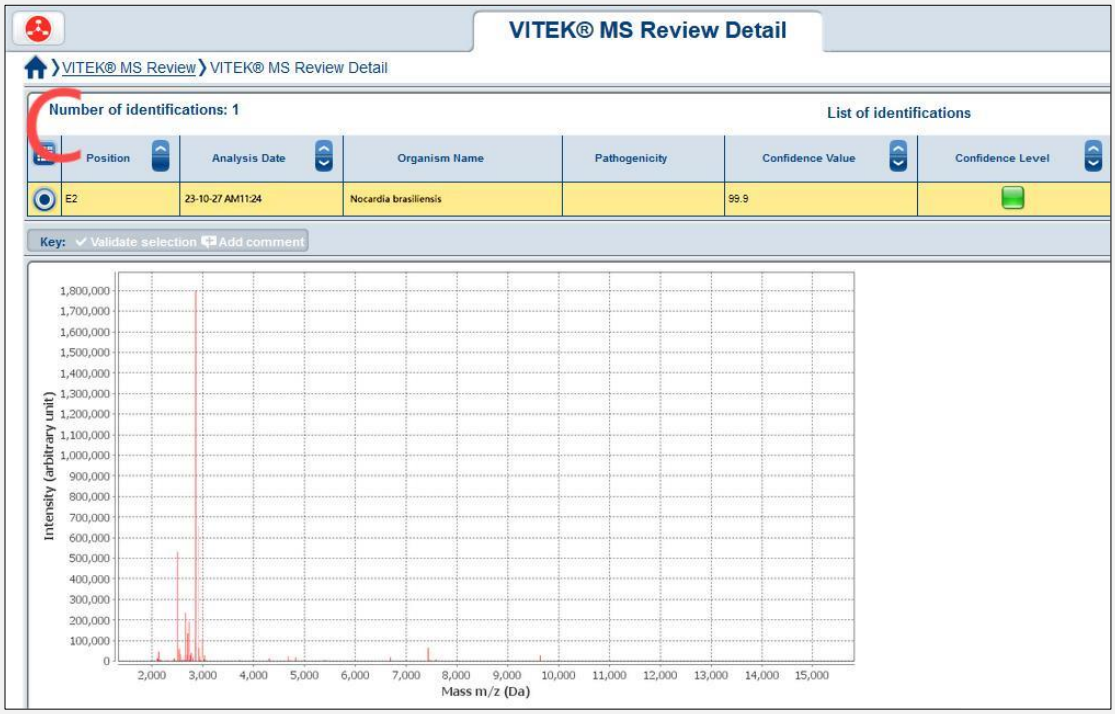

Figure C. Identification results of *Nocardia brasiliensis* MALDI-TOF MS.

tine + CRP (venous blood), total number of neutrophils, whole blood high-sensitivity C-reactive protein, and fibrinogen test. These laboratory test results indicated the presence of severe infection in the patient. The left hand abscess site of the patient was immediately incised, drainage was performed, and pathogenic testing was carried out. Finally, *Nocardia brasiliensis* was cultured from the pus. The antibacterial treatment plan for this case was trimethoprim/sulfamethoxazole 800 mg/160 mg oral administration twice a day. After 7 days of treatment, there were no new pustules, purulent or bloody secretions, and no tenderness around the ulcer. The treatment effect was significant. Due to the patient's need to seek treatment for diseases such as HIV and syphilis at a specialized infectious disease hospital, he was instructed to continue to receive antimicrobial treatment according to the course of treatment after discharge, at least 6 weeks after all symptoms and signs disappear.

Nocardia easily missed. The first reason is that the bacteria grow slowly and only grow very small colonies after 2 to 3 days of cultivation [8]. If the inspectors lack experience or do not pay attention to observations, it is easy to misdiagnose; secondly, if it is a respiratory specimen, the rapid growth of other respiratory bacteria can inhibit the growth of Nocardia [9]. Therefore, laboratories should attach great importance to smear detection. If gram-positive rod-shaped or branched filaments of varying lengths are found during microscopic examination of specimen smears, weak acid staining should be added, and the cultivation time should be appropriately extended to help detect Nocardia [10].

In this case, suspicious positive bacteria were detected during the Gram staining of pus, followed by weak acid staining and prolonged bacterial culture, ultimately isolating *Nocardia brasiliensis*. Thus, it could be seen that smear detection is crucial for the detection of *Nocardia brasiliensis*. *Nocardia brasiliensis* is mainly distinguished from erysipelas: erysipelas is an acute inflammatory skin disease caused by the invasion of beta hemolytic streptococcus into damaged skin and mucosal reticular lymphatic vessels. It is more common in the lower limbs and face, often accompanied by symptoms such as high fever and chills. Patient did not show any systemic symptoms before onset, and abscess formed locally on the back of his hand, which was not consistent with erysipelas [11].

There were also limitations in this case report. Most infections caused by Nocardia initially occur in the lungs, which can then spread through the bloodstream and cause systemic organ infections, often accompanied by brain abscesses, skin and soft tissue abscesses, etc. [12]. In this case, the patient's body temperature was normal and there were no symptoms such as coughing or sputum production. Clinical examinations such as sputum or lavage fluid bacterial culture and lung tissue biopsy were not conducted to rule out the possibility of pulmonary Nocardia infection.

In summary, this article reports a case of an HIV patient with concurrent infection with *Nocardia brasiliensis*. Clinical attention should be paid to HIV patients, as their weakened immune defense ability can easily lead to various types of infections, even some rare bacteria. With the rapid development of microbial identification technology, the importance of traditional smear detection methods cannot be ignored.

Ethics Approval and Consent to Participate:
Ethical review and approval was not required for this study. The patient provided written informed consent to participate in this study.

Consent for Publication:
The patient provided written informed consent for study publication.

Availability of Data and Materials:
The original data and materials presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Source of Funds:
This study was supported by the Chongqing Science and Health Joint Medical Research Project Fund (2022 QNXM034).

Declaration of Interest:
The authors declare no competing interests.

References:

1. Drobyshevskaya E, Lebedev A, Pronin A, Bobkova M. Factors Associated with Fatal COVID-19 Outcomes among People Living with HIV: A Cohort Study. Curr HIV Res 2023;21(6):367-77. (PMID: 38037993)

2. Fazili T, Bansal E, Garner D, Bajwa V, Vasudeva S. Septic arthritis due to Nocardia: Case report and literature review. Am J Med Sci 2022 Jul;364(1):88-91. (PMID: 35172188)

3. Gao H, He Q, Xu C, et al. The Development and Validation of Anti-paratuberculosis-nocardia Polypeptide Antibody [Anti-pTNP] for the Diagnosis of Crohn's Disease. J Crohns Colitis 2022 Aug 4;16(7):1110-23. (PMID: 35029687)

4. Ahammadunny R, Rathish B, Abraham M, Wilson A, Warrier A. A Case of Levamisole Induced Multifocal Inflammatory Leukoencephalopathy and Secondary Nocardia Veterana Brain Abscess. Ann Indian Acad Neurol 2021 Sep-Oct;24(5):814-6. (PMID: 35002165)

5. Hayashi Y, Kitajima T, Marumo S, Fukui M. Adult T Cell Leukemia/Lymphoma Becoming Apparent during Treatment of Pulmonary Abscess and Empyema Caused by Nocardia asiatica: A Case Report and Review of the Literature. Intern Med 2022 Jul 15;61(14):2227-32. (PMID: 34980794)

6. Lemaire V. [AMMA seated massage for people living with HIV, the relationship at your fingertips]. Rev Infirm 2023 Dec;72(296): 43-5. French. (PMID: 38071018)

7. Sun Y, Song B, Zhen C, Zhang C, Cheng J, Jiang T. The mediating effect of psychological resilience between social support and anxiety/depression in people living with HIV/AIDS-a study from China. BMC Public Health 2023 Dec 8;23(1):2461. (PMID: 38066520)

8. Kanchanasin P, Yuki M, Kudo T, Ohkuma M, Phongsopitanun W, Tanasupawat S. *Nocardia aurantiaca* sp. nov., isolated from soil in Thailand. Int J Syst Evol Microbiol 2020 Oct;70(10):5432-8. (PMID: 32897850)

9. Lebeaux D, Coussement J, Chauvet C, et al. Autoantibodies against granulocyte macrophage colony-stimulating factor and Nocardia infection in solid organ transplant recipients. Transpl Int 2020 Dec;33(12):1827-9. (PMID: 32881092)

10. Benndorf R, Schwitalla JW, Martin K, et al. *Nocardia macrotermitis* sp. nov. and *Nocardia aurantia* sp. nov., isolated from the gut of the fungus-growing termite *Macrotermes natalensis*. Int J Syst Evol Microbiol 2020 Oct;70(10):5226-34. (PMID: 32815801)

11. Ren Z, Silverberg JI. Burden, risk factors, and infectious complications of cellulitis and erysipelas in US adults and children in the emergency department setting. J Am Acad Dermatol 2021 May; 84(5):1496-503. (PMID: 33238162)

12. Clemente WT. Unanswered Questions on the Management of Nocardia Infections in Transplant Recipients. Transplantation 2023 Mar 1;107(3):582-3. (PMID: 36413148)