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CASE REPORT

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Primary cutaneous nocardiosis in an immunocompetent host

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Key Clinical Message

Nocardiosis is a rare opportunistic infection that is classically observed in immunocompromised patients but can also affect immunocompetent individuals. It tends to involve the lung, central nervous system, and skin and is often misdiagnosed.

KEYWORDS

cutaneous, immunocompetent, misdiagnosis, nocardiosis

A 53-year-old male patient presented to the hospital with swelling, nodules, and empyema of the right upper limb. In the previous 6 years, the patient had been treated with antibiotics several times but no significant improvement was observed. The local disease was prolonged, new rashes continued to appear, and the lesion area gradually expanded but the patient did not have chills, fever, fatigue, cough, expectoration, dizziness, and headache. He denied taking glucocorticoids and immunosuppressants and was free of tumors and acquired immune deficiency syndrome (AIDS). Upon detailed interrogation, we found that he had a history of soil exposure due to a skin abrasion on the right upper limb caused by an accidental fall before the onset of the disease. Therefore, we suspected the presence of special infections, such as nontuberculous mycobacteria, fungi, actinomycetes, and focused on the etiological examination.

Physical examination showed swelling of the right upper limb with multiple purplish-red nodules on the surface, some of which were suppurative and fluctuating, with scattered crusting and scarring (Figure 1). Laboratory evaluations revealed elevated C-reactive protein (31.8 mg/L, normal range: 0–5 mg/L), and other tests were negative. Ultrasonography revealed multiple swollen lymph nodes in the right axillary and inguinal regions. Plain CT scan of the head and chest did not reveal signs of infection. The pathology of the lesion was characterized by infected granulomas. Gram-positive bacilli were observed in the purulent discharge under the microscope (Figure 2). We first performed metagenomics next generation sequencing (mNGS) testing on clinical sample obtained from this patient, and 3 days later, the results revealed *Nocardia brasiliensis*. After 7 days, characteristic colony appeared on Columbia blood agar, appearing white with a wrinkled and granular surface (Figure 3). The causative agent was identified as *Nocardia brasiliensis* by 16S RNA sequencing and matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). We did not perform Grocott staining of skin tissue due to the lack of staining reagents. Eventually, the patient was treated with sulfamethoxazole-trimethoprim. The patient's right upper limb nodules subsided significantly after 2 months.

Nocardiosis is a local or disseminated infectious disease caused by *Nocardia* spp., which manifests as pyogenic or granulomatous. Nocardiosis is a sporadic global disease with no racial or age predilection.[1] It is more prevalent in males than in females, with an incidence rate of 3:1, and is associated with work and environmental exposures. Nocardiosis mainly occurs in people with immunodeficiency or lung disease; however, there has been a recent

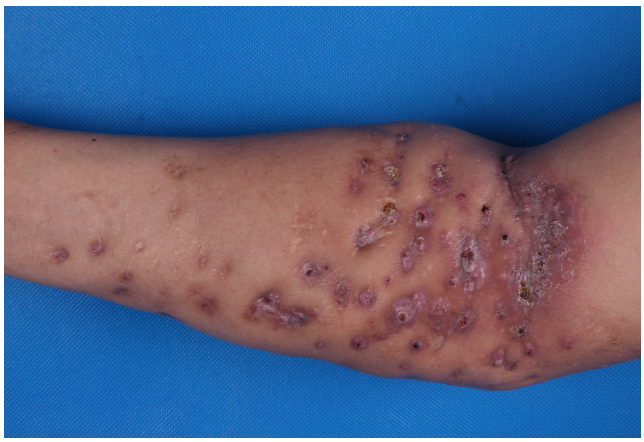

FIGURE 1 Multiple nodules and subcutaneous abscesses with scabs on the right upper limb.

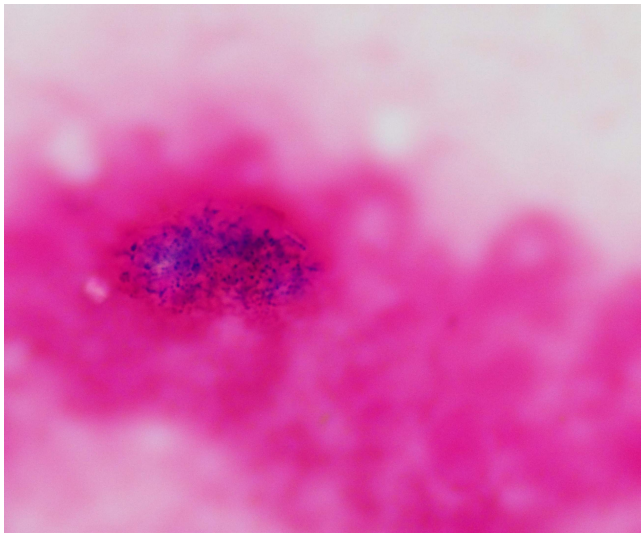

FIGURE 2 Results of gram staining of purulent secretions.

surge in the incidence of the disease in immunocompetent individuals, constituting approximately 18–45% of all cases, which may be correlated with undetected underlying immunodeficiency.[2]

Nocardia can involve different organs of the body, among which pulmonary nocardiosis is the most common, presenting with fever, cough, hemoptysis, difficulty breathing, weight loss, and fatigue. Brain abscesses usually affect patients with cellular immunodeficiency and manifest as fever, headache, vomiting, and even impaired consciousness. Skin involvement in nocardiosis accounts for about 20% of cases and is categorized into primary and secondary forms. Primary cutaneous nocardiosis often occurs in patients who are immunocompetent, and the most common species isolated is *Nocardia brasiliensis*. *N. brasiliensis* usually infects hosts by direct invasion through injured skin, forming nodules locally, abscesses or cellulitis, or spreading to distant locations along lymphatic vessels.[3]

FIGURE 3 Colony morphology.

Our patient had a definite exposure history and typical foci of cutaneous infection. Unfortunately, nocardiosis was not recognized at the initial visit.

Cutaneous nocardiosis, being highly deceptive, often poses challenges in differentiating it from superficial cellulitis, sporotrichosis, nontuberculous mycobacterial infection, leishmaniasis, and so forth. The lack of specific clinical manifestations makes it difficult to diagnose, as it primarily relies on pathogenic examination. The genus *Nocardia*, first reported by Edmond Nocard in 1888, is an aerobic, partially acid-fast, gram-positive bacterium that is widely distributed in soil and has the potential to cause disease in humans and animals. Traditional techniques, such as smear microscopy and culture, are laborious and inadequate for the identification of *Nocardia* species. Over the past few years, molecular biology methods like 16S rRNA gene sequencing, PCR, and MALDI-TOF MS have emerged as the widely accepted means to identify *Nocardia* species.[4] These diagnostic techniques offer greater precision and faster results, thereby contributing to timely diagnosis.

The management of nocardiosis should adhere to the fundamental principles of standardization, adequate dosage and full course. The use of sulfamethoxazole-trimethoprim as the initial treatment option is widely acknowledged. Studies have shown that amikacin, minocycline, moxifloxacin, linezolid and imipenem have good activity against *Nocardia*. It is important to emphasize that drug susceptibility testing is necessary to effectively direct treatment. For the majority of patients with primary cutaneous nocardiosis, it is advised to undergo monotherapy, while combination therapy may be opted for in cases

of severe infection. The treatment period varies from 2 to 6 months.[5] The approach to nocardiosis treatment should be individualized, taking into account the patient's immune status and the severity of the disease. After taking sulfamethoxazole-trimethoprim only for 2 months, the patient's condition showed remarkable improvement.

In conclusion, the clinical manifestations and laboratory findings of primary cutaneous nocardiosis are nonspecific. *Nocardia* infection should be suspected in patients with mycetoma, superficial skin infection or skin lymphatic infection with a history of trauma and poor response to conventional antibiotic treatment. Molecular tests of clinical sample should be performed as soon as possible to shorten the diagnosis time.

AUTHOR CONTRIBUTIONS

Shihuan He: Writing – original draft. **Youkun Lin:** Writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

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None.

DATA AVAILABILITY STATEMENT

Data sharing is available from the corresponding author.

DECLARATION OF PATIENT CONSENT

The patient has signed a written informed consent for publication of the case.

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