

Original Article

Extensive mycetoma in forearm, chest and neck due to *Nocardia mexicana*

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Abstract

Introduction: Mycetoma is a chronic granulomatous inflammatory disease of the subcutaneous tissue, which affects deep structures and bone. Most cases of actinomycetoma are caused by members of the genus *Nocardia*.

Case presentation: Here we report the case of a 43-year-old male who presented a disseminated mycetoma on the forearm, chest and neck, characterized by enlarged and erythematous lesions through which seropurulent material drains, and numerous atrophic scars. Molecular identification was performed by 16S gene amplification and sequencing. *Nocardia mexicana* was identified with 100% identity. Trimethoprim-sulfamethoxazole, diaminodiphenyl sulfone and amikacin was a successful treatment after 6 months.

Conclusions: *Nocardia mexicana* is a rare organism that causes mycetoma. We report a case of extensive mycetoma on the forearm with spread to the neck and thorax associated with manipulation of the mouth of a calf.

Key words: Mycetoma, *Nocardia mexicana*, tropical disease.

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Introduction

Mycetoma is a chronic, suppurative and granulomatous inflammatory disease of the skin and the underlying tissues, caused by bacteria or fungi. The most frequently reported bacterial mycetoma (actinomycetoma) is caused by bacteria of the genus *Nocardia*. These microorganisms are Gram-positive, aerobic actinomycetes found ubiquitously in soil, sand, plants, thorns and splinters and can enter through minor skin trauma to the subcutaneous tissue of a host. Usually, mycetoma displays a specific clinical triad which is composed of painless subcutaneous tumor-like swelling, multiple sinuses and fistulas, and festering grains [1].

The countries with the highest prevalence of the disease are Sudan, Venezuela, Mexico and India, with Sudan and Mexico having the highest number of reported cases.

Nocardia brasiliensis and *Nocardia asteroides* are considered the most frequently reported species worldwide [2]; however, there are reports of uncommon species being implicated, including *Nocardia otitidiscaviarum*, *Nocardia transvalensis*, *Nocardia mexicana*, *Nocardia harenae*, and *Nocardia takedensis*. *N. brasiliensis* is the most reported etiologic agent in Mexico [2,3], although *Nocardia mexicana* has also been recognized as a causal agent of mycetoma, being reported for the first time in 2004 in Mexican patients [4]. There have been few cases associated with *N. mexicana* since then, which have involved different anatomical regions and pathological conditions, such as brain abscess [5], cerebral nocardiosis [6], cutaneous botryomycosis [7], pulmonary infections [8], as well as a tenosynovitis and arthritis in bovines [9]. We report herein the case of an extensive mycetoma originated in

the forearm of a patient with dissemination to neck and chest, due to *N. mexicana*.

Case presentation

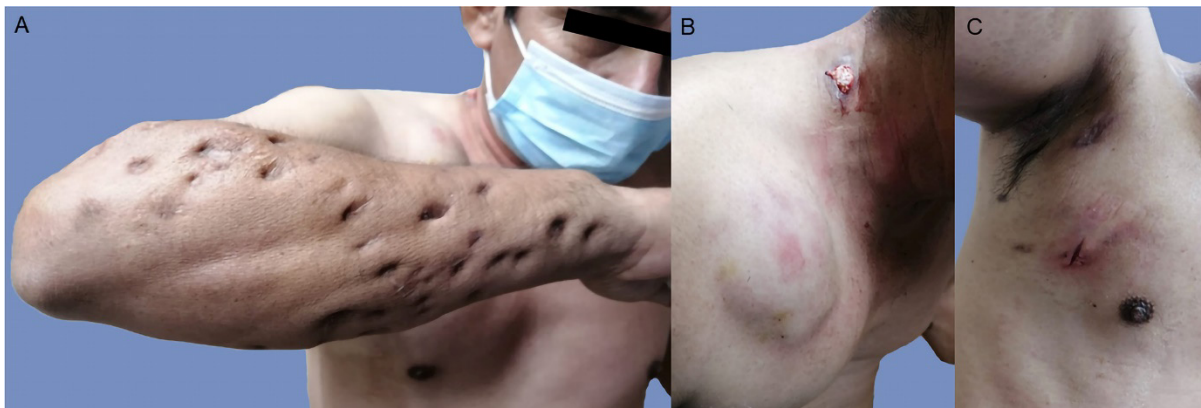
A 43-year-old male farmer from Acapulco Guerrero, Mexico, had history of trauma to the right upper limb after he introduced his hand and part of his forearm into the mouth of a calf. One month after the trauma (March 2022), he presented disseminated dermatosis on the right lateral face of the neck, anterior face of the thorax on its upper third, armpit and ipsilateral forearm, predominantly on the elbow and external face of the arm and forearm (Figure 1). The lesions were characterized by increased volume, fistulae through which seropurulent material drained, and numerous atrophic scars. He also presented pain and physical disability for flexion–extension movements of the affected limb, as well as local hyperthermia. He reported previous treatment with ceftriaxone, resulting in transient improvement. Hematic biometry results did not show any abnormalities and chest X-rays showed no bone or joint lesions.

An extensive mycetoma was suspected; therefore, a biopsy, bacteriological cultures, and smears were performed. Biopsy histopathological analysis showed pyogranulomatous dermatitis, and direct examination of exudate revealed small grains; however, no bacteria were visualized with Ziehl–Neelsen or Kinyoun stains. Bacterial culture was performed on Sabouraud dextrose agar at 37°C; after a 4-week incubation period, yellowish-white colonies with a chalky appearance were observed. Microscopically they stained weakly Gram-positive and had branched filamentous morphology; therefore, *Nocardia* spp. were strongly suspected. No antibiotic susceptibility tests were performed.

Treatment with trimethoprim-sulfamethoxazole (TMP-SMX) (800/160 mg BID for 6 months), diaminodiphenyl sulfone (100 mg SID) and rifampicin (600 mg SID for 3 months), was implemented with significant improvement (Figure 2). The patient did not completely recover, and has multifocal scars on arms, chest and neck; however, he is currently afebrile and there is no evidence of new lesions. He continues to be medicated with TMP-SMX and diaminodiphenylsulfone with the same previous indications.

For further species identification, 16S rRNA gene amplification and sequencing was performed. Briefly, genomic DNA was isolated from blood samples using a DNeasy blood and tissue kit (Qiagen, Ventura CA, USA) according to the manufacturer’s instructions. Polymerase chain reaction (PCR) was performed using a set of primers (5'-GGATCCTTTTGATCCTGGCTCAGGAC-3' and 5'-ACTTGACGTCGTCCCCACCTTCCTC-3') that were designed based on the 16S rRNA gene sequence of *Nocardia wallacei* ATCC 49872, formerly *Nocardia asteroides* (GenBank accession no. AY191251). A 1300 bp fragment of the 16S rRNA ribosomal subunit was amplified; this amplicon was purified and the nucleotide sequence was determined in both directions by fluorescence-based Taq FS Dye Terminator Cycle Sequencing. Consensus homologous sequence searching was performed in the GenBank database (nucleotide blast), and the sequence displayed 100% homology with *N. mexicana* strains OFN1325, PWQ2814 and DSM 44952, among others. The complete sequence obtained for *N. mexicana* has been deposited in the GenBank under accession no. OP858990.

Figure 1. Disseminated and extensive mycetoma: (A) sinus tracts on forearm; (B) abscesses and ulcers on the neck and chest; (C) axillary involvement.



Discussion

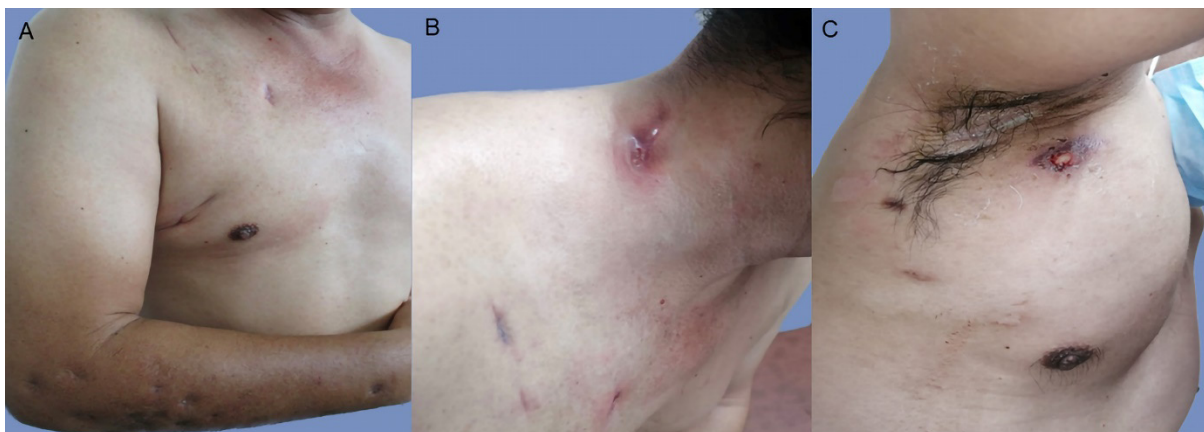
Mycetoma is a chronic inflammatory disease of the skin and subcutaneous tissue, which may involve deep tissues and bones, and is characterized by deformity and disability, especially in chronic phases. The etiologic agent enters the skin through some minor, often ignored, trauma. As the incubation period is long and variable, many patients do not clearly remember the history of trauma when they turn to a clinician. The lower extremity (foot) is the most commonly involved area, followed by the hand; other affected anatomical sites include the head, neck, chest, shoulders and arms [10].

N. mexicana was first reported in Mexico in 2004 when it was identified in three patients with mycetoma; its current epidemiological distribution includes reports in Japan, Australia, USA and Iran [4,6,8,9,11]. Among the few cases associated with *N. mexicana*, only one was reported in a veterinary patient and corresponded to a bovine with tenosynovitis and arthritis [9]. There are some reports of mycetoma associated with minor trauma from snake and insect bites, as well as the isolation of *N. asteroides* from cow dung [12]. The patient described in this report refers to a wound caused by inserting his forearm into the mouth of a calf, as the origin of the mycetoma; however, it is unknown if this injury started the mycetoma or whether it appeared after the injury due to contact with soil material. The role of animals in mycetoma development should be studied in endemic areas where people live in close contact with domestic animals, as well as in facilities where the floor is covered with animal manure [12]. *N. mexicana* could be considered an emerging pathogen and it deserves more attention from a clinical and epidemiological perspective, since it is involved in human and animal infections.

Diagnosis of mycetoma can be based on clinical presentation, direct examination of the discharges (presence of grains), conventional radiography, ultrasonography and MRI. Identification of the causative agent can be made by bacteriological culture and biochemical characteristics, but this process can be slow because of the 2- to 3-week incubation period and a series of specialized phenotypic tests. Furthermore, these methods allow identification only to the genus level. Further identification to the species level requires molecular techniques based on PCR amplification and sequencing of different molecular markers. Currently, molecular identification is more frequently achieved by sequencing of specific genes such as 16S rRNA, the 65-kDa heat shock protein (*hsp65*), *rpoB* and *secA1* [13,14]. We used the 16S rRNA subunit gene sequencing, allowing us to identify *N. mexicana* as the etiologic agent. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) is alternative method for rapid identification of *Nocardia* and other microorganisms, particularly when an in-house database is used and it is compared to commercial databases [15]. Final identification helps to better understand mycetoma epidemiology and to establish relationships between etiology and treatment response.

In general, the first-line treatment for actinomycetoma is TMP-SMX, in combination with amikacin, imipenem or linezolid. However, it has been reported that most strains of *N. mexicana* are resistant to TMP-SMX. In this case, treatment with TMP-SMX, diaminodiphenyl sulfone, and amikacin produced significant improvement for the patient. However, as we did not perform antibiotic susceptibility testing, the sensitivity of the isolate to TMP-SMX is unknown [16].

Figure 2. Evolution after treatment shows a significant improvement in forearm (A), neck and chest (B), and axillary area (C).



Conclusions

Mycetoma is a chronic, progressively destructive infection that is considered to be a neglected tropical disease. Here we describe an unusual case of an extensive mycetoma caused by *N. mexicana* associated with manipulation of a calf's mouth. The use of molecular methods allowed the identification of novel species of *Nocardia*, thus impacting the taxonomy and clinical aspects of mycetoma. It is strongly recommended to perform molecular identification at the species level in order to gather additional information pertaining to epidemiological and clinical data, and also to determine susceptibility to antibiotics.

Ethical approval and consent to participate

This study was approved by the Institutional Review Board of Hospital General “Dr. Manuel Gea Gonzalez”, Mexico City, Mexico (No. 06-19-2019). Patient confidentiality was maintained, no patient identifiers were used, and no experimental investigations were performed on the patient. Written informed consent for publication of this case report was obtained from the patient.

Declaration of competing interest

The authors have no competing interests to declare.

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Conflict of interests: No conflict of interests is declared.