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(CASE REPORT)

Mycetoma due to *Nocardia brasiliensis* (Maduromycosis) in the Mixteca Poblana: Case report with successful treatment

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Abstract

The case of a Mexican patient of the Mixteca Poblana, Region until today little studied, dedicated to domestic work with a skin infection caused by *Nocardia brasiliensis*, which evolved favorably despite taking more than 8 years with the injury is presented. The diagnosis was made by direct examination and culture of the specimen. The mycetoma is a progressive chronic localized infection caused by fungi or bacteria that affects the feet, upper limbs or back. The symptoms of the case include: edema, fistuous formation. The diagnosis is clinical, confirmed with microscopic examination of exudate and culture. The treatment consists of antibiotics for a long time 21 days central intensive phase and one year with supportive treatment orally and locally.

Keywords: Mycetoma; Nocardiosis; Mixteca Poblana

1. Introduction

Mycetoma is a local, chronic, and progressive disease of the skin, subcutaneous tissues, and bones, characterized by swelling that is often grotesque and disfiguring, with fistulas that drain a serosanguinous or purulent exudate containing grains (1). These are caused by various species of fungi (eumycetomas) or actinomycetes (actinomycetomas) that organize into aggregates of hyphae or bacterial filaments, respectively, constituting the grains that can vary in size, color, and consistency depending on the species causing the mycetoma (2).

There are at least 20 species of actinomycetes and higher fungi that can cause mycetomas, with the most frequent being Actinomycetes, *Nocardia brasiliensis*, and Actinomadura.

2. Case presentation

This paper presents a 18-year-old female patient, domestic, from Tepetzingo Tlapanalá (Sierra de la Mixteca Puebla, Mexico) and with a history of good health and who reports having suffered trauma with cactus thorns approximately 8 years ago Fig.1, which initially did not It caused more discomfort, only the appearance of a superficial skin lesion that was treated by various physicians without apparent improvement, with even resection of the same without reporting a specific lesion, only fibrosis in tissues. Subsequently, a circumscribed papular lesion appeared, soft to the touch and the color of the skin, which progressively spread throughout the entire back, pectoral region and the inner face of the axillary region, associated with a sensation of burning and type of pain. flashing flashing He was clinically diagnosed with superficial fungus, receiving irregular treatment with ketoconazole for 4 weeks, as well as various antimicrobials such as aminoglycosides, antiparasitics, and first-generation cephalosporins, in addition to local cures, without presenting improvement (stationary evolution). After 6 years of disease, new papular lesions were added to the existing

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lesions, which ulcerated and fistulized, draining purulent secretion, also presenting increased volume of the injured thoracic area, skin hyperpigmentation, sensation of heat, type of pain. permanent throbbing-throbbing and progressive deformation of the skin. Due to this, the patient decided to go to the Epidemiology Service of the University Hospital BUAP.

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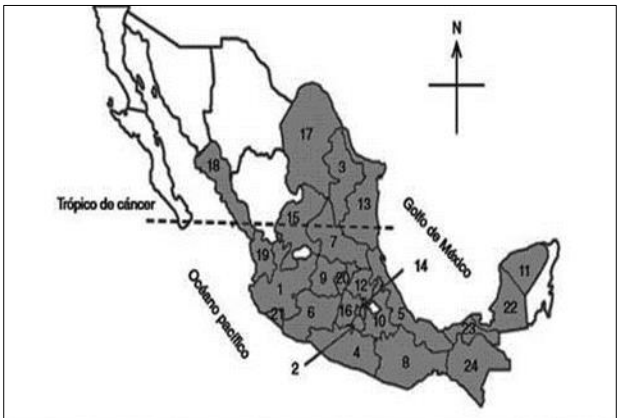
Mariat (1963) conducted the first global case study, compiling 854 cases, and noted that Mexico had the highest number of cases in the Americas, with *Nocardia brasiliensis* being the most frequently isolated agent (3). Other countries with high prevalence included India, Pakistan, and Indonesia. However, the highest frequency and historical importance of the disease are found in the Madura province in India, which is why it is also known as "Madura foot" and Maduromycosis. The region of Sudan in northeast Africa has reported the highest number of cases (4).

In Mexico, López-Martínez et al. have published several national case studies based on data from the country's main dermatomycological centers. In 2013, they compiled 3993 cases, with 96.52% of them being actinomycetomas. Of the total cases, 75.6% were male patients. The states with the highest number of cases were Jalisco, Morelos, Nuevo León, Guerrero, Veracruz, and Michoacán (5,6,7,8). Figure 1



Estado	Casos	Estado	Casos	Estado	Casos	Estado	Casos	Estado	Casos
(1) Jalisco	676	(6) Michoacán	243	(11) Yucatán	94	(16) Edo. de México	44	(21) Colima	13
(2) Morelos	429	(7) San Luis Potosí	229	(12) Hidalgo	67	(17) Coahuila	36	(22) Campeche	9
(3) Nuevo León	347	(8) Oaxaca	172	(13) Tamaulipas	66	(18) Sinaloa	34	(23) Tabasco	6
(4) Guerrero	302	(9) Guanajuato	163	(14) Distrito Federal	49	(19) Nayarit	24	(24) Chiapas	3
(5) Veracruz	264	(10) Puebla	138	(15) Zacatecas	49	(20) Querétaro	14	Sin reportar	462

Figure 1 Geographical distribution of 3933 cases of mycetoma in Mexico. From: López Martínez R*, et al.* Update on the epidemiology of mycetoma in Mexico. Review of 3,933 cases. Gaceta Médica de México. 2013;149:586-92

2.1. Examinations and assessments

Upon physical examination, generalized edema of the skin in the affected region was observed. The skin appeared hyperpigmented, with reddish and blackish areas, and had a shiny appearance. There were ulcerated and healed fistulous openings of approximately 1 cm in diameter, from which a seropurulent exudate containing whitish-yellowish grains drained. Additionally, there was increased pain upon palpation and a painless right axillary lymph node measuring 2 cm in diameter, without functional limitation but without affecting normal function (9,10). Figure 2,3.

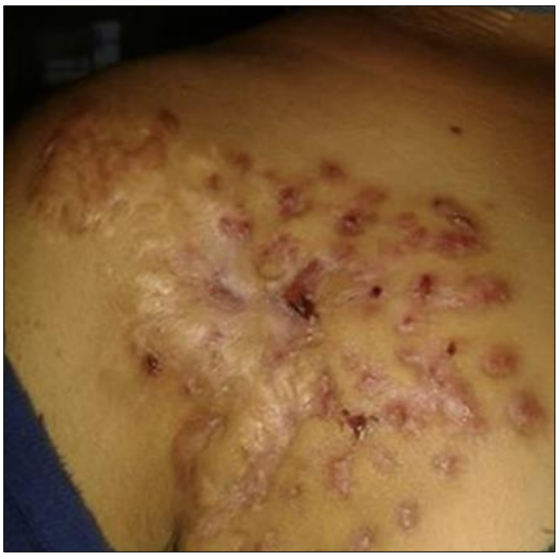


Figure 2 Nodular lesions of mycetoma at the beginning of treatment

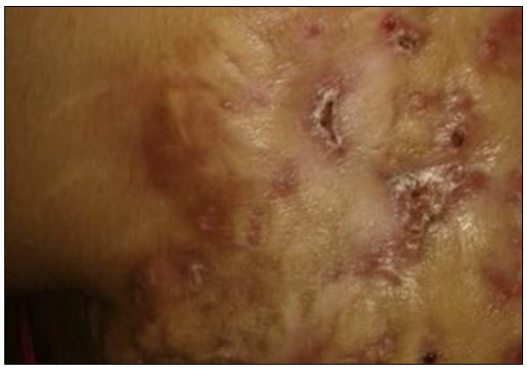


Figure 3 Nodular lesions with hyperpigmentation on the right thorax

Complete blood count: Hb 13.4 gr/dL, Hct 41.5%, Leukocytes 11,400 cells/mm3 (segmented 6,840 cells/mm3 , lymphocytes 2,736 cells/mm3 , eosinophils 0 cells/mm3 and monocytes 342 cells/mm3. PFH: BT:0.70, BD: 0.7, BI: 0.50, TGO: 15 U/L, TGP: 14 U/L, Alkaline Phosphatase: 178 U/L, Total Proteins: 7.35, A/G ratio: 1.48.

Radiological examination of the region showed no signs of osteomyelitis or soft tissue invasion (Figure 4).

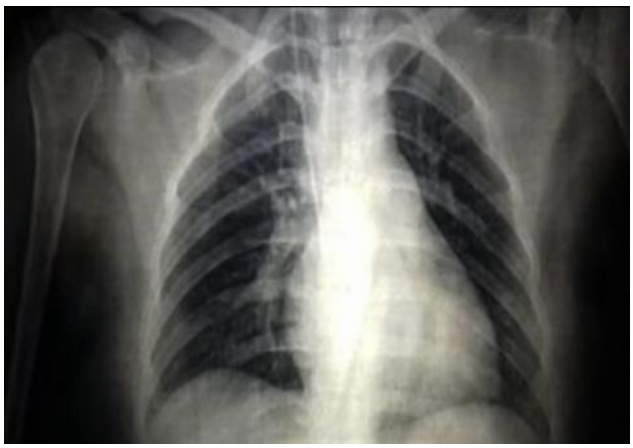


Figure 4 Radiological examination showing no evidence of injury or lesions.

Histopathological examination: In order to determine the bacterial or fungal etiology, tissue sections were stained using various techniques. Hematoxylin-eosin staining revealed kidney-shaped or lobulated grains, with a basophilic central area composed of very narrow filaments, surrounded by a hyaline eosinophilic band in a "radiating sun" pattern (Splendore-Hoeppli phenomenon), which constituted the sulfur granules. Ziehl-Neelsen staining showed acid-fast resistance. The periodic acid-Schiff (PAS) staining resulted in a magenta-red color. Silver metenamine staining did not reveal the typical brownish-black or black coloration seen in fungi, leading to the conclusion that it was a case of actinomycosis (11).

2.2. Diagnostic and intervention

In order to isolate the causative agent of the infection, the lesion walls were dissected, revealing sinuous and fistulous tracts containing abundant granules and seropurulent material, which involved the subcutaneous tissue without affecting muscles, tendons, nerves, or bones. Tissue samples and deep-seated granules were collected and transported in sterile saline solution to the Mycosis Laboratory at the Instituto GEA Gonzalez in Mexico City. Macroscopically, yellowish-white lobulated kidney-shaped granules measuring approximately 0.8 mm to 1 mm in diameter and having a soft consistency were observed. For microscopic examination, the granules were pressed between two slides, and Gram staining revealed gram-positive bacilli in chains and branching forms, as well as acid-fast bacilli with Ziehl-Neelsen staining (12, 13). The samples were cultured on thioglycolate medium, Sabouraud glucose agar with chloramphenicol, and brain heart infusion agar (BHI), and incubated under anaerobic and aerobic conditions at 25 °C and 37 °C. The etiological agent showed growth in ASG and BHA after approximately 15 days, at 25 °C and 37 °C under aerobic conditions, forming a rough, stacked colony with a yellowish-white color (Figure 6). Gram staining of the smear revealed gram-positive bacilli in chains and branching forms. For strain identification, the cultural, morphological, and biochemical characteristics were considered. Confirmation tests included casein hydrolysis, growth on Lowenstein-Jensen medium, and assimilation and growth in 0.4% gelatin. These tests successfully identified the agent as *Nocardia brasiliensis*5 (14,15, 16). Figura 5.

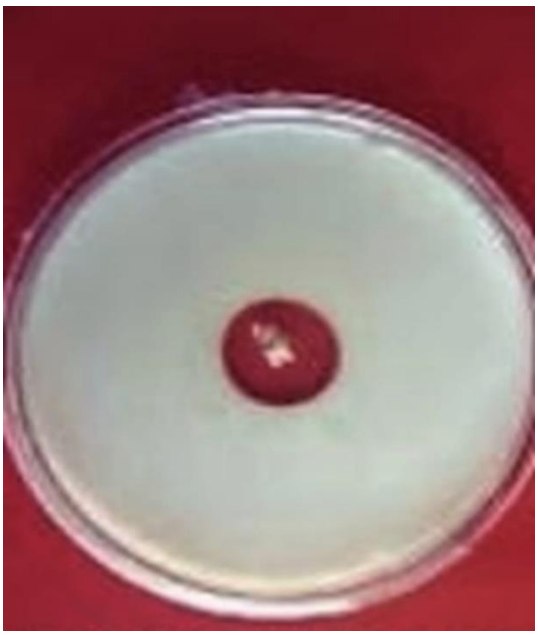


Figure 5 Casein hydrolysis and growth on Lowenstein-Jensen medium

2.3. Outcome

The patient was initially treated with a central venous catheter using Imipenem and Amikacin for 21 days. Subsequently, she underwent reevaluation and received treatment for one year with Trimethoprim-Sulfamethoxazole (TMP/SMX) tablets, each containing 800 mg and 160 mg, respectively, taken every 12 hours, along with 100 mg of Dapsone (DDS) once every 24 hours. Despite the advanced stage and poor management of the disease, the patient showed a significant improvement in the lesions, although there was residual cosmetic scarring in the form of keloid scarring (17,18,19). Figure 6.7.

Finally, the evolution and response to the treatment of the case was successful, and the patient was only left with keloid scar sequelae. Figure 8 .

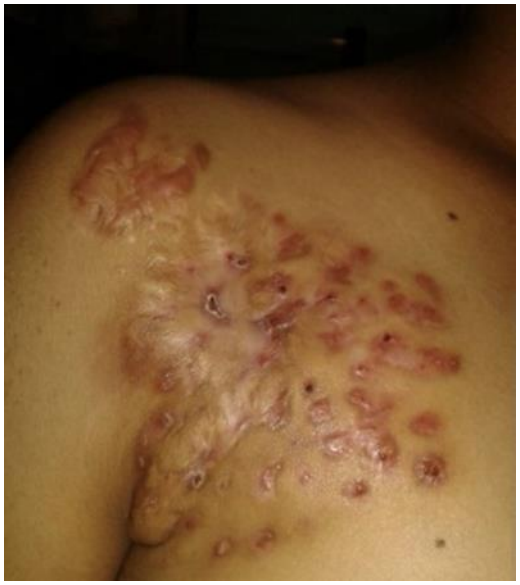


Figure 6 Nodular lesions with mycetoma at the end of treatment with 21 days of imipenem and amikacin

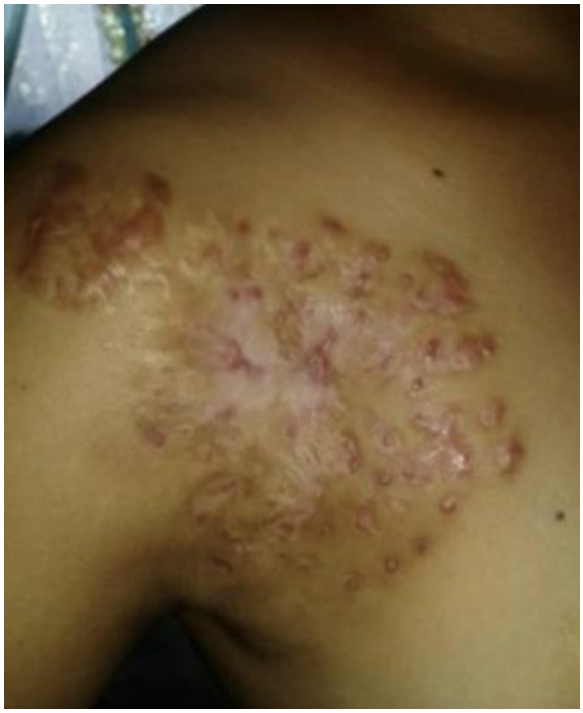


Figure 7 Scarring of the micetoma lesions after 6 months of treatment

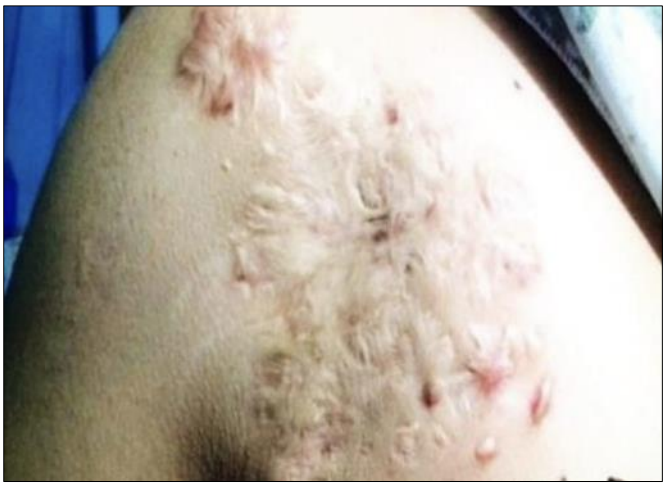


Figure 8 Scarred lesions of the micetoma at the end of the treatment. Patient with keloid scarring

3. Discussion

Nocardiosis, specifically micetoma caused by *Nocardia brasiliensis*, is a fungal infection that is reported in various parts of the world and presents in different clinical forms, the disease is commonly associated with minor traumas, where contaminated material from the soil comes into direct contact with the skin. Regarding the progression of the condition that our patient developed, as well as the clinical manifestations, they coincide with previous reports that state that these fungal infections develop in a slow and progressive manner. They produce multiple fistulas through which purulent material is discharged, and they can lead to the functional impairment of the affected limb due to the extensive destruction of both bone and soft tissues (18,19).

As it is a chronic problem, people who suffer from it often do not give it the proper importance and seek medical attention at a late stage (20). Another probable issue is that a precise etiological diagnosis is rarely made, and the therapy administered is generally inappropriate, as was the case in this instance. Therefore, it is important to emphasize the identification of the causative agent and establish the appropriate therapeutic approach (20,21,22).

4. Conclusion

This case highlights the risk of Mycetoma in patients with a history of skin trauma with cacti. Long-term follow-up with a multidisciplinary team is important to control the increased risk of developing the disease in advanced stages, which definitely affects the life of patients and their families due to the sequelae it generates. Indeed, early diagnosis with an appropriate study protocol is crucial to improve patient outcomes and achieve successful treatment in patients.

More research is needed in the endemic areas where cases occur as well as dissemination of information to the population to better understand the link between skin trauma and the development of mycetoma.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no competing interests to declare.

Statement of ethical approval

This work adheres to the regulations of the General Health Law on research, second title of the ethical aspects of research on human beings, Chapter 1, Article 17.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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