CASE REPORT

Mycetoma. Case report

María Caridad Arbolaez Goicochea[1]*, Yurexis Rodríguez Cruz[2], Damarys Nuria Salina Fernández[3]

[1]"Arnaldo Milián Castro" University Clinical Surgical Provincial Hospital, Santa Clara, Villa Clara, Cuba
[2]"Camilo Cienfuegos" University Polyclinic, Habana del Este, Havana, Cuba
[3]"Oscar Alberto Ortega Ortega" North Docent Polyclinic, Palma Soriano, Santiago de Cuba, Cuba

***María Caridad Arbolaez Goicochea.** mariacaridadarbolaez@gmail.com

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ABSTRACT

Introduction: mycetoma is a chronic inflammatory anatomoclinical syndrome consisting of enlargement, deformation of the affected region and nodular lesions.
Patient information: it was presented a case of mycetoma of the lower limb caused by *Nocardia* in a 48-year-old female patient with human immunodeficiency virus, who, after recurrent trauma to both lower limbs, reported to the dermatology office that four years ago he had lesions on his left foot, initially painless nodules that later began with yellowish exudation, moderate pain and inflammation in that area. The anatomopathological and microbiological studies confirmed the presence of the genus *Nocardia* as the causative agent of actinomycetoma. Antimicrobial therapy with trimethoprim/sulfametosaxol and diaminodiphenyl sulfone was started and total resolution of the lesions was achieved.
Conclusions: the diagnosis of this disease should be made from an integral perspective taking into account clinical, epidemiological, microbiological, anatomopathological and radiological aspects that contribute to establish the burden of morbidity and mortality caused by this clinical condition.
Key words: mycetoma; eumycetoma; actinomycetoma; nocardia

RESUMEN

Introducción: el micetoma es un síndrome anatomoclínico de tipo inflamatorio crónico constituido por aumento de volumen, deformación de la región que afecta y lesiones de aspecto nodular.
Información del paciente: se presentó un caso de micetoma de miembro inferior causado por *Nocardia* en una paciente con virus inmunodeficiencia humana, de 48 años de edad y sexo femenino, que tras traumas recurrentes en ambos miembros inferiores refirió, en la Consulta de Dermatología, que hace cuatro años comenzó con lesiones en el pie izquierdo, inicialmente nódulos indoloros que luego comenzaron con exudación amarillenta, dolor moderado e inflamación en esa área. El estudio anatomopatológico y el

microbiológico confirmaron la presencia del género *Nocardia* como agente causal de actinomicetoma. Se inició terapia antimicrobiana con trimetropim/sulfametosaxol y diaminodifenil-sulfona y se logró total resolución de las lesiones.
Conclusiones: el diagnóstico de esta enfermedad debe realizarse desde una perspectiva integral teniendo en cuenta aspectos clínicos, epidemiológicos, microbiológicos, anatomopatológicos y radiológicos que contribuyan a establecer la carga de morbilidad y mortalidad que aporta esta condición clínica.
Palabras clave: micetoma; eumicetoma; actinomicetoma; nocardia

INTRODUCTION

Mycetoma (madura foot, maduromycosis or fungal tumor) is a chronic inflammatory anatomoclinical syndrome characterized by an increase in volume, deformation of the affected region and nodular and fistulized lesions from which a filamentous exudate drains containing the parasitic forms called grains; it is a subcutaneous infection by implantation. By its etiology it is divided into two types: eumycetoma, caused by filamentous fungi, and actinomycetoma, caused by various aerobic filamentous actinomycetes (bacteria).[1,2,3,4] This disease has been reported in Asia, Latin America, Europe and Africa; however, most cases are reported in Sudan, India and Mexico and reports from Africa are scarce, but it is known to be a major health problem in tropical and subtropical regions. For this reason the World Health Organization (WHO) recently recognized mycetoma as a neglected tropical disease (NTD) during the 69th World Health Assembly.[2,3]
Epidemiological data from different areas show that males are more affected (sex ratio 3-4:1), with ages between the third and fourth decades of life (20-40 years). Some studies have reported that 3-5% of cases affect children engaged in field work.[1,2,3,4] Mycetoma is common in people working in rudimentary conditions, without protective clothing or shoes, leading to the presentation of the disease, mainly in poor rural workers or housewives involved in outdoor activities.[4] Several studies have been conducted from the African continent on the behavior of mycetoma;[3,4,5,6] however, there is no report of this condition in Botswana because this condition is not notifiable and because the magnitude and burden of disease are not well defined. For these purposes, sharing any available information is valid, which is why this case is presented.

PATIENT INFORMATION

A 41-year-old female patient, resident of Kasane District, approximately 550 km from Francistown City, Botswana, black, housewife, with a history of human immunodeficiency virus (HIV) positive, with eight years of evolution and adherent to antiretroviral treatment. She reported recurrent mild trauma to both feet and stated that she does not usually wear shoes at home. She came to the dermatology office because four years ago she started with lesions on her left foot, initially painless nodules that later started with yellowish exudation, moderate pain and inflammation in that area. The patient reported having undergone multiple treatments with analgesics and antibiotics, without clinical

improvement. Physical examination revealed faint yellow nodules on the left foot, with fistulous orifices and seropurulent exudate, with yellowish grains, as well as edema, pain and perilesional erythema with associated deformity (Figures 1 and 2); painful lymphadenopathies were observed in the left inguinal region. Initially the clinical diagnosis was mycetoma, without being able to define the bacterial or fungal etiology; complementary studies were indicated to determine the causal agent and the therapeutic strategy

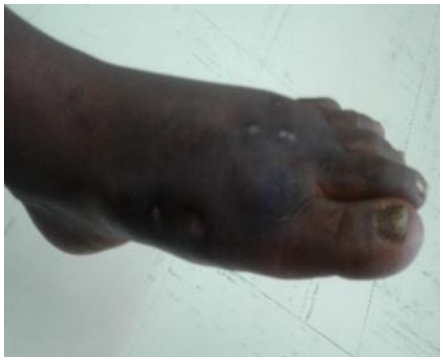

Figure 1. Clinical appearance of the lesions located on the dorsum of the left foot showing enlargement and deformity. Mycetoma

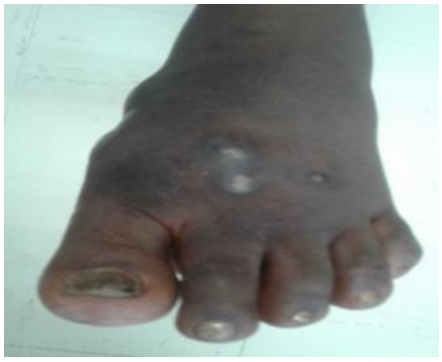

Figure 2. Chronic dermatosis on the left foot, showing fistulous orifices and yellowish-white granules. Mycetoma

Laboratory tests

Leukogram: 7.61x10^3U/l
Neutrophils: 64.3%
Lymphocytes: 28,3%
Monocytes: 7,00%
Eosinophils: 0,30%
Basophils: 0.10%
Red blood cell count: 3.93x10^6U/l
Hemoglobin: 11.3 g/dl
Hematocrit: 36.5%
Platelet count: 337x10^3 U/l

Urea: 2.93 mmol/l
Creatinine: 47.70 umol/l
Blood Sugar: 6.50 mmol/l
Aspartate amino transferase: 24 U/l
Alanine aminotransferase: 39.2 U/l
Total proteins: 86.80 g/l
CD4%: 21.22%
Absolute CD4 count: 260 cells
HIV viral load: <400

Histopathology

Macroscopic study from tissue (skin biopsy of the left foot) reported that a 1.3x0.7 cm skin tissue was received in which the surface showed a sinuous fistulous path with seropurulent exudate and yellowish-white granules inside; Microscopically, hematoxylin-eosin (H-E) staining evidenced a granulomatous reaction, a lobulated grain surrounded by polymorphonuclear cells, with an intensely basophilic area inside and a hyaline eosinophilic area around it (image in bright sunlight), this structure represents the actinomycetic grain characteristic of this disease (actinomycetoma) -Figure 3.

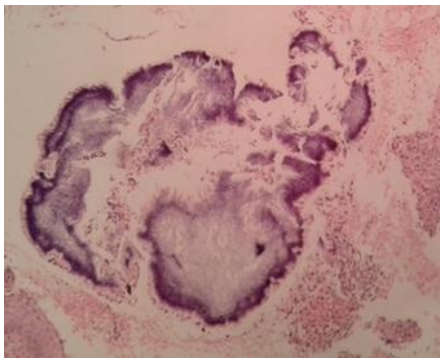

Figura 3. Actinomycetic granuloma, eosinophilic clavules, characteristic of *Nocardia spp*. are seen (H-E 40x)

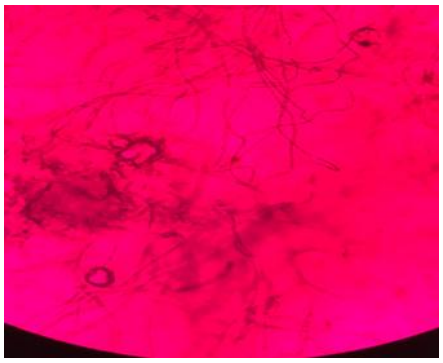

Figure 4. Gram stain, shows Gram-positive, branched, chain-positive bacilli

Microbiology

Microbiological examination was performed with traditional methods and revealed:

Gram stain: Gram-positive bacilli in chain, branched, non-sporulated (Figure 4). Ziehl-Neelsen staining showed acid fastness and no fungal structures were observed in the 10% potassium hydroxide (KOH) preparation. The sample was seeded on Sabouraud Dextrose Agar (SDA), SDA with chloramphenicol and cycloheximide (ADSCC), blood agar (BA), chocolate agar (CCA) and Mc Conkey agar (MCCA) and incubated at 25ºC and 35ºC, respectively, in the presence of oxygen. Growth of the causative agent was obtained at approximately 72 hours, a dry yellowish-white rough colony was produced (yellowish-white rough colonies impressed deeply anchored in the agar) -Figures 5 and 6-. The isolation and identification of the strain took into account its behavior against the stains used, its morphological cultural characteristics and some biochemical traits; not all culture media and the necessary reagents were available, which did not allow the identification of the species, but did allow the definition of the genus as *Nocardia*.

Figure 5. Colonies of *Nocardia spp*. on blood agar

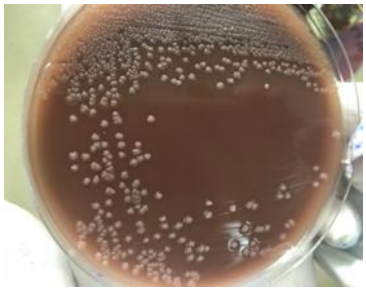

Figure 6. Colonies of *Nocardia spp*. on chocolate agar

Radiological report

There was an increase in the density of the soft tissues of the left foot with increased thickness, radiological signs of osteoporosis, predominantly juxta-articular. Decreased interphalangeal spaces and deformity in distal phalangeal tufts. No osteolytic or osteoblastic images are defined, no images of loss of bone

continuity suggesting fractures and no periostitis, confirming the absence of bone involvement related to the disease.
On regional radiography: left foot, frontal and lateral views (Figures 7 and 8).

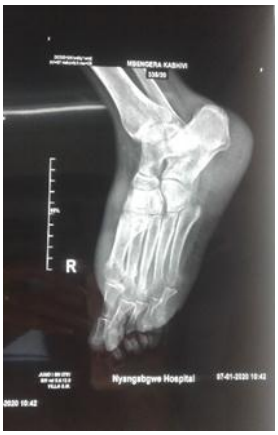

Figure 7. Lateral view of the left foot

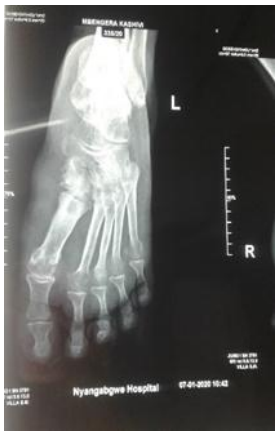

Figure 8. Front view of the left foot

The case was concluded as actinomycetoma due to *Nocardia spp*. and treatment was started with trimethoprim/sulfametosaxol (800/160 mg once a day), combined with dapsone (diaminodiphenyl sulfone) -100mg daily, single dose. Total resolution of the lesions was achieved in week 8 of evolution. After her remission the patient did not return to the office for follow-up.

DISCUSSION

Actinomycetoma or actinomycetic mycetoma is caused by filamentous, aerobic, Gram-positive actinomycetes; most cases are included in three genera: *Nocardia*, *Actinomadura* and *Streptomyces*; *Nocardia brasilensis* and *Nocardia asteroides* are frequently isolated species.[1,4,7] Eumycetoma or eumycetic mycetoma is caused by filamentous, septate, pigmented or black and hyaline or white fungi. The etiologic agents are included in several genera, among which black fungi (*Madurella, Pyrenochaeta, Exophiala, Leptosphaeria and Curvularia*) and white fungi (*Pseudallescheria, Acremonium and Fusarium*) stand out.[1] The clinical presentation can be similar, independently of the causal pathogen; however, the bacterial or fungal etiology of this disease defines its therapeutic management and, in many occasions, its evolution and prognosis.
Mycetoma is endemic in tropical and subtropical regions, between latitudes 15° South and 30° North (arid areas with short rainy seasons, countries located between the tropics of Cancer and Capricorn). This area has been called the "mycetoma geographical belt", which includes countries such as Saudi Arabia, Argentina, Brazil, Colombia, India, Mexico, Nigeria, Senegal, Somalia, Sudan, Venezuela and Yemen, among others.[1,2,3,4,5]
The causative agents of mycetoma present considerable variations in their geographical distribution but, in general, they have in common that they are most frequently reported in arid, dry geographical areas with short rainy seasons and

low relative humidity. Eumycetomas predominate in Africa, Asia and especially India, while actinomycetomas are more common in Latin America. Worldwide, 60% of reported cases are actinomycetoma and 40% are eumycetoma.[5,6] Only about 20% of African countries have published information.[4] The disease mainly affects young adult patients in productive ages of life; however, mycetoma has been described in all ages. Common risk groups include farmers, herders and workers in a low socioeconomic environment. It is a chronic subcutaneous granulomatous disease preceded by traumatic implantation of the pathogen, a classic example of neglected or neglected diseases.[1,3,6,7]

The condition described occurs in the skin and subcutaneous cellular tissue, but can also involve muscle fascia, tendons, muscles and bones. The lower limbs, followed by the upper limbs, are the most affected regions, but have also been reported in the thorax, abdominal wall, jaw, paranasal sinuses, orbit, eyelids, skull and central nervous system, vulva, scrotum and surgical incisions. The lesions are characterized by an increase in volume, which may be accompanied by the presence of fistulas and seropurulent exudate, with a slow and progressive evolution over months or years.[8] To achieve cure it is important to define the fungal or bacterial etiology because the treatment for each is completely different. Actinomycetoma is currently treated with antibiotics, which can be used alone or in different combinations, depending on the severity, dissemination and location of the disease. Medical cure is usually achieved if the patient receives adequate treatment; in contrast, treatment of eumycetoma consists of antifungals and surgical excision. Medical cure is more difficult to obtain and the extent and location of the disease can lead to chronic progressive lesions often leading to amputation; in both forms of mycetoma, prolonged treatment is necessary. Three genera (*Nocardia, Streptomyces* and *Actinomadura*) comprise the most frequent causative agents of actinomycetoma.[9] *Nocardia brasiliensis*, in particular, is cited by several authors as the most common cause of mycetoma so far.[6,10]

Nocardia spp. are Gram-positive, aerobic, filamentous, branched, Gram-positive bacilli, fragmenting into coccoid and bacillary, acid-fast elements, possessing a characteristic aerial mycelium, visible under the light microscope. These microorganisms are immotile, non-capsulated, non-sporulating, with oxidative metabolism, catalase-positive. Most of the species develop at 20°C and up to 45°C. Colonial appearance is variable: it can be smooth, granular, irregular, wrinkled or stacked. Carotenoid-like pigments impart orange, pink, red or yellow shades to colonies on solid culture media. Soluble brown or yellowish diffusible pigments may be produced. In the culture medium they give off a characteristic musty or wet earthy odor. They are present in soil, decaying organic matter and water. They are not part of the human or animal microbiota, but can cause various diseases in both species. Invasive forms include pulmonary nocardiosis and disseminated disease which notoriously affect immunocompromised patients. Primary cutaneous nocardiosis is seen in immunocompetent patients and may present as actinomycetomas and superficial skin infections, with pustules, abscesses, granulomas or cellulitis, or as lymphocutaneous forms.[10]

Effective medical treatment of actinomycetoma began in the early 1940s and 1950s with the use of sulfonamides and diaminodiphenylsulfone (DDS) and achieved cure in some cases. In the 1960s trimethoprim-sulfamethoxazole became the standard treatment for actinomycetoma. Currently other drug combinations are considered in its treatment such as: trimethoprim-sulfamethoxazole, dapsone, amikacin, amoxicillin/clavulanic acid, minocycline, moxifloxacin, linezolid and carbapenemics, among others.[9,11,12,13] Synergism from combined treatment guidelines is beneficial in order to reduce antimicrobial resistance, favored by the prolonged therapy that, in many occasions, this disease demands.

It is presented a case of actinomycetous mycetoma by *Nocardia spp*. in an HIV-positive patient, although the eumycetoma variant of this disease is frequent in the African continent and systemic forms of nocardiasis are usually more common in the presence of some degree of immunocompromise, this report corroborates that in medical practice any clinical variant is valid depending on the success of the interrelation between susceptible host, causal agent and environment. The diagnosis of this disease should be made from an integral perspective taking into account clinical, epidemiological, microbiological, pathological and radiological aspects that contribute to establish the burden of morbidity and mortality in Botswana.

Informed consent

Informed consent was obtained from the patient for the preparation of the case report.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.