A case report of black grain Mycetoma: The role of surgical intervention at a resource-limited center in Kilimanjaro region, Tanzania

N. Mosha[1,2], A. Mremi[2,4], L. Kini[1,2], G. Semango[3], J. Mshana[1], D. Mavura[1], J. Masenga[1,2]

Introduction

Mycetoma is a chronic, progressively destructive granulomatous infectious disease of the subcutaneous tissues that spreads to affect the skin, deep tissues, and bone. [1] Mycetoma is a neglected tropical disease caused by true fungi (eumycetoma) or aerobic actinomycetes (actinomycetoma). [1,2] So far, more than 90 different bacteria and fungi have been indicated as causative agents. *Nocardia brasiliensis*, *Streptomyces somaliensis*, *Actinomadura madurae*, and *Madurella mycetomatis* are the main species responsible for causing Actino- and Eumycetomas, respectively. [3] In East-Africa, *Streptomyces somaliensis* is more common than *Nocardia brasiliensis* and *Actinomadura madurae*. It affects mainly poor people in remote areas, which may explain why it did not appear on any list of neglected tropical diseases until a few years ago and was not considered a priority by health authorities. Since 2016, it has been recognized by the WHO as a neglected tropical disease (NTD). [4] Since 2023, eumycetoma causative agents have been listed as high priority fungal pathogens by the WHO. [5] It causes considerable chronic morbidity and often leads to the amputation of limbs after years of suffering. In severe cases, there is also mortality. Generally, when myceoma is diagnosed early, it can be treated by simple medical treatment with limited surgery when needed; therefore, it deserves far more awareness to allow early detection. [6]

Mycetoma usually starts following minimal trauma, e.g., a thorn prick that introduces the disease-causing organism into the subcutaneous tissue. The causative agent will form grains and tiny granules in this tissue. A small papule will grow and progressively develop into subcutaneous tumors, which progress to form multiple sinuses secreting pus-containing grains with extensive surrounding tissue granulation. Although mycetoma typically affects the foot, it can also affect other body parts, such as the hands. [3] The true incidence of mycetoma is not known; in many endemic areas, mycetoma occurs in remote places, and many patients lack the education or financial means to report to a hospital for treatment; others may fear amputation of the affected limb. [4] Most of the cases were found by searching archives from a single hospital in a single city in an area. [2,7] If the disease is left untreated, it significantly impairs the individual's quality of life since it can cause significant tissue disfigurement, deformity, joint ankylosis, and loss of function. In such a situation, amputation is advised.

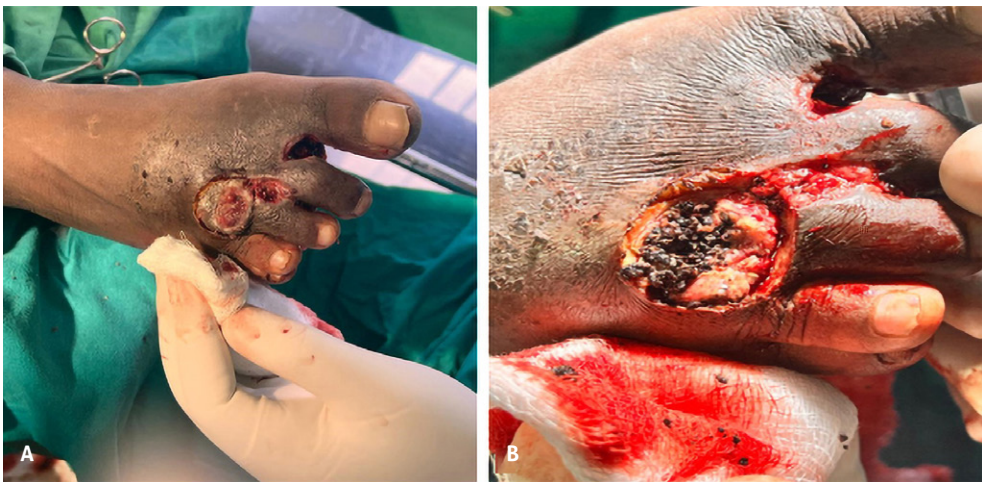

Figure 1. Clinical presentation of the patient with eumycetoma demonstrating multiple ulcerated nodules, granulation tissue and scars on the dorsal surface of the forefoot (A). A close view of same patient showing black grains from the lesions (B).

1. Regional Dermatology Training Centre, Box 8332, Moshi, Tanzania
2. Faculty of Medicine, Kilimanjaro Christian Medical University College, Moshi, Tanzania
3. School of Life Sciences and Bioengineering, Nelson Mandela-African Institution of Science and Technology, P.O. Box 447, Arusha, Tanzania
4. Department of Pathology, Kilimanjaro Christian Medical Centre, Moshi, Tanzania

Figure 2. Photographs of the patient showing the decontaminated mycetoma lesion (A), and appearance of the lesion after surgical debridement (B).

Case examination

A 26-year-old male from the Monduli area of the Arusha region, northern Tanzania, attended the dermatology clinic at our center for a progressive ulcerating swelling on the ventral and dorsal parts of his right forefoot. Though painless, the swelling was infiltrating the plantar surfaces, and it had been there for about two years. The onset of the lesion followed a minor injury he suffered when he stepped over thorns while working with his cattle. He had been using local herbs without improvement. Unfortunately, details on specific types of herbs are not available.

On examination of the right foot, there was soft tissue swelling associated with multiple sinuses discharging purulent material together with black grains (figures 1A-B). The toenails were undisturbed. The patient's past medical history and his general examination were essentially unremarkable. He had no enlarged regional lymph nodes. His laboratory workups, including the complete blood count (CBC), complete metabolism panel (CMP), hemoglobin level (Hb), lipid panel, and thyroid stimulating hormone (TSH), were within normal limits. The x-ray of the right foot showed soft tissue involved, while the bone cortex and density appeared normal. A clinical

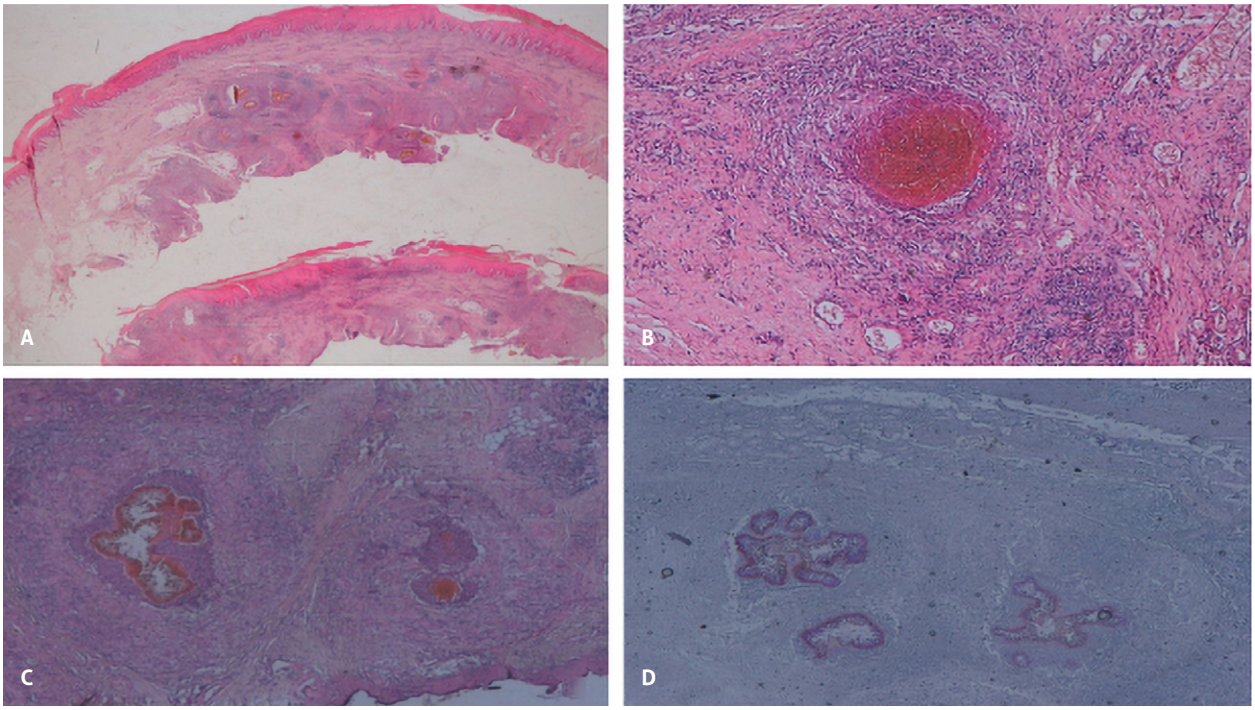

Figure 3. Microscopic images of the eumycetoma highlighting zones of suppuration and suppurative granulomatous inflammation in the dermis and subcutis, H&E staining at 20x original magnification (A), H&E staining at 100x original magnification; the fungal granules with interlacing hyphae embedded in interstitial brownish matrix demonstrated on Periodic Acid Schiff (PAS) at 40x original magnification (C &D).

diagnosis of mycetoma was entertained. An incisional biopsy was performed. Histopathology from the lesion demonstrated confluent zones of suppuration and longstanding suppurative granulomatous inflammation in the dermis and subcutis (figures 3A-B). The presence of granules with interlacing hyphae embedded in an interstitial brownish matrix was demonstrated with a Periodic Acid Schiff (PAS) stain. The fungal hyphae were embedded in a cement material, and the cement material was found throughout the grain, indicating Madurella species (figures 3C-D). Cultures of the grains on Sabouraud's and Mycosel agar were positive for *Madurella mycetomatis* with the typical diffusing pigment. An extensive surgical debridement was scheduled. A thorough decontamination of the skin surface and surgical debridement were undertaken, where black grains were extracted using a sterile spatula over filter paper and rinsed several times (figures 2A-B). The patient was kept on Cap Itraconazole 400 mg daily and showed considerable improvements afterwards. However, he got lost in the follow-up after a three-month follow-up.

Discussion

Mycetoma, previously known as 'Madura Foot', was first described by Vandyke Carter in the 1860s in Madurai, India. [8] As mirrored in our case, the typical clinical condition is made up of three components: subcutaneous mass, sinus formation, and purulent discharge that contains grains reflecting an infectious disease etiological agent. [9] In grains, fungal hyphae are found, often embedded in a cement material with a crust or shell of fibrin derived from host tissues. The color of the grain may indicate the etiological agent. Black grains are almost always fungi. There are no bacteria reported that cause black grain mycetoma. Actinomycetoma grains are most often white or yellow. Only the grains of *Actinomadura pelletieri* are red. [3] This differentiation is important due to the different treatments needed. Actinomycetomas are caused by filamentous bacteria. The commonest causative agent is Actinomadura madurae. Others include causative agents such as *Nocardia brasiliensis*, *Actinomyces israelii*, and *Streptomyces somaliensis*, which respond to antibiotics, e.g. trimethoprim-sulfametoxazole, amickacin, and amoxicillin-clavulanic acid. On the other hand, eumycetomas are caused by true fungi with thick septate hyphae, e.g. *Madurella mycetomatis*, *Trematosphaeria grisea*, and *Pseudoallescheria boydii* are resistant to most forms of treatment. [10] However, as evidenced in this patient, itraconazole can be useful. Our patient initially experienced a good treatment response following medical and surgical management before he lost track of follow-up.

As evidenced in the index case, mycetoma lesions are usually on the lower limb, involving one foot. Eumycotic mycetoma occurs after the traumatic inoculation of fungi through the skin. From there, local spread occurs to lymph nodes and bones; hematogenous metastatic spread may also occur to other parts of the body. Late complications of mycetoma include extension to the underlying bones and joints, leading to periostitis, osteomyelitis, and arthritis, and destruction of the bone, leading to gross deformity. [11] Our patient conforms only partially to this description because the disease was in an initial state. Though he had none of these, it is important to keep a regular follow-up to detect and manage these complications as and when they arise. Microscopic examination of grains shows whether the grain is composed of small actinomycetes or broader fungal filaments, as well as color.

Our patient was confirmed to have eumycetoma by histopathology examination and fungal cultures. Fungal cultures of the grains were positive for *Madurella mycetomatis* with the typical diffusing pigment. Modern methods like PCR were not available. Mycetma case studies have also been reported from Kenya and Uganda. [12,13]. In the study by Colom et al [14], molecular identification was performed in some of the cases. From the black grain eumycetoma, four *Madurella mycetomatis* and three *Madurella fahalii* were found. In their study, Kwizera et al, [13] identified 249 mycetoma cases in 70 times based on histology. Of these, 221 cases were fungal. Mavura et al, [15] in 2021, described a case series of mycetoma in Moshi, Tanzania. The findings from the previous studies and the index case suggest that mycetoma is prevalent in East Africa but underreported, possibly because of inadequate mechanisms for official reporting and the general lack of identification facilities in many limited-resource settings. A routine program and system should be developed to identify and document the burden of fungal infections in the region. Diagnosis and treatment guidelines should be developed.

Treatments for eumycetoma and actinomycetoma are different. The standard treatment for eumycetoma consists of itraconazole combined with surgery whereas actinomycetoma is treated with antibacterial agents. Both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) do not recommend the use of ketoconazole. [10,11,12,13,16]. A successful reconstruction surgery may be challenging, and recurrence is common. [6]

A potential caveat for our case study is the lack of essential information, such as the types of local herbs the patient used before attending the hospital. Similarly, because the patient lost follow-up, our case study lacks information on prognosis and treatment outcomes. Moreover, molecular subtyping of the mycetomas was not feasible in our setting due to resource constraints. Additionally, the details regarding the size of the grains were not recorded. Lack of essential information in the index case may imply that the preoperative diagnosis was inadequate, thus potentially leading to the patient's suboptimal treatment.

In conclusion, mycetoma is a common condition in Tanzania; though the number of reported or published cases is low, this could be attributed to several factors, including poverty and low diagnostic capacity, both clinical and laboratory. Therefore, clinicians need to recognize mycetoma early and institute treatment promptly to reduce the substantial morbidity associated with this devastating infection.

Abstract

Mycetoma is a chronic infectious disease of the skin and subcutaneous tissue leading to disfigurement and disability. Typically, mycetoma is characterized by the triad of tumefaction, draining sinuses, and the presence of grains in the exudate. It is caused by fungi or bacteria; hence, it is called eumycetoma or actinomycetoma, respectively. *Madurella mycetomatis* mostly causes eumycetoma, while *Nocardia brasiliensis* and *Streptomyces somaliensis* are the most common pathogens in actinomycetoma. Treatment approaches for the two groups are quite different. Actinomycetoma with antibiotics and Eumycetoma nearly always without success with antifungals. We present a patient with a diagnosis of mycetoma acquired through trauma to the foot. Histopathology results from the biopsy specimen reported black grains with filaments in an abscess surrounded by macrophages, giant cells, and lymphocytes. The lesion was surgically treated, followed by itraconazole for 3 months with a significant improvement. Unfortunately, the patient got lost in follow-up. Herein, we discussed the epidemiology, etiological agents, clinical presentation, diagnosis, and treatment of mycetomas.

Keywords

Mycetoma – eumycetoma – actinomycetoma - limited-resources - case report

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Correspondentieadres

Nelson Mosha

E-mail: nelsonmosha8@gmail.com