

Mycetoma of the Foot Caused by *Madurella Mycetomatis* in Immigrants from Sudan

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ABSTRACT: **Background:** Mycetoma is a chronic and destructive infection caused by either fungus or bacteria. Mycetoma has a characteristic clinical presentation of a triad of tumor-like swelling, draining sinuses, and macroscopic grains. Mycetoma infection is extremely rare in Israel; however, in view of the recent immigration from mycetoma-hyperendemic regions of Africa to Israel, physicians in Israel may encounter this infection.

Objectives: To present two cases of mycetoma caused by *Madurella mycetomatis* in immigrants from endemic regions in Sudan treated at our hospital, and review the current literature.

Conclusions: Health care professionals in Israel should suspect mycetoma in patients from endemic countries who present with tumor-like swelling especially in the lower extremity. Health care workers should be able to recognize mycetoma and provide the optimal treatment before the lesion progresses to an advanced and disabling disease.

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Mycetoma is a chronic and destructive cutaneous and subcutaneous infection caused by either a fungus (eumycetoma or mycotic mycetoma) or bacteria (actinomycetoma). The characteristic clinical presentation includes a triad of tumor-like swelling, draining sinuses, and macroscopic grains [1]. Soil is the natural reservoir for most of the numerous pathogens causing mycetoma, and the infection usually follows a traumatic inoculation of the pathogen into subcutaneous tissue via contaminated mechanical vectors (e.g., a thorn or splinter). This infection can spread and involve fascia, muscle, bone and regional lymph nodes [2].

Mycetoma has a particular geographic distribution, with the highest prevalence and incidence in equatorial, tropical and subtropical areas known as the “mycetoma belt” [3-5], although cases have been reported worldwide [6-8]. *Madurella mycetomatis* is the most prevalent cause of mycotic mycetoma worldwide [7], and this agent is particularly endemic in Sudan [9]. Mycetoma occurs typically in young men, especially farmers, who are exposed to contaminated soil [7].

Mycetoma infection is rare in Israel. There is sparse evidence in the literature of this infection, with only one case of locally acquired eumycetoma caused by *M. mycetomatis* reported [10]. In the last decade there has been significant immigration from mycetoma-endemic regions of Africa to Israel. We report here on two patients with eumycetoma of the foot treated at our hospital.

PATIENT DESCRIPTIONS

PATIENT 1

A 32 year old man from the Gezira region in Sudan (southeast of Khartoum) presented at our hospital with soft tissue swelling in his right foot and secreting sinuses [Figure 1]. The patient had immigrated to Israel several years before presentation. He did not recall any predisposing injury and did not suffer from systemic symptoms. Before presenting to our hospital, he underwent several surgical procedures in Sudan and in Israel.

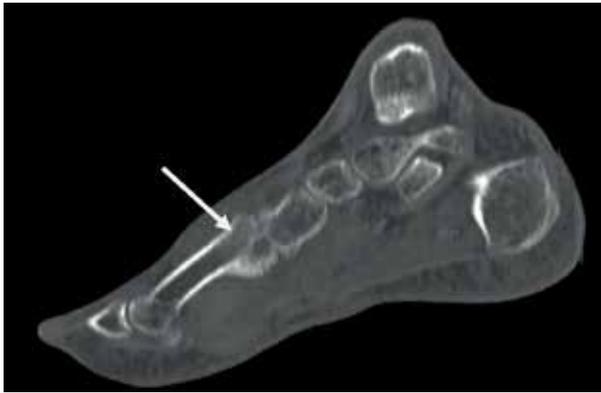
He was admitted to the orthopedic oncology department in our hospital for further investigation of suspected malignancy. On physical examination, the patient had a large swelling in the dorsum of his right foot with sinuses draining purulent fluid. Other than that his examination was unremarkable.

A computed tomography (CT) scan with radiocontrast agent demonstrated infiltrating and destructive process involving the first metatarsal bone and extending into the skin. In

Figure 1. Lesion, after incision and drainage, with secreting sinuses



Figure 2. Lesion in the first metatarsal bone with soft tissue swelling, infiltrating the bone and the soft tissue. Within the infiltrate are several hyperdense rounded lesions, the largest under the first metatarsal bone (arrow). In addition, there is an osseous remodeling component and a periosteal reaction



addition, there was tissue swelling in the medial aspect of the right foot with an osseous remodeling component and a periosteal reaction. Within the infiltration there were six hyperdense round lesions, the largest measuring 2.2 x 2.5 cm [Figure 2].

An open biopsy of the lesion was performed, and during the procedure a large amount of black grains was seen, with a reactive inflammatory process surrounding the lesion. Samples from the tissue and from the black grains were sent for microbiological and histopathologic evaluation [Figure 3A and B].

Specimens were negative on bacterial culture, Ziehl-Neelsen stain and culture for mycobacteria. Fungal culture was positive for *M. mycetomatis*, which grew slowly and was identified only after 6 weeks. The patient was treated with itraconazole, and examination a few weeks later showed mild abatement in the swelling.

PATIENT 2

A 23 year old man, also from the Gezira region in Sudan, was admitted to the orthopedic oncology department in our institution due to a large secreting tumor-like swelling in the distal dorsal part of his right foot [Figure 4].

The patient immigrated to Israel a year and a half before presentation and had been suffering from this lesion for more than 2 years. He could not recall any traumatic injury to the foot prior to the appearance of the lesion but did recall that a heavy object fell on his foot a few months earlier. Following that injury the lesion increased in size, reaching its current size of approximately 5 x 3 cm. In addition, a few sinuses secreting black material appeared on the foot. The patient's physical examination was unremarkable except for the lesion described here. X-ray images demonstrated an osteolytic lesion of the second metatarsal bone on the right.

Figure 3. [A] Fibrous tissue and bone fragments (black arrow) infiltrated by numerous fungal aggregations (white arrow) that are positive for periodic-acid Schiff and silver histochemical stains. There is also widespread chronic inflammation composed of lymphoid aggregates and plasma cells (magnification x100). **[B]** Magnification of the fungal aggregation: branching hyphae and septated filaments of *Madurella mycetomatis* (magnification x400)

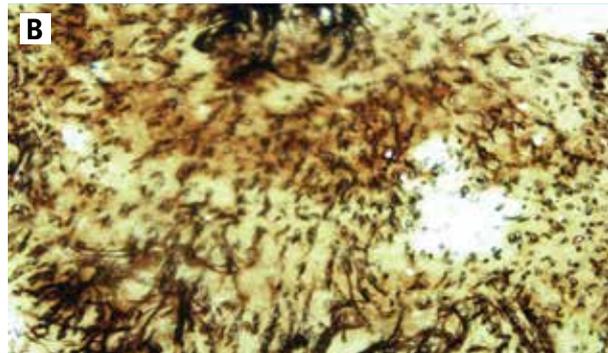
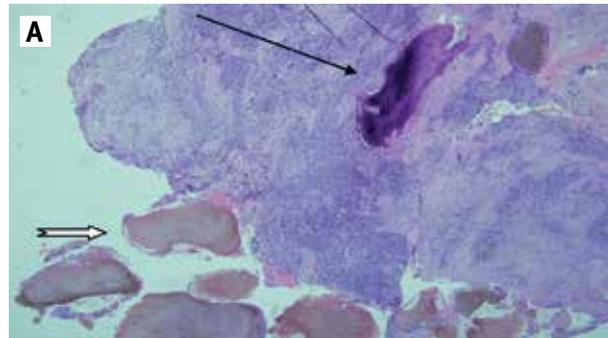


Figure 4. Large secreting tumor-like swelling on right foot



The purulent discharge from the wound, including the black grains, was sent for microbiological examination. On direct microscopic smear, no fungal elements were seen. Cultures were positive for *Staphylococcus aureus* and *Enterobacter cloacae*. After 6 weeks, *M. mycetomatis* was identified on culture.

Treatment was started with itraconazole and a short course of trimethoprim/sulfamethoxazole for the secondary bacterial infection. At a follow-up visit 6 weeks later, the lesion had significantly decreased in size with no discharge of pus or black grains.

DISCUSSION

Mycetoma is a chronic granulomatous inflammatory disease caused by true fungi (eumycetoma or mycotic mycetoma) or filamentous bacteria (actinomycetoma). It can spread from cutaneous and subcutaneous tissue to deep structures. This disease has a slowly progressive course and may evolve over years to decades.

Mycetoma infection is prevalent in the “mycetoma belt,” which stretches between the latitudes of 15 degrees south and 30 degrees north and is endemic in relatively arid areas [3]. At present, the global burden of mycetoma is still not known. The first documented cases of mycetoma were described in 1842 [4]. In 1956, Abott [12] published a series of 1321 mycetoma cases in Sudan during a 2.5 year period, which indicated that the burden of mycetoma was higher than previously thought. A meta-analysis published in 2013 by Van de Sande [7] included a total of 8763 mycetoma cases from around the world. It appeared that most cases were reported from Mexico, Sudan and India, and that the fungus *M. mycetomatis* was the most prevalent causative agent worldwide. Although their study represents the first indication of the global burden of mycetoma, the actual burden is probably much higher. The low numbers of documented mycetoma infection cases are probably due to under-diagnosing and under-reporting, mainly because mycetoma is not a reportable disease. Many reports of mycetoma, like the two cases presented here, are from Sudan [4,9,12,13]. Some even consider Sudan to be the “homeland of mycetoma” [4].

Mycetoma requires long-term treatment, consisting of a combination of surgical procedures (debridement, advanced excision or amputation) and prolonged medical therapy [14]. In the absence of a correct diagnosis and appropriate treatment, mycetoma can lead to significant morbidity due to bone destruction and deformities. Other complications that can occur include lymphatic obstruction, secondary bacterial infection, pathological fractures, osteopenia and osteoporosis [15,16].

Mycetoma infection is extremely rare in Israel [17-19]. However, due to recent immigration from mycetoma-hyperendemic areas, physicians in Israel may encounter this condition. Health care workers should be able to recognize mycetoma and provide the optimal treatment before the lesion progresses to an advanced and disabling disease. They should be aware of this entity and suspect mycetoma in patients from endemic countries, such as Sudan and Eritrea, who present with tumor-like swelling, especially when the patient is a young man and the lesion involves the lower extremity. In order to better recognize and manage this infection, there should be a high index of suspicion for mycetoma, and appropriate sampling of the lesion should include the grains.

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“Never idealize others. They will never live up to your expectations”

Leo Buscaglia (1924-1998), American author and motivational speaker, also known as “Dr. Love,” and a professor in the Department of Special Education at the University of Southern California