

## A 48-year-old male immigrant with a painful foot mass

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### CASE PRESENTATION

A 48-year-old male immigrant from Myanmar (Southeast Asia) presented with a right dorsal foot mass that had been progressively enlarging for the past five years. The patient could not recall any precipitating events or trauma. It caused him mild pain, especially with ambulation. His medical history was significant for hypertension and tobacco use. He did not have diabetes or history of peripheral vascular disease. He immigrated to the United States approximately four years previously. On examination, there was no ulceration or draining sinuses. He had a strong posterior tibial pulse bilaterally and good capillary refill time; however, the right-sided dorsalis pedis pulse was not palpable. He had no evidence of neuropathy. There was no associated fever, lymphadenopathy or weight loss. Laboratory test results revealed a hemoglobin level of 157 g/L and white blood cell count of  $5.4 \times 10^9$  cells/L without eosinophilia. Chemistry tests showed a creatinine level of 61.0  $\mu\text{mol/L}$ , aspartate aminotransferase level of 33 U/L and alanine aminotransferase level of 19 U/L. Magnetic resonance imaging of the foot showed an enhancing soft-tissue mass overlying the metatarsal bones (Figure 1). There was no bone erosion or fluid collections.

The patient underwent excisional biopsy of the lesion. A hematoxylin and eosin-stained section of the mass is shown in Figures 2 and 3.

What is your diagnosis?

### DIAGNOSIS

The patient underwent surgical exploration and mass resection. Histological sections from the surgical specimen showed eosinophilic structures composed of fungal hyphae and spores, highlighted by Gomori methenamine silver stain, surrounded by suppurative and granulomatous inflammation consistent with eumycetoma (Figures 2 and 3). The cultures were negative. After resection, the foot healed well without antifungal therapy. The patient continues to be followed in the outpatient clinic without any evidence of relapse.

Mycetoma, also known as Madura foot, is a chronic granulomatous infection of the skin and soft tissues with predilection for the lower extremities (1). Mycetoma is endemic in tropical and subtropical regions of the world. The majority of reported cases in North America are seen in the immigrant population; however, sporadic cases have been reported in the southern regions of the United States (2).

The culprit pathogens are either various genera of fungi (eumycetoma) or Gram-positive aerobic actinomycetic bacteria (actinomycetoma) (3). Common causative bacterial agents include *Actinomadura*, *Streptomyces* and *Nocardia* species, while common fungal agents include *Madurella*, *Scedosporium*, *Exophiala* and *Acremonium* (4). Other important differentiating points are: eumycetomas exhibit less inflammation and lesions are less aggressive with fewer fistulas; they tend to be encapsulated; and invasion of bone is slower than in actinomycetoma (5).

Human infection results from traumatic inoculation of these pathogens, usually by a thorn, splinter or other contaminated objects (6). Important factors in developing the infection are inoculum size and the host's immune response. Predisposing factors are walking bare-foot in agricultural fields in endemic areas. Once inside the host, mycetoma follows an indolent, progressive, usually painless course that is typically characterized by a localized tumour-like mass, with or without sinus formation and discharged granules, eventually leading to destruction and deformity of the involved site (6). In eumycetoma, discharged grains or granules are dark or pale/white in colour, while in bacterial mycetoma they are either white to pale yellow or red in colour. The infection may involve underlying structures such as tendons, muscles and bones.

Diagnosis of this uncommon condition requires a high index of clinical suspicion in a patient from an endemic area complaining of an extremity mass with multiple draining sinuses. The main differential diagnoses include cutaneous tuberculosis, chronic osteomyelitis, soft-tissue and bone tumours, and botryomycosis.

It is important to differentiate between bacterial and fungal mycetoma, given their different treatment and prognosis. Cultures, which provide the highest specificity in identifying the causative organisms, have a low diagnostic yield due to bacterial contamination and stringent growth requirements (7). Histopathological examination and special staining of tissue specimens or discharged granules are the most commonly used identification methods (7,8). Morphologically, actinomycotic species appear as poorly defined filamentous structures with variable size granules, while eumycotic species show typical branching septate hyphae with extensive surrounding suppurative granulomas and fibrotic reaction. Recent advances in molecular techniques using polymerase chain reaction have led to specific species identification, but are not widely available (7,9). Radiological imaging using computed tomography (CT) or magnetic resonance imaging is important in determining the

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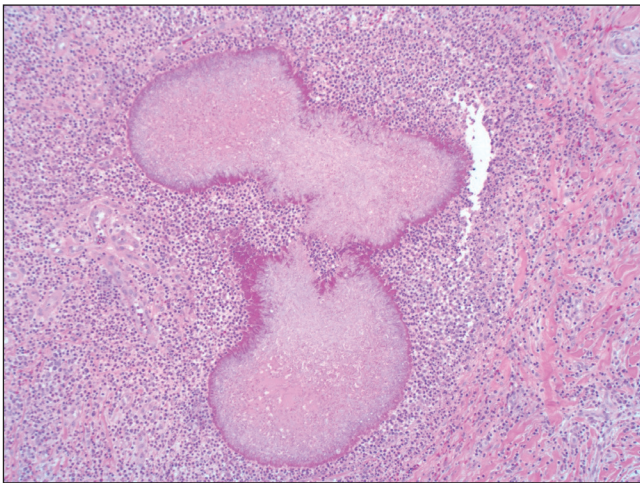
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**Figure 1)** The patient's chronically inflamed right forefoot mass

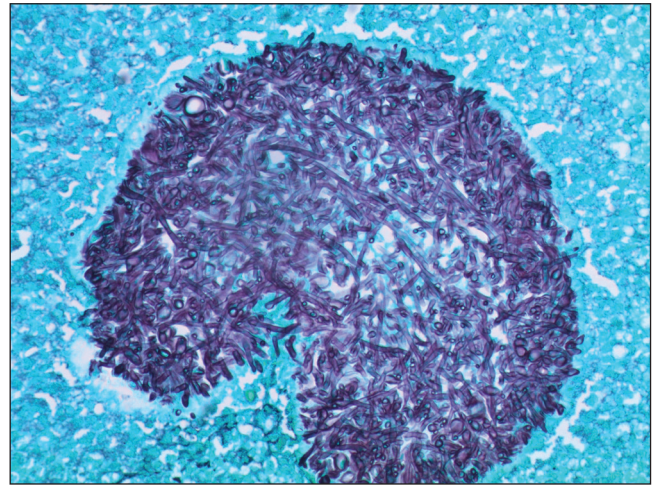


**Figure 2)** Hematoxylin and eosin-stained section of the foot mass showing eosinophilic structures composed of fungal hyphae and spores surrounded by suppurative and granulomatous inflammation (original magnification  $\times 200$ )

extent of soft tissue, bone and organ involvement and to guide further therapy (10).

While plain radiographs underestimate the extent of damage, early characteristic osteoarticular manifestations of mycetoma are best visualized on CT scanning, which demonstrates soft tissue infiltration, osteolysis and irregular periosteal reaction (10). Magnetic resonance imaging is considered to be less sensitive than CT scanning during the early stages of disease; however, it is very helpful in measuring the depth of tissue invasion, which aids in staging the disease and planning surgical therapy (11). Furthermore, the presence of dot-in-circle sign – a tiny, hypointense foci representing grains within hyperintense spherical lesions representing inflammatory granulomata on magnetic resonance imaging – is considered to be diagnostic of mycetoma (11,12).

Contrary to the therapeutic approach in actinomycetoma, which is treated primarily with antibiotics while surgery is reserved to drain abscesses and debride necrotic tissue, an early surgical intervention followed by antifungal therapy is the standard in the treatment of eumycetoma (13). Commonly used antifungal medications include azoles and terbinafine (14). The use of amphotericin B has been



**Figure 3)** Gomori methenamine silver-stained section of the foot mass showing septate branching fungal hyphae and spores (original magnification  $\times 400$ )

largely abandoned because of its toxicity and lower efficacy. The most commonly described regimen to treat actinomycetoma is streptomycin plus either trimethoprim-sulfamethoxazole or dapsone (15,16). The duration of therapy depends on the patient's response and ranges from several months to two years. The prognosis of mycetoma depends on how early the diagnosis is established and when appropriate management is initiated. Furthermore, the degree of fibrosis and underlying deep tissue damage could hinder functional recovery despite aggressive management.

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