

## Mycetoma: Management for the First Contact Doctor

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### ABSTRACT

Mycetoma is a chronic infection of the skin and underlying tissues caused by fungi or bacteria. It is endemic to tropical regions, mainly affecting men, peasants, between the third and fourth decade of life. The clinical picture is characterized by increased volume, deformity of the anatomical area, and fistulas that drain a stringy exudate with the presence of "pimples." The diagnosis and determination of the etiological agent is carried out by direct analysis and culture of the secretion.

### ARTICLE DETAILS

**Published On:**  
**16 March 2023**

**Available on:**  
<https://ijmscr.org/>

### INTRODUCTION

Mycetoma is a local, chronic and progressive disease of the skin, subcutaneous tissues and bone, characterized by a swelling that is often grotesque and disfiguring, with fistulas that drain a serosanguinous or purulent exudate containing granules. These are caused by various species of fungi (eumycetomas) or actinomycetes (actinomycetomas) that are organized in aggregates of hyphae or bacterial filaments, respectively, constituting granules that can be of different size, color, and consistency depending on the species that causes the mycetoma.<sup>1,2</sup>

Mycetomas are chronic, granulomatous, suppurative inflammatory lesions that can be caused by fungi (eumycetoma) or bacteria (actinomycetoma). Clinically it is characterized by the formation of nodules, abscesses, fistulous tracts and areas of fibrosis that cause an induration with a woody consistency. They can compromise the skin, soft tissues, bones and joints. Purulent or serosanguineous discharge with colored granules and variable dimensions, which correspond to microcolonies of the causative agent, drain through the fistulas. Mycetomas caused by fungi occur mostly in tropical areas, while actinomycetomas can occur anywhere in the world.<sup>3,4</sup>

### EPIDEMIOLOGY

Mycetomas are more frequent in men, with a ratio of 3 to 5, and actinomycetomas produced by *Actinomyces madurae*

are more frequent in women. They are more common in individuals who are exposed to the environment through outdoor activities such as farmers, herders, and hunters; however, it can also be observed in people who work in cities, victims of traffic accidents, or travelers to endemic areas.<sup>5</sup>

The disease usually affects adults between the ages of 20 and 40; however, it can be seen in children and the elderly in endemic regions. It is not considered a disease that is transmissible from animal to human or from human to human.<sup>6</sup>

The most common cause of mycetoma in the world is eumycotic, particularly *Madurella mycetomatis*, which accounts for 70% of cases in Central African regions. There is a predominance of certain agents depending on the region, e.g. In Central America and Mexico, mycetoma is most commonly caused by actinomycetes such as *Nocardia brasiliensis*, *Streptomyces somaliensis*, *A. madurae*, and *Actinomyces pelletieri*, and in the US it is caused by the fungus *Pseudallescheria boydii*.<sup>7</sup>

Mycetoma, whether actinomycotic (bacteria) or eumycotic (true fungi), is a chronic granulomatous process, usually unilateral and subcutaneous. The characteristic clinical triad is an enlargement of the affected tissue, sinuous tracts, and discharge of granules. Initially a painless papule or nodule is produced at the inoculation site. Subsequently, new lesions and fistulous tracts appear that intercommunicate with each

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other, draining granules of different colors, chronically. As the nodules evolve, they form retractile scars. On some occasions they invade underlying structures, causing periostitis and osteomyelitis with the formation of small bone cavities (2-10 mm). The involvement of nerves and tendons is very rare and occurs in extensive and long-standing injuries. The skin surface appears shiny with local hyperhidrosis and frequently hyperpigmented.<sup>8,9,10</sup>

The natural habitat of *A. madurae* is soil and plants. When a trauma occurs that causes loss of skin continuity, the entry of the causative agent into the body is facilitated, with people who live in rural areas and who walk barefoot being at greater risk. Despite the inoculation of the causative agent in the affected area, a history of trauma is present in only one third of the cases. Because the incubation period is variable and not well defined (some begin symptoms after several weeks or even years), only a small percentage of patients remember this history.<sup>10</sup>

### **CLINICAL PRESENTATION**

Mycetoma is a pathology that affects the skin, subcutaneous tissue and bone tissue. The characteristic clinical presentation is localized, suppurative and progressive; it involves subcutaneous edema, sinuous tracts, cream-colored granules (1 to 10 mm in diameter), abscesses, and subcutaneous granulomas.<sup>5,8</sup>

There may also be fistulas that drain seropurulent fluid (more frequent in eumycetomas due to *Nocardia*). The pain has a slow and insidious onset, which is why most patients tend to consult late (the average evolution time at the time of consultation is approximately 5 years).<sup>7,11</sup>

The clinical presentation of actinomycetoma and eumycetoma are theoretically identical, regardless of the microorganism; however, actinomycetomas are more aggressive and destructive, and invade bone more easily than eumycetoma. Both the morphology and the topography of the dermatosis in our patient corresponds to the most frequently reported in the literature. Bonifaz et al. as well as López Martínez and Cols, highlight that the lower extremities are the most commonly affected topography, in 70.74% and 60.29% respectively. The classic triad is the most frequent clinical form; It is reported in the literature that up to 97% of the cases will present fistulas with exudate, only a small proportion lack them,<sup>4</sup> which may be associated with the time of evolution at the time of diagnosis. Bone damage identified by radiography is extremely common.<sup>11,12</sup>

### **DIAGNOSIS**

The histopathological study with hematoxylin-eosin staining shows large multilobed grains with scalloped or cartographic borders, with a peripheral band that stains intensely blue and a clear center. These grains are surrounded by stripes (pink in color due to eosin) with long, forked fringes, made up of filaments.<sup>12</sup>

The genus *Actinomadura* is considered to be among the aerobic actinomycetes with medical relevance and has been in continuous taxonomic revision. Currently, 27 species are associated with it, with the species *latina*, *madurae* and *pelletieri* being clinically important.<sup>12</sup>

*Actinomadura madurae* is a ramified Gram (+) bacillus, which does not stain in Ziehl Neelsen or Kinyoun staining (it does not have micholic acids) and is slow-growing on Sabouraud and Lowenstein Jensen Agar, where cerebriform colonies are observed, depending of the crop temperature. Bacterial identification is complex and susceptibility studies are not standardized, although resistance to penicillin, cephalosporins, and trimethoprim-sulfamethoxazole has been described.<sup>12</sup>

Currently, the use of universal PCR with amplification of the gene that codes for 16S rRNA in microbiological diagnosis allows the identification of the agent from cultures or directly from samples. In the latter case, the literature recommends it for the diagnosis of osteoarticular infections. Fenollar et al. studied 518 patients with suspected osteoarticular infection who underwent culture and Universal PCR simultaneously. The sensitivity of the universal PCR was 92% and the specificity was 99%.<sup>12</sup>

Plain radiography shows intraosseous radiolucent images, mainly at the level of the 5th metatarsal and 17th hallux phalanges, but they can occur in any bone. Condensing images such as periostitis<sup>18</sup> can also be found.<sup>12</sup>

On MRI it can present as a heterogeneous plantar mass that involves the plantar fascia, similar to plantar fibroma<sup>2</sup>, or with diffuse involvement of all tissues of the foot. Bone involvement shows an increase in signal on T2 and a decrease on IT. A characteristic lesion is the presence of ovoid areas of 3 to 10 mm with low signal on IT and T2.<sup>13</sup>

### **TREATMENT**

The management of actinomycetomas is of a medical nature (86.7% remission in patients treated only with medical management), while eumycetomas also require surgical management.<sup>14</sup>

Currently, the treatment of actinomycetomas includes multiple antibiotics such as diaminodiphenylsulfone, streptomycin, trimethoprim sulfamethoxazole, rifampicin, and amoxicillin with clavulanic acid, which are usually used in combination in different schemes until clinical cure and microbiological negative results. Oliverio Welsh has used amikacin in combination with trimethoprim sulfamethoxazole in the treatment of cases of actinomycetoma not cured with trimethoprim sulfamethoxazole in monotherapy or with extensive lesions that include bone or visceral involvement.<sup>14</sup>

An appropriate treatment regimen is Amoxicillin/clavulanate 500/125 mg every 8 hr and diaminodiphenylsulfone 100 mg

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every 24 hr, with which clinical and mycological cure was achieved in 4 months. Due to the chronicity of this pathology and its conditions, it is extremely important to make an early diagnosis and provide timely treatment to avoid future complications.<sup>14</sup>

### **CONCLUSIONS**

Mycetoma is a chronic and inflammatory pathology that affects subcutaneous tissue, which can be caused by fungi (eumycetoma) or bacteria (actinomycetoma), the latter being the most prevalent. It is a disease that occurs mainly in tropical and subtropical areas, and in rural populations. So the people who suffer from it are mostly peasant men who do not wear shoes and hurt their feet causing the causative agent to enter through the traumatized skin. The identification of this pathology as well as its timely treatment is necessary to avoid future complications as well as systemic damage to patients.

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