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Mycetoma

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Mycetoma is a chronic infective condition of tropical and subtropical regions. It is commoner in males, especially those in their third or fourth decade who work on the land. The clinical triad of subcutaneous nodule, sinuses and discharge usually leads to diagnosis; the disease is commonly painless. Treatment is by extensive surgical excision of affected areas and may include limb amputation. Recurrence is common, rates ranging from 20 to 90 per cent. Medical treatment may be used on its own or as an adjunct to surgery. Although such therapy may cure over half of those with actinomycetoma (caused by bacteria, mainly aerobic actinomycetes), those affected by eumycetoma (caused by fungi) have a poorer prognosis and may require many years of drug therapy.

Mycetoma is a chronic subcutaneous granulomatous lesion caused either by true fungi (eumycetoma) or by higher bacteria, mainly aerobic actinomycetes (actinomycetoma)[1]. It was first described by Gill of Madura in south India in 1842, hence the name 'madura foot'. In 1860 Carter introduced the term mycetoma ('fungal tumour') to indicate the origin of the disease[2]. Although it has a worldwide distribution, mycetoma constitutes a major health problem primarily in tropical and subtropical regions[3]. It is endemic in the mycetoma belt between latitudes 15°S and 30°N, which includes Sudan, Somalia, Senegal, Mexico, India, and Central and South America[4–7]. Areas where mycetoma is endemic have a short rainy season of 4–6 months with a relative humidity of 60–80 per cent and a fairly constant temperature of 30–37°C both day and night, followed by a dry season of 6–8 months with a relative humidity of 12–30 per cent, a day temperature of 45–60°C and a night temperature of 15–18°C[8,9]. The disease has also been reported in areas of temperate climate[10,11]. Conservative estimates of the incidence of mycetoma in the Sudan vary from 300 to 400 new hospital cases annually[8]. This figure does not take into account the considerable number of outpatients and those seen at peripheral dispensaries where qualified doctors might not even be present. Although studies on patients with mycetoma have indicated a deficiency in cell-mediated immunity, there has been no report of the effect of the spread of human immunodeficiency virus infection in Africa on the incidence of the disease.

Eumycetoma is caused by a variety of fungi, including *Madurella mycetomi*, *M. grisea* and *Pseudoallescheria*, while actinomycetoma is caused by *Actinomadura madurae*, *A. pelletieri*, and species of *Nocardia* and *Streptomyces*[12,13]. The causal organism is usually found in the soil and enters the host through a breach in the skin or the mucosal membrane caused by sharp objects such as a thorn. The disease is not contagious. Its incubation period is unknown because of difficulty in determining the time of initial infection. However, in experimental animals the development of mycetoma has been noted[14,15] after an incubation period of 3 weeks.

Clinical presentation

Mycetoma is five times commoner in males than females and generally occurs in adults between 20 and 40 years of age, although in endemic zones children and the elderly may also be affected[16]. No occupation is exempt, but the disease typically affects cultivators, field labourers and herdsmen.

The clinical triad of subcutaneous nodule, sinuses and discharge is diagnostic (*Figure 1*). Mycetoma usually presents as a slowly progressive painless nodule at the site of previous trauma, commonly in the dorsal aspect of the forefoot; this occurs in 70 per cent of cases (*Figure 2*)[17]. The hand, affected in 12 per cent of cases, is the next commonest location (*Figure 3*); in endemic areas other rarer sites may be affected e.g. the thigh, orbit, air sinuses, testes, ear and mandible[18–20] (*Figure 4*). The subcutaneous nodule gradually increases in size and multiple secondary nodules may develop, suppurate and drain through multiple sinuses that may temporarily close. These sinuses are usually connected with each other, and with deep sterile abscesses and the skin. They show very little tissue reaction at their cutaneous openings[21,22]. The discharge is usually serous, serosanguinous or purulent. Quite often the pus associated with mycetoma is sterile; this is probably the effect of antibiotics produced by the mycetoma itself[23]. Staphylococci or streptococci may occasionally be isolated. During the active phase of the disease, the sinuses discharge grains of a colour that depends on the type of organism; they may be black (*M. mycetomi*), white (*A. madurae*), red (*A. pelletieri*), or yellow (*S. somaliensis*). The grains are of variable size and consistency[24].

The clinical picture of mycetoma is almost uniform, irrespective of the causal species. The organism multiplies in the subcutaneous tissue, forming colonies that spread along fascial planes to involve skin, deep structures and bone. It eventually causes bone destruction with cavities and deformity; tendons and nerves are usually not affected[25]. In eumycetoma the lesion grows slowly and remains encapsulated for a long time, whereas in actinomycetoma it is more aggressive, more destructive and involves bone at an early stage[26,27]. In 1–3 per cent of cases there is genuine lymphatic spread of mycetoma to regional nodes; this type of spread is more common with actinomycetoma. Other causes of enlarged regional lymph nodes are secondary bacterial infection or local immunological reaction to the disease[28].

Although mycetoma is generally painless, in about 18 per cent of patients it is painful because of secondary bacterial infection or, in some cases, bone expansion by the mycetoma[29]. Constitutional symptoms and signs are rare, but when they occur generally result from secondary bacterial infection of open sinuses. Lymphoedema and varicose veins are rarely observed in infected patients. The disease is rarely fatal but produces disabilities and deformities in its later stages[30]. Primary osseous mycetoma without soft tissue involvement is sometimes encountered; the route of infection is unclear. There is no report of blood-borne spread of the disease.

The radiological features of mycetoma are interesting. In the early stages there may be a soft tissue mass with obliteration of fascial planes. Bone cortex may be compressed from outside by the mass, producing scalloping which is followed by a

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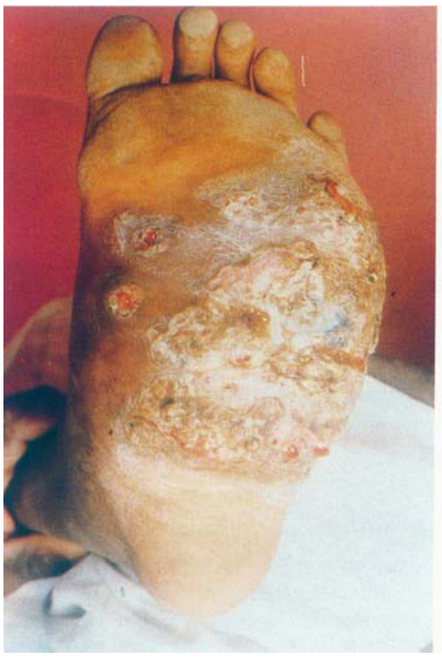

Figure 1 *Mycetoma foot with the triad of a mass, sinuses and discharge*

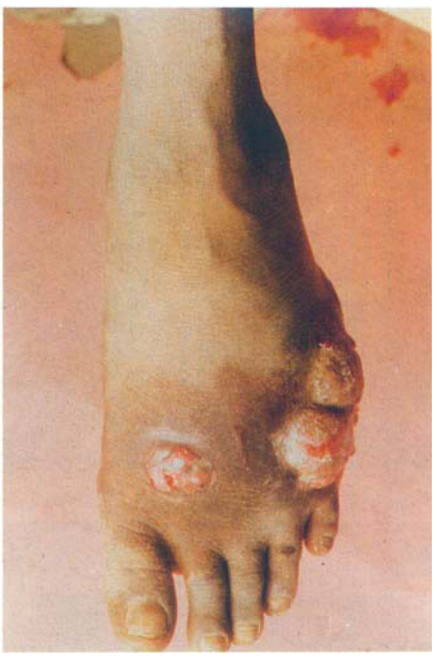

Figure 2 *Mycetoma involving the dorsal aspect of the forefoot*

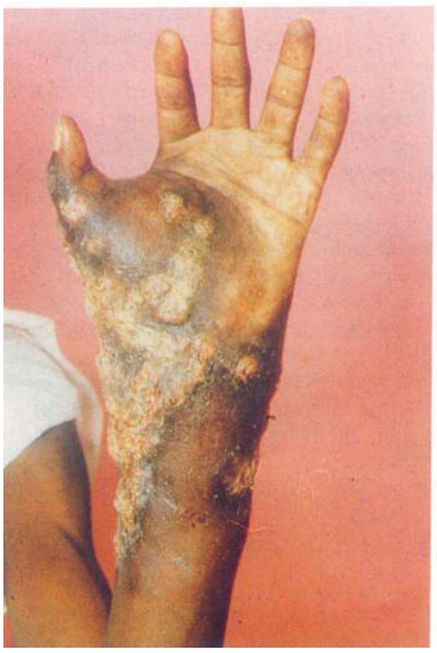

Figure 3 *Eumycetoma involving the hand and forearm with multiple healed sinuses*

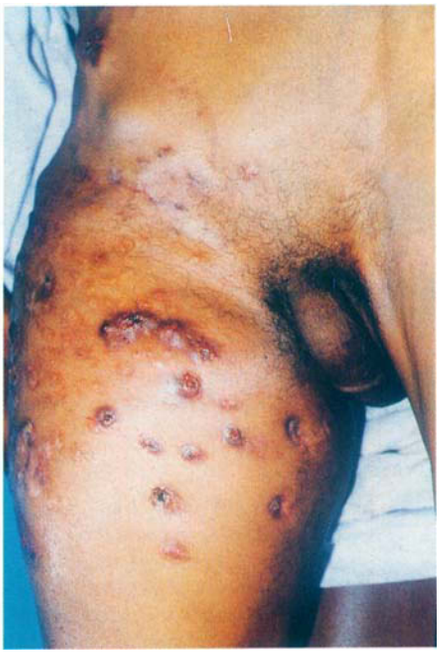

Figure 4 *Actinomycetoma involving the upper thigh and the lower part of the anterior abdominal wall*

variable amount of periosteal reaction. Sunray appearance and a Codman's triangle may be present, producing a picture similar to that of osteogenic sarcoma (*Figure 5*). There may be multiple cavities within normal-density bone. These cavities are large, few in number, and in eumycetoma have well defined margins (*Figure 6*). In actinomycetoma they are small, numerous and their edges ill defined (*Figure 7*). The size of the cavities is a function of the size of the grains[31]. Osteoporosis is common in late mycetoma due to disuse atrophy and to pressure on blood vessels supplying the bone. Pathological fractures are unknown, because bone is replaced by grains, giving the bone some support[32].

The differential diagnosis includes soft tissue swellings such as thorn granuloma, fibrolipoma, neurofibroma, Kaposi's sarcoma and malignant melanoma. Osteogenic sarcoma and bone tuberculosis may have similar radiological appearances to mycetoma but sequestration does not occur in mycetoma. Primary osseous mycetoma must be differentiated from chronic osteomyelitis, osteoclastoma and syphilitic osteitis[33,34].

Diagnosis

The condition is usually diagnosed clinically. Confirmation is possible by demonstrating significant levels of antibodies against the different types of causal organisms by counter-immunoelectrophoresis, immunodiffusion or enzyme-linked immunosorbent assay[35–39]. Histological examination of the surgical specimen using haematoxylin and eosin or periodic

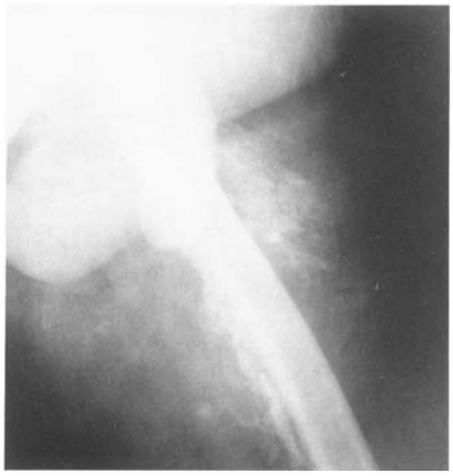

Figure 5 *Radiograph of the femur of a patient with actinomycetoma showing periosteal reaction, new bone formation and sunray appearance*

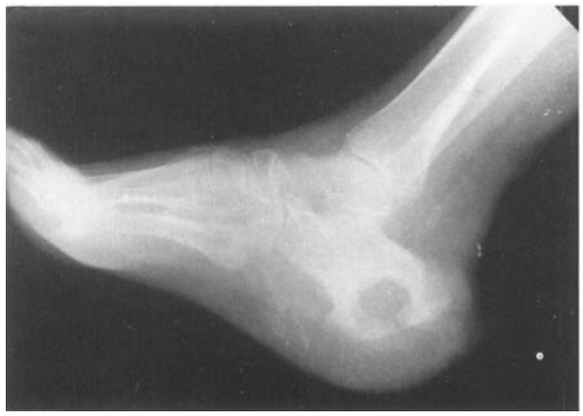

Figure 6 *Radiograph of foot showing a big cavity in the calcaneum with well defined edges and sclerosis typical of eumycetoma*

acid–Schiff stains can identify the causal organism and demonstrate the type of local tissue reaction against it[40,41].

Surgical treatment

Surgery for mycetoma ranges from local excision to mass reduction and occasionally to amputation of an affected limb. The aim of such treatment is complete removal of the lesion. This is possible in about 30 per cent of patients who have early disease in which the granuloma is localized. Actinomycetoma has ill-defined limits, so a wide margin of healthy tissue should be excised with the lesion if possible. Great care must be exercised during surgery to minimize the spread of grains along fascial planes if recurrence is to be avoided. The surgeon should not cut across the lesion or see the grains; a bloodless field, using a tourniquet, is mandatory. Some authorities advise flooding the wound at the end of the procedure with iodine solution to destroy any missed grains, but there is no firm evidence to support this technique. Surgical mass reduction of a lesion that cannot be completely excised greatly facilitates the response to medical treatment. Approximately one-quarter of all mycetomas require amputation of part or all of the foot and, rarely, of the hand[17]. To avoid the socially disastrous consequences of amputation, a programme of extensive repeated excision of diseased tissue, including bone, may be carried out preferentially[42]. Such debulking procedures are carried out in about one-fifth of patients. The recurrence rate after surgical treatment is high, ranging from 20 to 90 per cent[43]. Medical treatment before and/or after surgery may be used in certain circumstances[44].

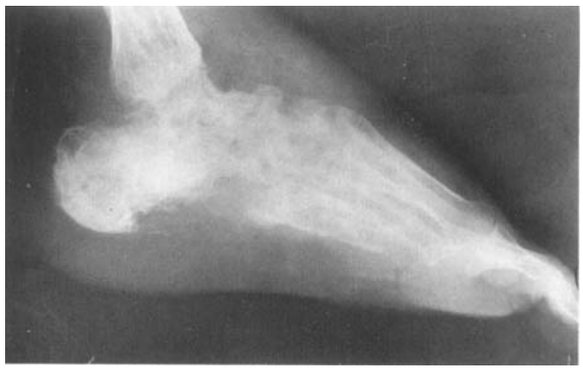

Figure 7 *Radiograph of foot showing advanced actinomycetoma with multiple small cavities with ill-defined edges*

Medical treatment

Medical treatment alone or in combination with surgery is used in about one-quarter of patients. It is indicated for those with massive or inoperable lesions, and in those with recurrent lesions after surgery. It is more effective in actinomycetoma than in eumycetoma; the latter may produce a cement substance around the organisms demonstrable by ultrastructural studies. Many drugs and drug combinations have been tested both *in vivo* and *in vitro* against mycetoma pathogens. Mahgoub[45] reported 144 patients with actinomycetoma treated medically; 63 per cent were cured, 22 per cent enjoyed great improvement, and 11 per cent showed some improvement. Treatment may be successful even when there is bone involvement[46]. In patients with actinomycetoma, medical treatment consists of dapsone 100 mg twice daily and streptomycin 1 g daily for 1 month. The streptomycin dosage is then reduced to 1 g on alternate days[47]. If the response is not satisfactory dapsone is replaced by co-trimoxazole 980 mg twice daily. In resistant cases rifampicin and sulfadoxine–pyrimethamine can be tried[48].

The results of medical treatment in patients with eumycetoma have not been encouraging. Griseofulvin 500 mg three times daily and penicillin 600 000–800 000 units daily have shown promising results when given for a long period, ranging from 1 to 10 years. Ketoconazole and itraconazole have been tried with some success[49]. However, these drugs are rather expensive and therefore not readily available in endemic areas[50]. Another disadvantage is that such drugs must be given for long periods (from 6 months to 10 years) to effect cure[45,49].

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