Mycetoma- A resurgence

M. Mani Surya Kumar[1], V. Senthil Kumar[2,*], Parimalam Kumar[3], V. Anandan[4]

[1,2]Senior Assistant Professor, [3]Professor and HOD, [4]Professor, Dept. of Dermatology, Government Stanley Medical College, Chennai, Tamilnadu, India

***Corresponding Author:**
Email: vskumarveerappan@yahoo.in

Abstract
Mycetoma is a localized chronic, suppurative granulomatous disorder of subcutaneous tissue, skin and bones, mainly of feet, characterized by a triad of grains, tumour and tracts. It is commonly seen in tropical and subtropical areas. Based on causative organisms it is classified into eumycetoma caused by fungus, and actinomycetoma caused by bacteria. Color of grains also helps in differentiating the organisms. Black grains are always produced by fungi; pale grains are produced by bacteria and fungus. Diagnosis is based on the classical clinical presentation, histopathology and microbiological examination. Serological tests are not helpful. Molecular techniques to detect antigens are still under study. Eumycetoma is very resistant to treatment. Actinomycetoma responds well to prolonged antibiotic therapy.[1,2] We present here in detail a series of five cases of mycetoma diagnosed in our hospital in a span of six months.

Keywords: Actinomycetoma, *Eumycetoma*, Madura foot.

Introduction
Mycetoma is a chronic suppurative granulomatous infection of skin, subcutaneous tissue, and bones. It is highly prevalent in tropical and subtropical regions. In the Indian Sanskrit text Atharva Veda, mycetoma has been described as *padavalmikam*, meaning "anthill foot. Gill first recognized mycetoma as a disease entity in 1842 in the southern province of Madura from where the commonly used name "Madura foot" got prevalent. However, the term "Mycetoma" (meaning fungal tumor) was proposed by Carter.[3] Pinoy classified mycetoma based on causative organisms, and the formal classification was framed by Chalmers and Archibald.[4, 5]

Mycetomas are caused by various species of fungi and bacteria. They occur as saprophytes in soil or on the plants. Actinomycotic mycetoma is usually caused by species like Nocardia brasiliensis, *Actinomadura madurae, Actinomadura pelletieri* and *Streptomyces somaliensis*.

Eumycotic mycetoma is caused by a variety of fungi. The most common species are *Madurella mycetomatis and madurella grisea*. Actinomycetoma species produce only pale grains. Eumycetoma species produce both black and pale grains. Actinomadura pelletieri produces red grains.[6, 7]

Mycetoma is endemic in tropical and subtropical regions. It usually occurs between latitudes 15° S and 30° N, also known as the "Mycetoma belt" which includes countries like Sudan, Somalia, Senegal, India, Yemen, Mexico, Venezuela, Colombia, and Argentina. Worldwide, *M. Mycetomatis* is the most common cause of mycetoma. In India, *Nocardia* species and *Madurella grisea* are the most common causes of myeloma.[8.] Actinomycetoma is more prevalent in dry conditions, whereas eumycetoma is more common in sites were rainfall is more prevalent[9] Mycetoma is usually seen in males than females. The ratio of males to females is (3:1). The reason is because men are more involved in agricultural work.[10, 11] It usually involves young adults of age 16–40 years.[12] It is rarely seen in children**.** We describe in detail about five cases diagnosed in our hospital during six month period. The summary of all five cases are given in table 1.

Case 1

A 40-year-old male farmer presented with swelling and multiple discharging sinuses over dorsum of left foot of 2 years duration. A painful nodule developed at the injury site which gradually increased in size. On examination there was a diffuse, ill-defined, indurated swelling over dorsa of left foot. It was studded with multiple, nodules; and a few sinuses having sero-purulent discharge and black crusts (Fig. 1). Routine investigations, including complete blood counts, urinalysis, and chest x-ray films did not show any abnormality. X-ray films of the foot showed osteosclerotic lesion. Skin biopsy showed chronic granulomatous inflammatory infiltrate comprising neutrophils, lympho-histiocytes and a few plasma cells; and fibroblastic and vascular proliferation were seen. Sabouraud's dextrose agar (SDA) without antibiotics was used as culture medium. The colonies grown were wooly; yellow- brown in color, with radial grooves (Fig. 2). A diagnosis of *Madurella grisea* was made.

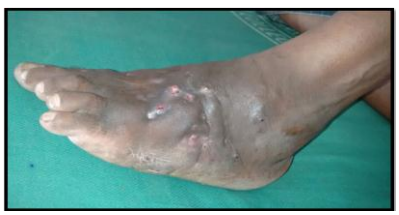

Fig. 1:

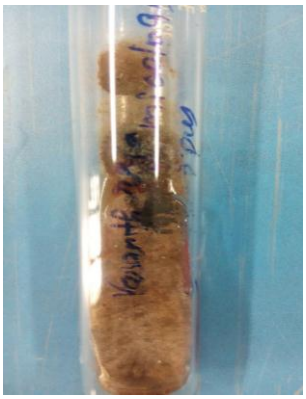

Fig. 2: Culture of *Madurella grisea*

Case 2

A 29-year-old female who was an agricultural labourer by occupation came with chief complaints of swelling over dorsum of base of left great toe for more than 2 years duration. She took some native medications in the form of topicals subsequently she developed ulceration along with the preexisting nodules. Cutaneous examination showed a diffuse swelling of base of left great toe with nodules and ulceration. Pus was discharging from few active sinuses. Few sinuses were discharging black granules (Fig 3). Systemic examination and routine investigations, including chest x-ray, were normal. X-ray films of the involved leg showed soft tissue swelling and underlying bones showed osteiscerotic changes. Grains were subjected to KOH mount which showed septate hyphae. Histopathology showed acanthotic epidermis and epithelioid cell granulomas with minimal caseation necrosis. Culture on SDA produced colonies which were white and wooly at first, then turning olivaceous, producing a brown diffusing pigment. Diagnosis of *Madurella grisea* was made.

Fig. 3:

Case 3

A 71-year-old male who was a labourer by occupation presented with swelling over sole of right foot for 1-year duration. He had a thorn prick over sole of right foot. Few months back, he developed painful swelling with multiple sinuses and discharge. Cutaneous examination showed diffuse swelling over sole of right foot which was indurated. Multiple discharging sinuses were present over the swelling (Fig. 4). Few sinuses were discharging black grains. Systemic examination and routine laboratory investigations, including chest x-ray, were essentially normal. X-ray of right foot showed osteosclerotic changes in underlying bones. Histopathology showed mixed suppurative and granulomatous inflammation. Repeated KOH mounts of grains showed hyphae. Culture was done in 2 sets of SDA; one set was incubated at 27°C and one at 37°C. Growth was seen in both but was seen early at 37°C where the colony matured within 1 week. The growth was identified to be *Madurella grisea*.

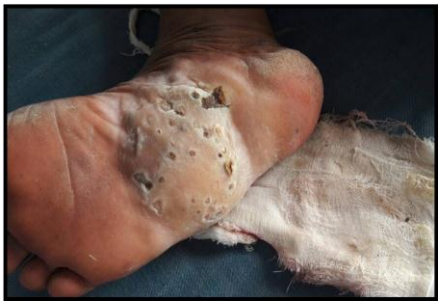

Fig. 4:

Case 4

A 40-year-old male construction laborer presented came with chief complaints of swelling over lateral border of sole of right foot for 1-year duration. He had an injury over sole of right foot. Later he developed painless swelling with multiple sinuses and seropurulent discharge. Cutaneous examination showed swelling over lateral border of right foot which was indurated. Multiple discharging sinuses, covered with black crusts, were present over the swelling (Fig 5). Few sinuses were discharging black grains. Systemic examination and routine laboratory investigations, including chest x-ray, were normal. X-ray of right foot showed osteosclerotic changes in underlying bones. Histopathology revealed mixed suppurative and granulomatous inflammation. KOH mounts from grains, demonstrated hyphae. Culture on SDA agar at 37 °C showed growth of brown colonies with woolly appearance. Growth of *Madurella grisea* was made.

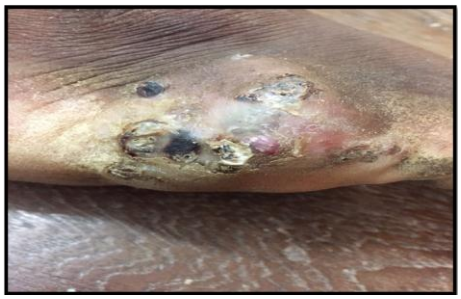

Fig. 5:

Case 5

A 24 year old male, studying in college, came with complaints of swelling over dorsum of left foot for past 4 years and multiple pus discharging tracts in the swelling for past 4 years. The patient denied history of trauma or thorn prick in that foot, but gave history of going barefoot occasionally in fields. The disease began as a painless swelling which gradually increased in size over the past 4 years. History of development of multiple serous fluid discharging tracts in the beginning which now shows seropurulent discharge (Fig. 6). Patient also gave history of black colored grains in the discharge. The tracts heal over varied time period with scarring on surface and new tracts starts appearing nearby with increase in the size of swelling. He underwent treatment in a nearby hospital where he was treated with incision and drainage of swelling and oral antibiotics. This reduced the purulent discharge but not the size of the swelling. When he presented in our hospital, his dermatological examination showed presence of an ill defined diffuse swelling over the dorsum of left foot with multiple healed sinus tracts forming scars and few seropurulent discharging sinuses on the lateral aspect of swelling. Since no visible grains were seen, overnight saline soaked gauze was applied and it showed to contain 2-3 black colored grains in the morning. The granules were crushed and examined under microscope with 5-10%KOH, which showed broad, septate branching brown hyphae with chlamydospores. AFB staining was negative. Specimen for histopathology was obtained as a deep wedge biopsy and stained with eosin and hematoxylin, in which the grains appeared as a brown, oval structure with radiating hyphae and chlamydospores at the periphery surrounded by eosinophilic precipitate called Splendore Hoeppli phenomenon (Fig. 7, 8, 9). Staining with periodic acid Schiff was also positive. Culture was consistent with M*adurella grisea*

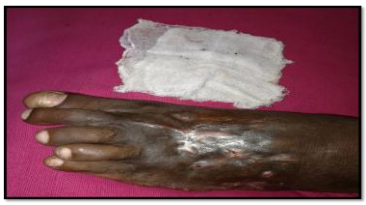

Fig. 6:

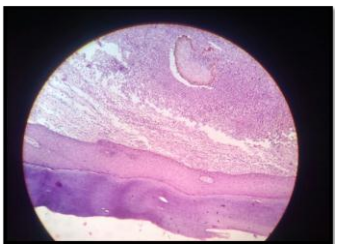

Fig. 7: HPE – Epidermal Changes

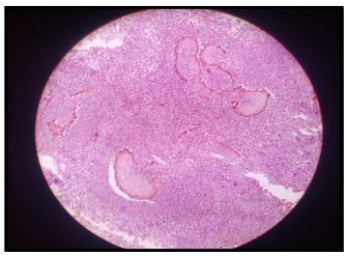

Fig. 8: Splendore Hoeppli Phenomenon

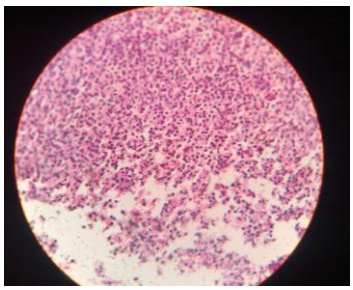

Fig. 9: Dense Infiltrate

Table 1: Summary of the 5 patients

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	m	f	m	m	m
Age	40	29	71	40	24
Occupation	Farmer	Farmer	Labourer	Labourer	College student
H/o injury	+	-	+	+	-
Duration	2 years	2 years	1 years	1 years	4 years
Nodules	+	+	+	+	+
Discharge	Seropurulent	Purulent	Purulent	Seropurulent	Serous
Grain	+	+	+	+	+
Colour of grain	Black	Black	Black	Black	Black
X-ray	Osteosclerotic lesion	Osteosclerotic lesion	Osteosclerotic lesion	Osteosclerotic lesion	Osteosclerotic lesion
Culture	*Madurella grisea*	*Madurella grisea*	*Madurella grisea*	*Madurella grisea*	*Madurella grisea*

Discussion

Mycetoma is a chronic, granulomatous, mostly localized infection of the dermis and subcutaneous tissue with classical triad of tumour, tract and grains. The grains are aggregates of microcolonies of the organism. More than 20 species of fungi and bacteria have been identified as etiologic agents of mycetoma. Approximately 40% of cases are due to true fungi (eumycetoma), and 60% are caused by aerobic actinomycetes (actinomycetoma). It occurs due to traumatic implantation or contamination of a wound involving the foot in majority of the cases. Involvement of other parts of the body is unusual and reported rarely. It usually involves men 20 to 40 years of age, walking barefoot, rural settings.

All our five cases had involvement of lower extremity, most commonly in the foot. The incubation period is highly variable from months to years. Because of the long incubation period, patients do not remember the history of trauma. The clinical features will be the same irrespective of the organism involved. The diagnostic criteria are a triad of painless firm nodule, sinus formation, and grains. All our patients had similar clinical features, foot involvement and long incubation period.

Most of our cases started as small, painless nodule at the site of injury which later ulcerates to discharge a purulent, or serosanguinous fluid containing grains. The grains are microcolonies of causative organism which is the hallmark of mycetoma. The grains vary in size, color, and consistency. The type of mycetoma can be diagnosed by the color of grains. Red color grains indicate actinomycotic mycetoma, black color grains indicate eumycotic mycetoma and pale grains indicate both actinomycotic and eumycotic mycetoma. Overlying skin may be hypo- or hyper-pigmented and sometimes ulcerated. Active sinus tracts and old healed tracts can be seen. All our cases had black grains.

The disease is usually progresses and entire foot may become swollen, indurated, and deformed due to fibrous tissue reaction and multiple sinus formation. The condition is usually painless. Sometimes patients may complain of pain due to secondary bacterial infection and involvement of bones. Disease may spread along fascial planes to involve the subcutaneous tissue, fat, ligaments, muscles, and bones. Osteolytic and osteosclerotic lesions are classical bone changes seen in mycetoma. Sometimes osteomyelitis can ensue. Actinomycetoma tends to progress more rapidly, with greater inflammation and tissue destruction and earlier invasion of bone. In all our cases there were osteosclerotic lesions.

Management of mycetoma depends on the etiological agent, whether it is actinomycotic or eumycotic. Diagnosis is made based on the classical clinical features, colour of grains, histopathology and culture. Early intervention and effective treatment is very important for arresting the disease progress. The duration of treatment is highly variable and prolonged. All our patients were eumycotic and started on tablet Voriconazole 400mg daily along with potassium iodide. Surgical excision was done for large nodules. The treatment response was assessed based on factors like skin becoming normal, disappearance of nodules, healing of sinuses, and absence of grains in discharge.

Conclusion

Mycetoma is usually diagnosed at an advanced stage because of the painless nature of the disease and hence permanent deformity of affected part would have already occurred. The disease is usually chronic and progressive with increased risk of secondary bacterial infection and bone involvement. This can cause increased pain and disability. The sudden increase in the prevalence of mycetoma in our department where we mycologically confirmed six cases within a span of six months indicates an upsurge in the occurrence of the disease. One of them being a college student also indicates that any age group irrespective of their profession can be affected. Thus, there is a need for awareness and early diagnosis of mycetoma based on the clinical features, histolopathology and microbiological studies. Effective and prolonged treatment can prevent development of deforming complications.

References

1. McGinnis MR., Mycetoma. Dermatol Clin 1996;14:97-104.
2. Mahgoub ES., Medical management of Mycetoma. Bull World Health Organisation 1976;54:303-10.
3. Carter HV., On a New and Striking form of Fungus Disease Principally Affecting the Foot and Prevailing Endemically in Many Parts of India. Transactions of the Medical and Physical Society of Bombay 1860;6:104-42.
4. Pinoy E., Actinomycoses and Mycetomas. Bull Inst Pasteur 1913;11:929.
5. Chalmers AJ, Archibald RG, A Sudanese Maduromycoses. Ann Trop Med 1916;10:169.
6. Palestine RF, Rogers RS 3rd., Diagnosis and Treatment of Mycetoma. J Am Acad Dermatol 1982;6:107-11.
7. Magana M., Mycetoma. Int J Dermatol 1984;23:221-36.
8. Green WO Jr., Adams TE., Mycetoma in the United States; a review and report of seven additional cases. Am J Clin Pathol 1964;42:75-91.
9. Taralakshmi VV, Pankajalakshmi VV, Arumugam S, Subramanian S., Mycetoma caused by *Madurella mycetomii* in Madras. Australas J Dermatol 1978;19:125-9.
10. Fahal AH, Sabaa AH., Mycetoma in children in Sudan. Trans R Soc Trop Med Hyg 2010;104:117-21.
11. Zarei Mahmoudabadi A, Zarrin M., Mycetomas in Iran: a review article. Mycopathologia 2008;165:135-41.
12. López Martínez R, Méndez Tovar LJ, Lavalle P, Welsh O, Saúl A, Macotela Ruíz E., Epidemiology of Mycetoma in Mexico: Study of 2105 cases. Gac Med Mex 1992;128:477-81.