CASE REPORT

Alleviating Diagnostic Dilemma of Maduramycosis: A Case Series

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Summary

Maduramycosis[1] is chronic infection of cutaneous and subcutaneous tissue caused by bacteria and fungi. It involves skin, subcutaneous tissue and bones.[2] Here we report a case series of 14 patients of mycetoma describing their epidemio-clinical features and laboratory investigations. The most common clinical presentation in the patients were infiltrated subcutaneous swelling with multiple discharging sinus tracts (fistulas). Lesions were located on the foot in all the cases.

Key words: *Mycetoma, actinomycetoma, deep fungal infections,diagnosis, management*

Introduction

Maduramycosis[1] also called as mycetoma is chronic granulomatous suppurative mycosis.[2] It is caused by traumatic implantation of causative organism on exposed area of the body most commonly lower extremity.[3] Broadly, mycetoma is etiologically classified as eumycetoma and actinomycetoma as caused by filamentous fungi or aerobic actinomycetes respectively.[2,3,4]

Case Series

We present our experience of management of fourteen cases of leg mycetoma who presented to us in our OPD section in the preceding two years (Table 1). Presenting complaints of the patients were swelling with or without erosions, discharge or ulcer for duration ranging from 3 months to 10 years. All the cases gave prior history of trauma with a wooden splinter while doing outdoor work. The incubation period for developing clinical signs and symptoms ranged from three months to six years.

Samples from all the patients presenting with clinical features of mycetoma were sent for Fine Needle Aspiration Cytology (FNAC), biopsy and tissue culture & sensitivity. FNAC samples were stained with Giemsa stain and for histopathological examination H & E staining method is used. As we were not having facility for PCR-RFLP analysis was not done.

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Out of the fourteen cases, 8 cases were of actinomycotic mycetoma and 6 were eumycotic mycetoma (Figure 1). Histology of biopsied tissue (Figure 2) and FNAC from discharging sinuses were performed and was confirmatory in them. However; the culture studies did not yield growth of causative organisms in all the cases as were cultured for 7 days only.

One of our patients required debulking of the growth along with concomitant antimycotic therapy and all of them responded well to treatment. Simple treatment by 160 mg trimethoprim and 800 mg sulfamethoxazole till lesions heal and minor surgical interventions were sufficient on treatment part.
After relief from the symptom, patients were lost to follow up.

Figure 1. Swelling with multiple discharging sinuses. Grains are seen on the surface of the discharging sinuses.

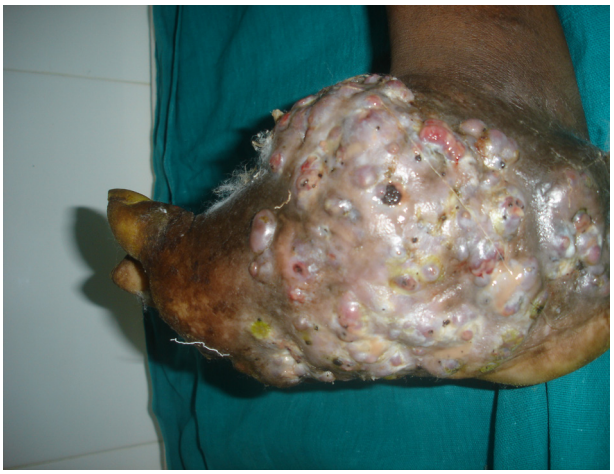


Figure 2. H&E stained histopathology slide of Eumycetoma showing thin layer of neutrophils adherent to outer surface of grain.

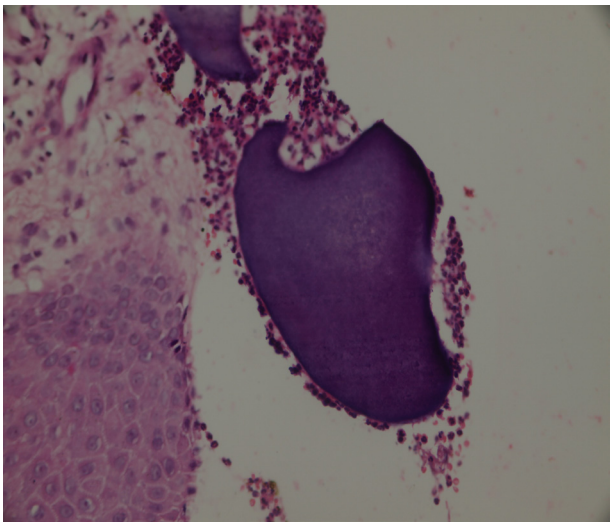
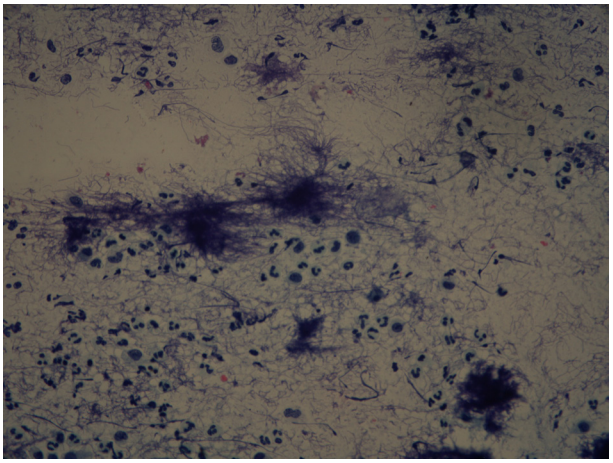


Figure 3. Giemsa stained FNAC slide of Actinomycetoma showing Grains with homogenously blue centre and radiating filaments at the periphery. Grains are surrounded by neutrophils, macrophages, and lymphocytes.



Discussion

Maduramycosis or mycetoma is chronic granulomatous suppurative[1,2] mycosis caused by traumatic implantation of soil organisms on subcutaneous tissue.[3] It characteristically presents with triad of painless[8] localized tumor-like swelling, underlying sinus tract and presence of grains.[2,3] Mainly located over extremities.[5] More than 75% cases involve leg and lower extremity.[3]

The oldest description about mycetoma is found in Atharva Veda as “padavalmikam”, meaning “Anthill Foot”. In 1842, Gill recognized a disease entity prevalent in Madura from where name “Madura Foot” came. Later, Carter proposed a term Mycetoma meaning “Fungal tumor”[1,2]

Carter also classified Mycetoma on the basis of colour of grains. Later a formal classification based on causative organism was put forward by Chalmers and Archibald, they grouped mycetoma as Group 1-maduramycosis caused by fungi, Group 2- actinomycosis caused by actinomycetes (Higher bacteria).[2]

Madura foot is classical example of neglected disease which primarily affects the poor and rural population of Tropic and Sub-tropic climate. These regions are located between latitudes 15 degrees to 30 degrees and defined as “Mycetoma belt”. It includes countries with highest occurrence of mycetoma, India is one of those. Mycetoma belt is characterized by low humidity and low rainfall with well-defined alternating rainy and dry seasons[3],but disease can occur sporadically in any part of the world.[6]

Table 1: The clinical and laboratory data of our patients.

SN	Age (years) /Sex	Morphology	Average duration	Histopathology Examination	FNAC	CULTURE
1.	78/Male	Multiple swellings with discharging sinuses over left foot.	6 months	Fragments of the destroyed grains are within multinucleated giant cells. Few neutrophils present	On Giemsa staining grains appear homogeneous blue in centre, at periphery fine granules with pink radiating filaments seen	No growth seen
2.	56/Male	Multiple discharging sinuses over left sole.	2 years	Fragments of the destroyed grains are within multinucleated giant cells	Inflammatory Granuloma with multinucleated giant cells, lymphocytes eosinophils and fibrosis surrounding the grains is seen	No growth seen
3.	27/Male	Swelling with multiple small erosions over right sole.	9 months	Grains surrounded by neutrophils and layer of fibrous tissue is seen	Oval grain surrounded by neutrophils is seen.	No growth seen
4.	38/Male	Multiple nodules with discharging sinuses over left foot.	1 year	Grains surrounded by neutrophils and layer of plasma cells, macrophages, granulation tissue & fibrous tissue is seen.	Oval grains surrounded by neutrophils is seen	No growth seen
5.	41/Male	Swelling over left ankle with multiple discharging points.	5 years	Fragments of the destroyed grains are within multinucleated giant cells seen	deep granulomatous inflammation consisting of multinucleated giant cells, lymphocytes and plasma cells surrounded by fibrous tissue is seen	
6.	52/Female	Multiple swellings over ankle.	6 years	Well organised inflammatory granuloma with Langerhans giant cells without grains is seen	Grains with homogenous blue centre and peripheral pink filaments seen with multi-nucleated giant cells, lymphocytes and few neutrophils in the background.	No growth seen
7.	24/Male	Swelling with sinuses with small ulcer over right ankle.	1year	Grains surrounded by neutrophils and layer of fibrous tissue is seen	Grains with homogenous blue centre and peripheral pink filaments with predominantly polymorphonuclear cells surrounding the grains.	No growth seen
8.	42/Male	Swelling with multiple discharging sinuses over left sole.	2 years	Fragments of the destroyed grains are within multinucleated giant cells	few destroyed bluish grains with poorly appreciated peripheral pinkish filaments seen	No growth seen
9.	68/Male	Multiple discharging sinuses over left leg.	5 years	Fragments of the destroyed grains are within multinucleated giant cells	Well differentiated granuloma with predominantly multinucleated giant cells, and lymphocytes surrounded by fibrosis is seen	No growth seen
10.	32/Male	Swelling over left ankle with discharging sinuses and small ulcer.	3 years	Fragments of the destroyed grains are within multinucleated giant cells	Well differentiated granuloma with predominantly multinucleated giant cells, and lymphocytes surrounded by fibrosis is seen	No growth seen
11.	44/Male	Swelling with multiple discharging sinuses over left foot.	5 years	Well organised inflammatory granuloma with predominant Langerhans giant cells is see	few destroyed bluish grains with poorly appreciated peripheral pinkish filaments seen	No growth seen
12.	26/Male	Swelling with multiple discharging sinuses over left foot.	5 months	Grains surrounded by neutrophils and macrophages seen	Inflammatory granuloma with black grain at the centre surrounded by neutrophils, few macrophages, plasma cells and granulation tissue are seen	No growth seen
13.	36/Male	Swelling with multiple discharging sinuses with black grains over right foot.	18 months	Grains surrounded by neutrophils is present. Plasma cells and fibrous tissue surround this layer.	Suppurative granuloma consisting of neutrophils, macrophages, few giant cells are seen	No growth seen
14.	28/Female	Swelling with multiple discharging sinuses over left foot.	10 years	Fragments of destroyed grains within multinucleated giant cells seen	Grains homogenously blue at the centre and radiating pink filaments at the periphery are seen	No growth seen

This deforming granulomatous disease is common in poor rural workers and homemakers who work outdoors without protective garments and shoes.[3] Host factors such as immune status, adaptive humoral response and nature of occupation as well as organism related factors such as virulence and size of inoculum are related to the development of disease.[2,3,6] Male to female ratio is 3-4:1.[3] The age group most commonly affected is 20-40 years.[6]

Although various studies have been done for estimation of burden of disease, the estimated prevalence does not reflect the actual magnitude of disease. The gap lies in the fact that the studies done were single center studies.[5]

The three subtypes based on etiology are (1) Actinomycotic mycetoma – caused by filamentous aerobic and anaerobic organisms, e.g. *Nocardia brasiliensis, Actinomadura madurae*; (2) Eumycotic mycetoma – caused by true fungi; and (3) Botryomycosis – caused by true bacteria, e.g. *Staphylococcus aureus, Pseudomonas spp*.

Mycetoma is differentiated from other mycoses by its characteristic draining sinuses containing grains (sclerotia, sulfur granules).[1] Grains contain organism both inside and outside the grains.[7] Various questions remained unanswered till date regarding route of transmission. These questions include – Where the causative organism resides? What is its natural habitat? Soil and dung are most probable habitat but there can be other possible habitat). How the organism introduced in subcutaneous tissue (thorn prick is estimated but intermediate hosts can be involved). Will the organism always cause mycetoma? Does co- infection play role?[5] What is incubation period?[3]

In host, T- cell mediated immune responses play important role.[2] Three types of responses to grains of mycetoma have been described which include: Type-1: Degranulation and adherence of neutrophils to the outer grain surface leading to gradual destruction of grains. Outside this layer of neutrophils macrophages, lymphocytes, plasma cells and a granulation tissue present enclosed in a fine layer of fibrous tissue. Type-2: Disappearance of neutrophils and predominant presence of macrophages for clearance of grains and neutrophils debris owing to presence of disintegrated grains inside the multinucleated giant cells. Type-3- development of epithelioid cell granulomas and with few or no remnants of grains and presence of a fibrous tissue in abundance.[2,8]

As it is a painless condition it usually presents in advanced stage.[8] Diagnosis of the disease is essential as left untreated can invite superimposed infection sometimes leading to septicemia and can cause fatal outcome.[2] Also disfigurement of the limb is an important concern.

Another need for diagnosing the disease is that, mycetoma is caused by taxonomically different organism i.e fungi, bacteria which require different approaches for the treatment.[5] Diagnosis is made by classical triad, histopathology, FNAC, culture studies, ultrasonography, Magnetic resonance imaging, skin testing, serology etc[7].

As of today, no protective vaccine is available against any of the causative agents of mycetoma.[9] One of our patient required debulking of the growth along with concomitant antimycotic therapy and all of them responded well to treatment. Wearing of protective shoes and clothing prevent against trauma from thorn pricks and its importance should be emphasised. Knowledge and early identification by examination and minimum investigation of the condition leads to alleviating the poor farmer's anguish. Moreover we found simple treatment by 160 mg trimethoprim and 800 mg sulfamethoxazole till lesions heal and minor surgical interventions prevent patients from the debilitating disease.

Differential diagnosis included infectious- such as cutaneous tuberculosis, nontuberculous mycobacterial infections of skin, osteomyelitis, chromomycosis, sporotrichosis, blastomycosis, dermatophyte pseudomycetoma etc. Non- infectious such as mossy foot or podoconiosis, malignant tumors (sarcoma of skin and soft tissue or bones and Kaposis's sarcoma).[2]

Conclusion

When left untreated, disease continues to progress, and bacterial superinfection can lead to increased morbidity from local abscess formation, cellulitis, bacterial osteomyelitis and, rarely, septic death. It enjoys little attention by health and social sectors across the world, as it is a non-glorious (and, indeed, low-priority) disease. There is no consensus on treatment that is often prolonged with numerous relapses. Also, to combat the globally prevalent disease condition, actual prevalence of the disease should be known for this integrated approach with use of standardised forms and establishment of

national reference centres is expected.

Conflict of Interest Declaration
The authors have no conflict of interest to declare.

Acknowledgement
Nil

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