

# Detection of slow growing *Actinomadura* species proved a key for management of mycetoma: A case report from Chhattisgarh

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### ABSTRACT

Mycetoma is disorder of subcutaneous tissue, skin, and bones, mainly the feet. Etiologically divided in Eumycetoma and actinomycetoma, since the treatment of both is different, the diagnosis is mandatory. This is the case of 35-year-old lady with swelling in left foot with multiple discharging sinuses for 5 years that was none responding to antifungal treatment. Change of treatment after the culture confirmation of *Actinomadura* species improves patient condition drastically.

**Keywords:** Actinomycetes, actinomycetoma, discharging sinuses, eumycetoma, magenta colonies on LJ, mycetoma

### Background

Mycetoma also called Madura foot or Maduramycosis is slowly progressive, chronic granulomatous infection of skin and subcutaneous tissue with involvement of underlying fasciae and bones, usually the lower extremities. Broadly there are two categories namely, eumycetoma caused by fungi and actinomycetoma caused by higher bacteria of the class actinomycetes. It is prevalent in almost all part of the world but mainly found in countries lying in Mycetoma belt that include Sudan, Mexico, and India.<sup>[1]</sup>

On the basis of clinical diagnosis, the causative agent cannot be ruled out. But it is must for appropriate and timely management of patients. In the present case, patient was treated with antifungal as fungus is one of the predominant causative agents. But as it had not responded, the specimen was cultured repeatedly and but the growth of slow

growing unusual species of *Actinomadura* was detected in the third attempt and the appropriate management received to the patient.

### Case

A 35-year-old lady presented with complaint of swelling of left foot from last 5 years. The swelling started as tender nodule on lateral aspect of the plantar surface, gradually extended to involve the whole foot and forming multiple sinuses with granular serous discharge. Incision and drainage of a nodule was done, but there was no symptomatic relief. Development of swelling was continued followed by discharging sinuses. Punch biopsy was suggestive of mycetoma. Patient was started on itraconazole 200 mg therapy twice daily for 5 months but there was no improvement. New nodules were continued to appear. Patient had given history of nodule formation 15 years back on same foot for which she underwent incision and drainage and was relieved temporarily. Patient could not recall the history of local trauma.

On local examination there were multiple nontender nodules over the dorsum and lateral aspect of the left foot with several

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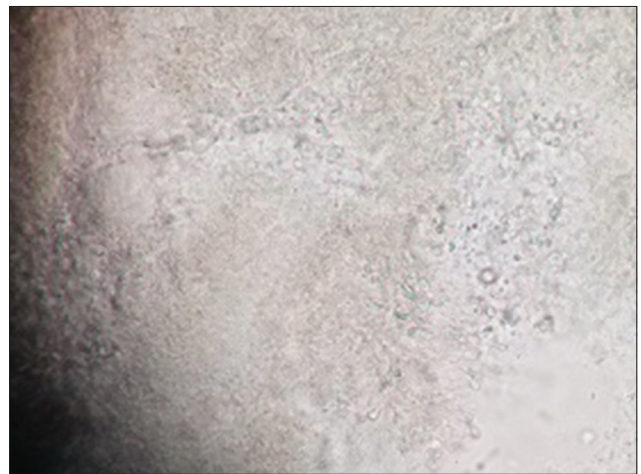
active and healed sinuses [Figure 1]. After cleaning of the affected area with 70% ethyl alcohol, yellowish granules were collected along with the serous fluid from an active sinus by pressing the periphery of sinus. Grains were yellowish in color and size was size 1 to 2 mm. After washing with the sterile saline, it was inoculated on two slants Sabouraud dextrose agar (SDA) media of which one was incubated at 25°C and another at 37°C BOD incubator, Brain heart infusion agar media and Lowenstein Jensen media were also inoculated and incubated at 37°C BOD incubator. KOH (10%) Mount of granule by crushing between sterile slides was made. It was examined under high power field which revealed thin intertwined filaments [Figure 2]. Grams and Ziehl-Neelsen (ZN) stain could perform with serous fluid only as granule was not sufficient to process and it revealed plenty of pus cells with no organisms.

Till 4 week of incubation there was no growth on SDA and brain heart infusion agar (BHIA), but on Lowenstein Jensen (LJ) medium pinkish rough colonies were started to appear. As the colonies were immature and less in number; it was incubated

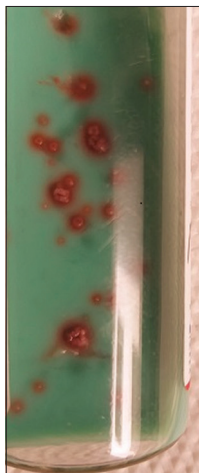
for another one week. On further incubation colonies become dark magenta pink [Figure 3]. Gram stain of colonies showed gram-positive thin branching filaments not more than 1 µm in diameter [Figure 4] and modified Z N stain of the colonies showed non acid-fast filaments. The probable diagnosis of actinomycetoma was made and she was treated with intramuscular injection Gentamicin 80 mg twice daily, Cotrimoxazole 960 mg twice daily along with Mupirocin ointment. Patient had no history of diabetes mellitus, thyroid problem, and tuberculosis in the past. Her viral seromarkers were normal. The patient had successfully responded to the treatment and the sinuses healed completely after 5 months of treatment [Figure 5]. Special features of this isolates were grew only on LJ, slow grower as growth started after 4 weeks. So, for confirmation and to differentiate it from *other Actinomyces* the isolate was sent to National Culture Collection of Pathogenic Fungi (NCCPF), Mycology Division, Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. There it was subculture on various media but could not grow and it was identified as *Actinmadura* genotypically but species remain undetected. It could identify at genus level only.



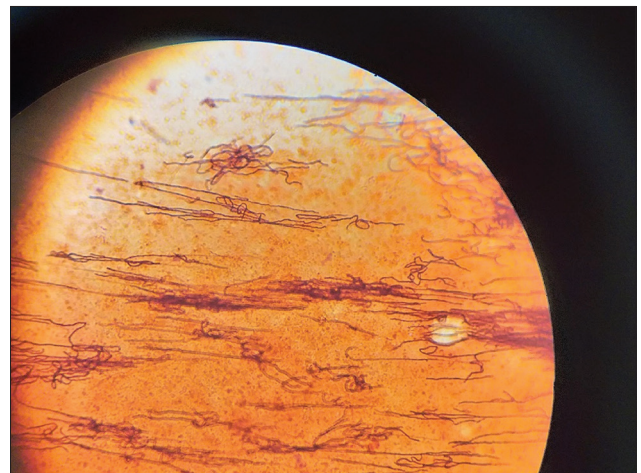
**Figure 1:** Mycetoma foot with the active and healed sinuses with granular discharge



**Figure 2:** KOH Mount showing narrow intertwined filaments



**Figure 3:** Growth on LJ medium after 5 weeks of incubation showing rough magenta colour colonies



**Figure 4:** Gramstain of colonies from LJ Medium showing long filamentous thin bacilli



**Figure 5:** Presentation of patient (Foot) after 5 months of treatment

## Discussion

Diagnosis of mycetoma is usually made clinically by presence of triad tumefaction, draining sinus with discharging granules. In an old study by Taraklaxmet al. (1978) in India, *Nocardia* species and *Madurellagrisea* are the most common causes of mycetoma.<sup>[2]</sup> *Madurellamyctomatis* is also reported from India as well as outside recently.<sup>[3,4]</sup> In India, there is wide variation in the cases, as eumycetoma is common in Rajasthan, whereas other states, namely, Andhra Pradesh, Punjab, Madhya Pradesh, Tamil Nadu, and West Bengal, Uttar Pradesh report most cases of actinomycetoma.<sup>[5-7]</sup> Because of the variation in the climate, socioeconomic factors, and the variations as well as lack of reporting of case in literature, epidemiology of India is undetermined. Though lower limb is common site of mycetoma various sites of actinomycetoma has been reported cervicofacial as well as severe peidonitis due to actinomycetes have also been reported.<sup>[8,9]</sup>

Two cases of Mycetoma from State of Chhattisgarh were reported by Sawatrkar *et al.* but etiological agents were not mentioned.<sup>[10]</sup> Scarcity of reports or underreporting of cases from the Chhattisgarh causes ambiguity in predominance of eumycetoma or actinomycetoma.

In this case clinical presentation was typical of mycetoma and histologically findings were suggestive of mycetoma. KOH of granules had played a crucial role and directed to appropriate processing of the sample. The processing of single grains could get the etiological agent. As presentation was typical, we prolonged the incubation of medium. There was no growth on SDA and Brain heart Infusion Agar (BHIA) till 4 weeks of incubation but on LJ media pinkish colonies were started to appear and could miss if incubation was not prolonged. It grew only on LJ was also characteristic of this species. In literature, it is mentioned that colonies of *Actinomadura* starts with appearance of white areal hyphae which was not seen in the strain and it was slow grower.<sup>[7]</sup> So, for confirmation and to differentiate it from *Streptomyces*, the isolate was sent to National Culture Collection of Pathogenic Fungi (NCCPF), Mycology Division,

Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. Molecular techniques to identify relevant antigens had shown promise. It was identified as *Actinomadura* species by molecular method. Species identification was not mentioned by NCCPF, PGIMER Chandigarh. The reason could not make out. Before microbiological investigations, on clinical suspicion, patient was treated with itraconazole but clinically there was no improvement. After the information of culture findings treatment was changed to modified Welsh regimen. Patients gradually improved without appearance of active sinus later. After taking 5 months of treatment swelling reduced and all sinuses were resolved. Modified Welsh regimen showed excellent response in most of the cases of actinomycetoma and can be considered as first-line therapy for the same.<sup>[11]</sup> Present study wanted to focus on two important aspects, one is, this species of actinomycetes is slow growing and it took around 6 weeks to grow which is usually required around 2 weeks or 4 weeks for fungus. Another important fact is usual culture media for isolation is SDA and BHIA or blood agar but it could obtain growth only on LJ media which was not routinely the media of choice for the isolation of mycetoma causing fungi. A study by Sawatrkar *et al.* from central India had all actinomycetoma cases were culture negative.<sup>[10]</sup> It may be due to shortage in the incubation period which might be possible in our case if incubation was not prolonged. Culture positive *Actinomadura* cases are less reported in literature and diagnosis was made on microscopy.

Isolation and identification of *Actinomadura* had great impact on treatment of this case since the treatment of these two aetiologies is entirely different. For definite diagnosis histopathological and microbiological examination is mandatory, though it is difficult. In the present study histopathology did not gave definitive diagnosis. Report by Alam *et al.* made diagnosis on the basis of Gram stain and histopathology.<sup>[12]</sup>

Serological test though available but are not so reliable; however. Eumycetoma not respond to standard antifungal therapy. Confirmation of identification of organisms by molecular diagnostic techniques can lead to better treatment outcomes reducing the disability and disfigurement associated with this condition though was not available always. Mycetoma is a common neglected tropical disease through leads to deformity.<sup>[13]</sup> Due to its sporadic occurrence exact prevalence in all the part of the India is unknown. There is need of detail investigations like culture of all samples and identification of it. Reporting of more and more cases which will also help to know the prevalence of Actinomycetoma and eumycetoma in the state. It will help to standardise the methods of antimicrobial sensitivity testing to implement the appropriate therapy and management of patient of the rare isolates.

## Conclusion

Diagnosis of mycetoma depends on clinical, histopathological and microbiological background. Clinical and histopathological

findings was not confirmatory and required culture confirmation of *Actinomadura* species which remained key for management of the patient and obtained good recovery. Itraconazole was not effective and modified regimen has to be used for treatment.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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