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A Case Report on Actinomycetoma of the Left Foot: Highlighting a Neglected Tropical Disease and the Consequences of Poor Medication Adherence

Sanatkumar Bharamu Nyamagoud[1*], Agadi Hiremath Viswanatha Swamy[1], Ancy Chacko[1], Jibin James[1]

[1]Department of Pharmacy Practice, KLE College of Pharmacy, Vidyanagar, Hubballi-580031. A Constituent Unit of KLE Academy of Higher Education and Research, Belagavi, Karnataka, India.

***E-mail** ✉ dr.sanathnyamagoud@gmail.com

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ABSTRACT

Mycetoma is a slowly progressive, chronic granulomatous infection that primarily affects the skin, subcutaneous tissue, and deeper structures, with a predilection for the lower limbs. In this report, we describe a case of a 26-year-old male construction worker who presented with complaints of painful, elevated lesions on his left foot. On examination, there were multiple, well-defined, erythematous to skin-colored plaques with erosions and crust formation, predominantly over the left foot and extending to the left thigh region. The patient had a history of repeated hospital admissions due to exacerbation of symptoms, largely attributed to his poor compliance with prescribed medications and disregard for medical advice regarding inpatient care. Microbiological examination confirmed the presence of *Actinomadurae* species. Consequently, the patient was managed with a modified two-step Ramam therapeutic protocol. This case highlights the critical impact of medication non-adherence and limited healthcare access, both of which can prolong the duration of treatment and complicate disease management. Prompt diagnosis, accurate identification of the causative pathogen, and a patient-centered therapeutic approach are essential to achieve favorable clinical outcomes.

Keywords: Actinomadura Madurae, Actinomycetoma, Modified 2-step Ramam Regimen, Eumycetoma

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Introduction

Actinomycetoma represents a chronic, gradually evolving infection of the subcutaneous tissue, typically developing following the traumatic implantation of specific organisms — either bacteria (actinomycetoma) or true fungi (eumycetoma) — commonly found in soil and water environments [1]. It is crucial to differentiate between actinomycetoma and eumycetoma because their respective therapeutic strategies differ significantly [2, 3]. The entry of these pathogens into the body usually occurs through skin injuries or minor trauma, often associated with walking barefoot on contaminated soil or through thorny vegetation [4]. Once introduced into the host tissue, these organisms form compact structures known as grains, which help shield them from the host immune response. These grains vary in color, texture, and size depending on the species of the causative microorganism involved [5].

Mycetoma predominantly affects individuals residing in rural or isolated regions, where access to healthcare services and medications is often severely limited [6, 7]. This infection can occur in people of all age groups, although it tends to be more frequently reported in males [5, 8]. The increased incidence among men may be attributed to higher environmental exposure during outdoor labor, while hormonal factors like the protective effect of progesterone in females could also play a role. However, in endemic zones, females remain equally susceptible due to environmental exposure [9]. Following injury, the pathogen may disseminate via the bloodstream, initiating colonization by circumventing host immune defenses through several survival mechanisms, including cell wall

modification and melanin synthesis. Early cutaneous manifestations often include hypo- or hyperpigmentation, along with both active and healed sinus tracts, which contribute to the spread of infection to adjacent tissues [10, 11].

The occurrence of actinomycetoma is particularly common among individuals engaged in occupations such as farming, fieldwork, or those adhering to certain ritual practices, often those from economically disadvantaged backgrounds. These vulnerable populations frequently experience disruption in education and employment opportunities due to resulting disabilities. Additionally, poor health awareness and delayed medical consultation often lead to advanced disease stages where amputation becomes the only feasible intervention [12]. This case is reported to emphasize the profound influence of patient awareness, healthcare accessibility, community practices, and lifestyle factors on disease progression and health outcomes.

Case Report

A 26-year-old male engaged in construction work sought medical attention at the Skin and STD Centre of Karnataka Institute of Medical Sciences (KIMS), Hubli — a tertiary-level teaching facility — with a prolonged history of painful, elevated lesions ranging in color from erythematous to skin-toned, localized over his left foot. These lesions had persisted for two and a half years, with a recent worsening of symptoms noted over the past week. Additionally, for the preceding two years, the patient reported associated constitutional symptoms, including low-grade fever, unintentional weight loss, and episodes of nausea.

Clinical evaluation revealed multiple well-defined plaques, varying from red to skin-colored, accompanied by distinct erosions and crusting, distributed over the left foot and extending to the left thigh region. Before this illness, the patient was asymptomatic. However, approximately two and a half years ago, he sustained a thorn prick injury over the left sole, which subsequently led to the development of intermittently occurring, mildly itchy, and painful reddish lesions over the affected area (**Figures 1** and **2**).

For initial management, the patient attended the Dermatology Outpatient Department (OPD) at KIMS Hubli in August 2020. At that time, he was prescribed an intramuscular injection of Amoxiclav, oral Paracetamol, and topical Soframycin 1% cream. Despite adherence to the treatment regimen, there was no significant resolution of his symptoms. Consequently, he returned to the Dermatology OPD six months later with exacerbated lesions. Considering the chronic and progressive nature of his presentation, a wedge biopsy was performed on 7th January 2021 for further evaluation.

The biopsy specimen obtained from the patient's lesion consisted of subcutaneous tissue measuring 1.2 cm in length, 0.6 cm in width, and 0.3 cm in thickness. On its outer surface, a sinus tract approximately 0.3 × 0.1 cm in size was identified. Upon sectioning, the tissue displayed a grey-brown appearance. Microscopic analysis showed features indicative of granulation tissue formation. To investigate potential fungal involvement, special staining techniques — including Gomori methenamine silver stain and periodic acid Schiff stain — were utilized, both of which yielded negative results for fungal elements.

Further diagnostic evaluation involved aspirating material from the lesion for microbiological analysis. Gram staining demonstrated abundant pus cells accompanied by a few clusters of Gram-positive cocci. Microbial culture of the aspirate isolated Staphylococcus aureus as the causative organism. Ziehl Neelsen staining was also conducted to screen for acid-fast bacilli, but this test returned a negative result. Additionally, fungal culture of the lesion sample showed no fungal growth even after a 10-day incubation period.

A peripheral blood smear analysis revealed the presence of microcytic hypochromic anemia, along with relative neutrophilia and reactive thrombocytosis. Radiographic imaging of the affected left foot (**Figure 3**) did not show any evidence of bone involvement.

Based on the histopathological findings, the patient was diagnosed with actinomycetoma, clinically identified as Madura Foot. Accordingly, treatment was initiated following the Modified 2-step Ramam regimen. The initial intensive phase included intravenous Gentamicin 80 mg administered every 12 hours, along with Cotrimoxazole DS 960 mg given twice daily for four weeks. This was to be followed by a maintenance phase consisting of Doxycycline 100 mg capsules twice daily combined with Cotrimoxazole DS 960 mg twice daily for a duration of 5 to 6 months.

However, the patient presented for the third time to the outpatient department (OPD) on 17th August 2022, reporting a worsening of symptoms. Upon detailed history, it was revealed that he had self-discontinued the prescribed Gentamicin injections and Cotrimoxazole DS tablets after taking them for just one and a half weeks.

The reason cited was a burning sensation experienced at the injection site. The patient was firmly instructed to comply strictly with the treatment regimen to avoid further complications.

Despite advice, the patient returned for the fourth time on 26th December 2022 with disease progression, as lesions had extended to the thigh region. Owing to poor adherence to the therapeutic plan, he was readmitted to the male ward for proper monitoring and re-initiation of the modified 2-step Ramam protocol. The intensive phase was resumed with Inj. Gentamicin 80 mg twice daily and Cotrimoxazole DS 960 mg twice daily for 28 days. Supportive medications included Tab Pantoprazole 40 mg for 22 days, Tab Serratiopeptidase thrice daily for 22 days, FS/BC/Calcium supplements once daily for 22 days, Tab Paracetamol 500 mg as needed, and Inj Ondansetron as needed.

The lesions initially began as pea-sized nodules, gradually enlarging over time before rupturing spontaneously, releasing a yellow-colored discharge containing granules for approximately four days. The condition had an insidious onset, beginning over the anterior sole and progressively expanding in size and number to affect the entire sole and dorsum of the left foot over one and a half months.

Laboratory investigations revealed normal renal function and blood counts, apart from low hemoglobin levels, for which iron supplementation was administered. An ENT evaluation, including pure tone audiogram (PTA), demonstrated normal hearing function.

Following completion of the intensive treatment phase, the patient showed significant improvement in lesion healing, as observed in follow-up examinations (**Figures 4 and 5**). He remained hospitalized for a total duration of 35 days for supervised care. On 30th January 2023, he was discharged on maintenance therapy, with strict instructions to adhere to the prescribed medications and attend regular follow-ups [13]. Subsequent evaluations revealed favorable wound healing and overall clinical improvement.

Figure 1. Painful red to skin colored raised lesions present over the entire sole and dorsal of the foot region

Figure 2. Multiple discrete erythematous to skin colored plaques with well-demarcated erythematous erosions and crusting present over the left foot

Figure 3. X-ray of the left foot showed no body involvement

Figure 4. Improvement in lesion size and number with no active sinuses

Figure 5. Wound healed with no new or active sinuses

Results and Discussion

Mycetoma is a chronic subcutaneous infection caused by aerobic bacteria, known as actinomycetoma, and fungi, referred to as Eumycetoma [14]. The incidence of actinomycetoma accounts for 60% of global cases, while Eumycetoma makes up 40%. Identifying the specific microorganisms responsible for the infection is crucial, as the treatment protocols differ between the two [15]. The condition is often considered a mixed infection due to the presence of multiple microorganisms within the same environment.

In addition to *Propionibacterium* species such as *P. propionicum*, other bacteria such as coagulase-negative staphylococci, *Staphylococcus aureus*, beta-hemolytic streptococci, microaerophilic organisms, and anaerobic streptococci may also be involved. In cases where *S. aureus* or beta-hemolytic streptococci are present, the lesions are typically painful and exhibit inflammatory features early in the infection [16].

Mycetoma predominantly affects males, with a male-to-female ratio of 3.7:1. This disparity is largely due to higher rates of exposure to contaminated soil during outdoor work activities. However, since females in endemic areas also engage in similar outdoor work, it is possible that other genetic or immune factors could influence susceptibility to the disease [10].

The pathogenesis of mycetoma involves a complex interaction between the host's immune system and the pathogen, which results in a compromised ability to contain the infection. This leads to chronic granulomatous inflammation, which can eventually cause the spread of foreign bodies containing granules to adjacent bone structures [17]. Factors such as poor overall health and malnutrition can exacerbate the infection, as undernutrition weakens the body's defense mechanisms, increasing vulnerability to infection and facilitating its spread. Malnutrition, for example, impairs gut barrier function, which further increases the risk of infection [18].

Microscopic and macroscopic examinations reveal that the color of the grains varies between bacterial and fungal infections. When *Actinomadura madurae* grains are identified, they typically exhibit large, multilobular structures with peripheral basophilic and central eosinophilic or pale-stained filaments. Fungal hyphae and spores can be detected under direct microscopy using KOH stain, while Lugol's iodine stain highlights filaments that are 0.5–1 micrometer in width. Histological stains such as PAS and *Gomori methenamine* silver are positive for fungi, while bacterial grains, including those of *Staphylococcus aureus*, are gram-positive cocci. The acid-fast bacillus (AFB) stain remains negative in bacterial cases [19].

Several other skin conditions, such as plantar or acral psoriasis, sporotrichosis, and botryomycosis, can mimic mycetoma. In the early stages of the disease, lesions appear as firm subcutaneous nodules, which can easily be confused with other benign or inflammatory conditions such as dermatofibromas or hypertrophic scars. This makes early diagnosis challenging based solely on visual inspection. Timely identification of the disease's visible signs, along with prompt treatment, is essential to prevent the severe and often fatal complications associated with mycetoma [10].

The diagnosis of mycetoma is determined by examining clinical signs, including the wound and lesion characteristics, swelling, deformities, granulation tissue, scars, abscesses, sinus tracts, and purulent exudates containing microorganisms, which influence the treatment plan [15]. The treatment strategies differ for eumycetoma and actinomycetoma. Eumycetoma is typically managed using antifungal agents, such as itraconazole, voriconazole, posaconazole, and terbinafine, with early treatment using itraconazole showing potential for lesion reduction. Actinomycetoma is treated with antibiotics like dapsone, amikacin, trimethoprim, and sulfamethoxazole (TMP-SMX), and combinations of streptomycin may be added depending on the specific microorganism involved [19]. In the case presented, the patient tolerated the prescribed medications well under careful monitoring, with PTA and creatinine levels remaining within normal ranges.

Effective treatment of mycetoma often involves the combination of antimicrobials and surgical removal of larger lesions. Trimethoprim and sulfamethoxazole are the standard combination therapy for this condition. Combination therapies are preferred over single-agent treatments for better efficacy and to reduce the likelihood of resistance. For patients unresponsive to cotrimoxazole, alternative treatments such as meropenem and amoxiclav can be utilized. As noted by Agarwal *et al.* [20], premature discontinuation of systemic antimicrobials, coupled with prolonged disease duration and limited healthcare access, significantly raises the risk of disease recurrence.

Bonifaz *et al.* [21] conducted a study with 18 patients suffering from actinomycetoma caused by *A. madurae*. They were treated using two different drug combinations: streptomycin with cotrimoxazole and DDS, and streptomycin with cotrimoxazole and ciprofloxacin. The results indicated that the combination including DDS was less effective in comparison to ciprofloxacin, particularly when bone involvement was minimal [21]. A retrospective analysis involving 31 patients (with a male-to-female ratio of 3.4:1) revealed that Nocardia brasiliensis was the most common pathogen, accounting for 83.9% of cases, followed by *A. madurae* (12.9%) and *Actinomadura pelletieri* (3.2%). Notably, half of the patients exhibited bone involvement. Among the treatment regimens, the Welsh regimen was most frequently used. Treatment selection was influenced by the size of the lesions and the presence of other health conditions. For lesions under 5 cm, trimethoprim and sulfamethoxazole monotherapy was effective. Larger lesions without bone or organ involvement were treated with a combination of trimethoprim, sulfamethoxazole, and amoxicillin-clavulanic acid. The majority of patients showed favorable responses to this combination therapy [22].

In another study by U.S. Agarwal, ten actinomycetoma patients (eight males and two females) were treated with various regimens, including the Ramam regimen, modified Ramam regimen, Welsh regimen, and its modification. Of the 8 patients who received the Ramam regimen, 6 fully recovered. One patient, allergic to penicillin, was

switched to the modified regimen, leading to a full recovery, while another patient, who didn't respond to the Ramam regimen, was transitioned to the modified Welsh regimen and fully recovered. The remaining patient on the modified Ramam regimen also experienced complete recovery. The study indicated that the Ramam regimen was highly effective for patients with minor bone involvement, while the Welsh regimen should be reserved for severe cases [23].

Cure verification typically involves confirming the absence of clinical symptoms, grains, and negative culture results [24]. Patient progress can be monitored through clinical evaluation and laboratory tests, such as hemoglobin levels, white blood cell count, C-reactive protein, erythrocyte sedimentation rate, and, when available, enzyme-linked immunosorbent assay (ELISA), as well as biopsy and culture. Treatment plans for actinomycetoma should be personalized, with consideration of economic factors, especially in low-resource settings [16].

Conclusion

Actinomycetoma is a rare and often overlooked tropical infection that develops subcutaneously, caused by either bacteria or fungi. Typically, it presents with a triad of painless, firm swelling, the presence of grains, and the formation of multiple sinus tracts. Identifying the responsible microorganism is essential for effective treatment. This case highlights the significance of medication adherence and its influence on treatment outcomes. The patient demonstrated a remarkable response to the prescribed therapy, with notable improvement in the lesions upon follow-up.

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