Case Report

Actinomycetoma of Left Foot - A Case Report of Neglected Tropical Disease and Medication Non-adherence

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Abstract

Mycetoma is a chronic localized progressive granulomatous infection of the skin involving subcutaneous and deeper tissues, commonly affecting the lower extremities. We report a case of a 26-year-old male construction worker presented with chief complaints of painful red to skin-colored raised lesions present over his left foot, lesions were multiple discrete erythematous to skin-colored plaques with well-demarcated erythematous erosions and crusting present over the left foot and left thigh region. The patient had been hospitalized several times due to worsening symptoms because of his nonadherence to medications and negligence toward health and medical advice of hospital inpatient admissions. Actinomadurae was isolated and a modified 2-step Ramam treatment regimen was initiated. This case is presented to signify how medication non-adherence and poor health facilities can lead to an increase in treatment course and duration. Early detection and identification of the causative organism and individualized treatment plans are necessary for a better clinical outcome.

Keywords: Actinomycetoma, Eumycetoma, Modified 2-step Ramam regimen, Actinomadura madurae

Introduction

Actinomycetoma is a slowly progressing subcutaneous infection that develops after a traumatic inoculation of the bacteria (actinomycetoma) or true fungi (Eumycetoma) which is seen in soil and water [1]. These causative agents, actinomycetoma and eumycetoma, must be distinguished as their treatment is different [2, 3]. The agents are introduced into the body by traumatic inoculation or minor trauma which is found by walking barefoot in soil and thorny vegetation [4]. On further inoculation with the causative organism, they aggregate into grains, which serve as a protective mechanism against the human immune system. These grains have different colors, consistency, and sizes according to the type of microorganism [5].

People affected by mycetoma often live in remote areas where they have limited access to health care and medication [6, 7]. Mycetoma affects people of all ages and is more common in men., and males are most affected than females [5, 8]. Two Possible reasons may be due to progesterone inhibiting the growth of organisms and men having a higher risk of exposure to soil-borne microorganisms while working outside, but in mycetoma-endemic locations, females are equally at risk [9]. After a traumatic injury, there will be a hematogenous spread due to which there will be an initial colonization of organisms invading the human host defense mechanism through a variety of adaptations like cell wall thickening and melanin production. Initially, there will be hyper or hypo skin pigmentation with signs of active and old sinus and which simultaneously spreads the infection to new areas [10, 11]. The probability of occurrence of actinomycetoma is more likely to be seen in people like (fieldworkers, farmers, ritual beliefs, and workers of low socioeconomic status) these people lose their chance of education and jobs due to disability and due to their lack of health-consciousness they present to the doctor late and due to that amputation is usually the only available treatment [12]. Hence this case was reported to address that lack of knowledge and attitude, health facility, lifestyle, and community can impact patient health.

Case Report

A 26-year-old male worker (construction) was presented to the Skin and STD Centre of Karnataka Institute of Medical

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Sciences, Hubli, a tertiary care teaching hospital, with chief complaints of painful red to skin-colored raised lesions present over a left foot for two and half years and exacerbations of symptoms in the last 1 week. He had a history of fever of low grade, weight loss, and nausea for 2 years. On examination, the lesions were multiple discrete erythematous to skin-colored plaques with well-demarcated erythematous erosions and crusting present over the left foot and left thigh region. Two and half years before, the patient was all right, then he had a throne prick following which he developed itchy painful red lesions intermittent in nature, mild grade over the left sole region of the leg **(Figures 1 and 2)**. The patient visited the skin outpatient department (OPD) of KIMS Hubli in August 2020 and was prescribed an injection of Amoxiclav, Tab Paracetamol, and Soframycin 1% cream. There was no cure for the symptoms after taking these medications and again he revisited Skin OPD after 6 months with the same chief complaints which were exaggerated and for which a Wedge biopsy was done on 7th January 2021. According to the skin biopsy, the gross appearance - specimen consists of subcutaneous tissue measuring 1.2×0.6×0.3cm, in the external surface a sinus present measuring 0.3×0.1cm and the color of the cut surface was grey-brown. Features suggestive of granulation tissue, special stain for fungus Gomori methenamine silver stain, and periodic acid Schiff stain are negative. Aspirate from the lesion was sent to the microbiology lab for Gram staining and Ziehl Neelsen staining. Gram's staining picture revealed numerous puss cells and a few pairs of Gram-positive cocci and the organism isolated was Staphylococcus aureus. Ziehl Neelsen's stain report showed negative for acid-fast bacilli. The fungal culture report showed no growth after 10 days of incubation. Peripheral smear test showed microcytic hypochromic anemia with relative neutrophilia and reactive thrombocytosis. X-ray of the left foot showed no body involvement **(Figure 5)**. The report showed features suggestive of actinomycetoma diagnosed as Madura Foot and started with a Modified 2-step Ramam regimen (Step 1-Intensive Phase: IV Gentamicin 80mg 12 hourly + Cotrimoxazole DS 960mg BD for 4 weeks, Step 2-Maintenance Phase: Cap Doxycycline 100mg BD + Cotrimoxazole DS 960mg BD for 5-6 months). On 17th August 2022, the patient had been in OPD third time with exacerbation of symptoms, and he had said about taking medications continuously for 1 and half weeks then he stopped taking the Gentamicin injections and Cotrimoxazole DS tablet of his own choice because of the burning sensation on the site of injection. Further, the patient had been strictly advised to continue the medications regularly. On 26th December 2022, the patient revisited for the fourth time because lesions were spread to his thigh region. He was readmitted because of his non-adherence to the course of treatment again. He was then admitted to the male ward and was restarted with a Modified 2-step regimen (Inj Gentamicin 80mg twice a day for 28days, Cotrimoxazole DS 960mg Tab twice a day for 28 days for the initial phase along with the Pantoprazole 40mg Tab for 22 days, Serratiopeptidase Tab thrice a day for 22 days, FS/BC/Calcium Tab once a day for 22 days, Paracetamol 500mg Tab SOS, and Ondansetron Inj SOS). The lesion was initially pea size which was gradually increased in size and burst on its own and released a yellow discharge with granules for four days. Lesions were insidious and onset initially present over the anterior aspect of the sole later progressed in size and number to involve the entire sole and dorsal of the foot region for one and half months. Investigation showed normal limits of renal parameters and blood counts except low hemoglobin levels for which iron supplements were given. His Ear Nose Throat (ENT) evaluation was done which showed a normal Pure Tone Audiogram (PTA). After the completion of the intensive phase of treatment, the lesions were improved **(Figures 3 and 4)**. The patient was admitted to the hospital for the entire treatment a total of 35 days. On 30th January 2023, the patient was discharged with maintenance therapy. The patient was advised to strict medication adherence and follow-up [13]. During the follow up the wound was found to be better and healing.

Pretreatment

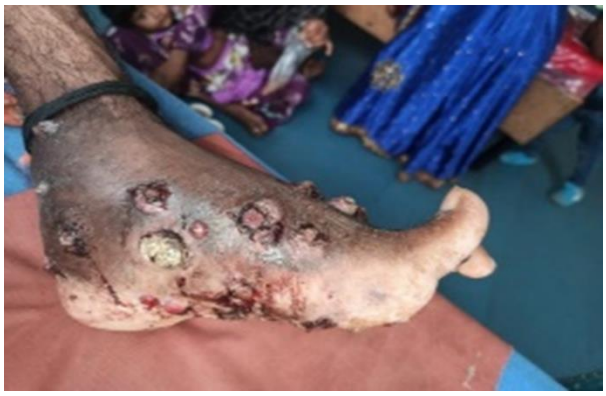

Figure 1. Painful red to skin colored raised lesions present over entire sole and dorsal of the foot region.

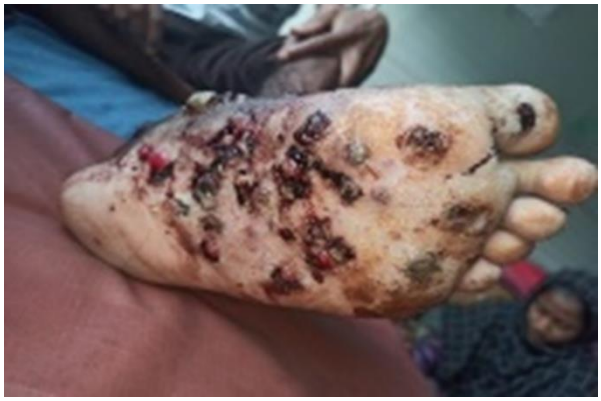

Figure 2. Multiple discrete erythematous to skin colored plagues with well-demarcated erythematous erosions and crusting present over the left foot

Post Treatment

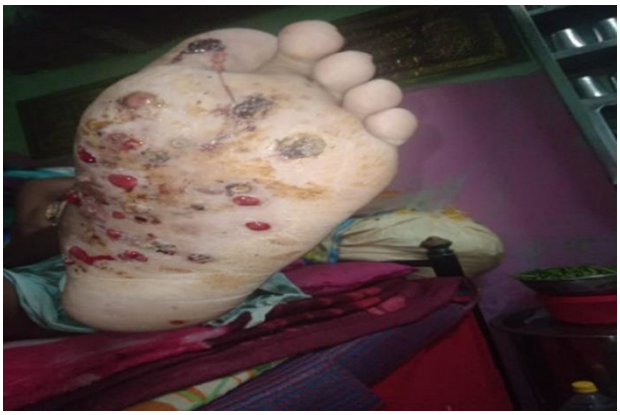

Figure 3. Shows improvement in lesion size and number with no active sinuses

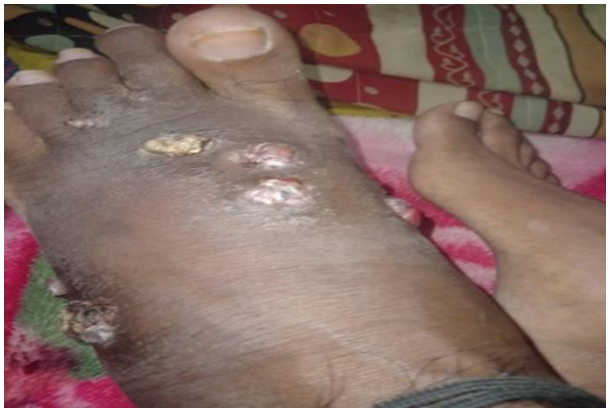

Figure 4. wound healed with no new or active sinuses

Investigations

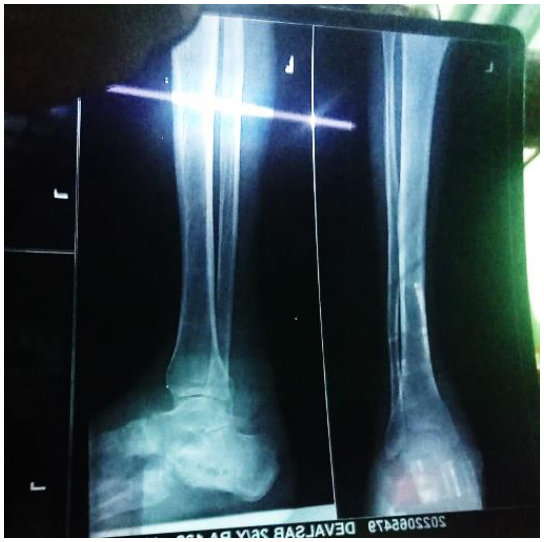

Figure 5. X-ray of the left foot showed no body involvement.

Results and Discussion

Mycetoma is a subcutaneous disease that is caused by aerobic bacteria (Actinomycetoma) and fungi (Eumycetoma) [14]. The worldwide disease population in actinomycetoma is 60% and Eumycetoma is 40%. Therefore, it is necessary to identify the disease-causing microorganisms since their treatment varies [15]. This condition should be classified as a synergistic infection since, in the majority of cases, it is a mixture of several microorganisms that reside in the same habitat.

Other Propionibacterium species besides P. propionicum may also be present, along with coagulase-negative staphylococci, Staphylococcus aureus, beta- and -hemolytic streptococci, microaerophile, and anaerobic streptococci. S.aureus or β-hemolytic streptococci the lesion will be usually painful and inflammatory at the onset of infection [16].

Mycetoma consistently exhibits male dominance, with a gender ratio of 3.7:1. This is mainly attributed to the increased risk of soil exposure while engaging in outdoor work-related activities. However, considering that females undertake outdoor job activities in mycetoma-endemic regions, it is impossible to rule out the possibility of other genetic or immunological variables [10].

The disease progression is a complex process of interplay between host and pathogen, leading to reduce immunity to engulf the pathogen, subsequently, chronic granulomatous inflammation occurs. Therefore, foreign bodies with granules may spread into the bony structure [17]. Predisposing factors that may worsen the condition of the patient like poor general health, and malnutrition thus leading to more invasion and widespread infection. Undernutrition drives an increased risk of infection by reducing gut barrier function [18]. In the microscopic and macroscopic study, the color of grains varies with fungi and bacteria, and when grain morphology in identified actionomadura madurae will have large and multilobulate peripherally, basophilic and centrally eosinophilic or pale stained filaments grow from the peripheral zone. Under direct microscopic stain with KOH fungal hyphae and spores, are found for fungus and stain with Lugol's iodine stain- filaments with a width of 0.5-1micro meter. Histological staining in fungi PAS staining and Gomori methenamine silver will be positive and in bacteria that is Actinomadurae grains are gram-positive cocci (Staphylococcus aureus) and acid-fast bacillus (AFB) is negative [19]. Many skin disorders, including plantar or acral psoriasis, sporotrichosis, and botryomycosis, can mimic mycetoma. The lesion simply resembles a firm subcutaneous nodule in very early mycetomas, before the first sinuses appear. This makes it difficult to diagnose the condition from a visual examination because the differential includes a wide range of benign and inflammatory conditions, from dermatofibromas to hypertrophic scars. Early case diagnosis, which depends on identifying the disease's visible warning signals, and treatment are the only ways of avoiding this and stopping the numerous and deadly sequelae of mycetoma [10].

Diagnosis is based on clinical manifestation, features of wound and lesions, swelling and deformity of affected areas, presence of granulation tissue, scars, abscesses, sinus tracts, and purulent exudate that contains microorganisms according to this treatment varies [15]. Treatment for eumycetoma and actinomycetoma are different, eumycetoma is managed with Antifungal agents that as itraconazole, voriconazole, Posaconazole and terbinafine, and early administration of itraconazole have shown to reduce the size of the lesion. Actinomycetoma is treated with an antibacterial agent such as dapsone, amikacin, trimethoprim, and sulfamethoxazole (TMP-SMX), and depending on the infecting species, different combinations of streptomycin are used to treat actinomycetoma [19]. In our case study, the patient was well tolerable to the medications when carefully given and he was monitored for PTA and creatinine clearance which showed in normal limits.

Antimicrobials along with surgical debulking of larger lesions are found to be effective. In antimicrobial agents, Trimethoprim and sulphamethoxazole are a gold standard combination. Combination therapy is preferred over monotherapy due to several reasons which may be to improve response and to prevent resistance. Those patients who are not responding to cotrimoxazole can be treated with meropenem and amoxiclav. According to Pooja *et al*., the early stoppage of systemic AMA and long-standing disease with the scarcity of medical and health facilities have a higher chance of relapse of the disease [20]. In this study conducted by Alexandro Bonifaz *et al*., 18 subjects of actinomycetoma caused by A madurae they were given 2 treatment modalities that includes streptomycin + cotrimoxazole + DDS and streptomycin + cotrimoxazole+ ciprofloxacin and it was found that treatment including DDS was less effective when compared to ciprofloxacin in treating patients with Actinomycetoma caused by A madurae due to minimal bone involvement [21]. From the retrospective study conducted on 31 patients (male to female ratio is 3.4:1) diagnosed with actinomycetoma, Nocardia brasiliensis (83.9%) was the most common potential cause of lesions, followed by A. madurae (12.9%), and actinomadura pelletieri (3.2%) and it was stated that 50% of patients had bone involvement. Out of all regimen Welsh regimen was the most commonly used. Treatment was provided according to the lesion size and other patient-related comorbidities. Trimethoprim and Sulfamethoxazole monotherapy was used in a patient with lesions size under 5cm. Trimethoprim and sulfamethoxazole combined with Amoxicillin and clavulanic acid was used in larger lesions without bone/ internal organ involvement. It was found that most cases responded effectively to a treatment regimen consisting of Trimethoprim and Sulfamethoxazole combined with Amoxicillin and clavulanic acid [22]. In another prospective study conducted by U.S Agarwal, 10 patients (8 males and 2 females) who were diagnosed with actinomycetoma were enrolled in the study and were treated with different treatment regimens like Ramam regimen, Modified Ramam regimen, Welsh regimen, and its modification. Eight patients had been treated with Ramam regimen out of which Six patients had a full recovery, one had a penicillin allergy and was switched to a modified regimen; this patient also had a full recovery., whereas another patient had no response to the ramam regimen and then was shifted to the modified Welsh regimen and showed a complete response. And the other patient who was treated with a modified ramam regimen showed a complete response. Patients with actinomycetoma who only had minor skeletal involvement responded well to the Ramam regimen., according to the author, whereas the Welsh regimen and its modification should be reserved and should only be used for severe diseases [23]. The cure can be confirmed by a lack of clinical activity, absence of grain, and negative culture [24]. Clinical evaluation and laboratory tests, such as those for hemoglobin level, total count, C-reactive protein, erythrocyte sedimentation rate, enzyme-linked immunosorbent assay (where available), biopsy, and culture, might be used to follow up on a patient's progress. Therapy for patients with actinomycetoma should be individualized. Economic considerations may influence the choice of therapy, particularly in developing countries [16].

Conclusion

Actinomycetoma is a neglected and rare tropical disease that is a subcutaneous progressive infection caused by bacteria or fungi. Usually, it follows with a clinical triad of painless hard swelling, grains, and multiple sinus tracts. Determining the causative organism is fundamental to the treatment process. This case was reported to address the importance of medication adherence and its impacts on the treatment outcome. The patients showed excellent response to the treatment and on follow up showed improvement in lesions.

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