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# A Forgotten Case of Madura Foot

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**Abstract:** Mycetoma is a chronic, suppurative, and debilitating granulomatous infection primarily found in tropical and subtropical regions. The World Health Organization has classified it as a neglected tropical disease. The clinical diagnosis is typically based on a classic triad of localized swelling, the formation of sinus tracts, and the production of grains or granules. However, atypical presentations of the disease are also observed. Mycetoma is divided into two categories: eumycetoma, which is caused by fungal organisms, and actinomycetoma, which is caused by bacterial agents. While the clinical features of both types are similar, a precise diagnosis is crucial, as treatment approaches differ between the two. The treatment of mycetoma involves surgical debulking to remove the bulk of the lesion, followed by an extended course of medical therapy. This combined approach has become the standard due to the long duration of the disease and the often suboptimal response to treatment. The prolonged course of mycetoma necessitates careful management, as the disease can be difficult to treat effectively with just one modality. Therefore, early detection and accurate diagnosis are key to determining the most appropriate treatment plan for each patient.

**Keywords:** actinomycetoma, eumycetoma, treatment

## INTRODUCTION

Mycetoma, also known as Madura foot, is a rare and chronic tropical disease that primarily affects the skin, subcutaneous tissue, and bones, especially in the foot. This condition is characterized by a distinct combination of localized swelling, the presence of multiple sinus tracts, and the discharge of granular material or grains. The causative microorganisms of mycetoma typically enter the body through small skin abrasions caused by minor injuries. This disease is categorized into two main types: eumycetoma, caused by fungi such as *Madurella mycetomatis*, and actinomycetoma, caused by bacteria like *Actinomadura madurae*. In India, approximately 75% of mycetoma cases are classified as actinomycetoma. Actinomycetoma generally responds well to antibacterial treatment, whereas eumycetoma is less responsive to antifungal therapy and is often associated with recurrent episodes.

Recently, the World Health Organization (WHO) has officially recognized mycetoma as a "neglected tropical disease," highlighting the lack of attention the condition has received despite its considerable impact on both public health and economic resources. Mycetoma is a

persistent infection that primarily affects the skin and subcutaneous tissue, and in advanced or neglected cases, the infection may extend to involve the bones. While mycetoma is found worldwide, it is most prevalent in tropical and subtropical regions, particularly within an area known as the "Mycetoma Belt," which spans between latitudes 30° N and 15° S (Garg, 2017).

The earliest descriptions of mycetoma date back to ancient Indian scriptures, including the Atharva Veda (Kwon-Chung, 1992). Over time, the disease has been referred to by various names, such as "Anthill foot" and "Madura foot." It was not until the disease's fungal origin was established that the term "mycetoma" was proposed by Carter in 1860 (Carter, 1860). As further research revealed that both bacterial and fungal organisms could cause mycetoma, the condition was formally classified into two categories: Maduramycosis, caused by fungi, and Actinomycosis, caused by bacteria. Actinomycotic mycetoma is caused by aerobic species of actinomycetes, with *Nocardia brasiliensis*, *Actinomadura madurae*, *Actinomadura pelletieri*, and *Streptomyces somaliensis* being the most common causative organisms. On the other hand, eumycotic mycetoma is associated with various fungi, the most prevalent being *Madurella mycetomatis* (Garg, 2017).

Actinomycetoma typically responds positively to antibacterial therapy, with most cases being manageable through antibiotics. In contrast, eumycetoma is more difficult to treat with antifungal medications and often leads to repeated infections or relapses. This difference in response to treatment underscores the distinct nature of the two types of mycetoma. While actinomycetoma remains a significant public health issue, eumycetoma presents even more challenges due to its resistance to treatment.

The global distribution of mycetoma further complicates efforts to control the disease. While it affects populations worldwide, it is most common in regions with warm climates, especially those in the tropics and subtropics. Despite being recognized as a significant medical condition, mycetoma continues to be underreported and underdiagnosed, which has contributed to its classification as a neglected tropical disease.

By focusing on both the scientific and public health aspects of mycetoma, it is hoped that greater awareness, improved diagnostic methods, and more effective treatment options will be developed to combat this debilitating and often neglected disease.

**Clinical Presentation of the Disease**

The causative microorganism of mycetoma enters the skin through minor injuries, which are often unnoticed or trivial in nature. Due to the long and variable incubation period, which can range from 3 months to several years, many patients cannot clearly recall the specific incident that led to the trauma when they seek medical attention. This delayed onset often complicates the diagnosis.

In terms of gender distribution, mycetoma is more commonly observed in males, with a male-to-female ratio of approximately 3:1. This higher prevalence in men is likely attributed to their increased exposure to the pathogens, particularly through activities such as agricultural work, which often involves direct contact with soil and other potential sources of infection. Additionally, some researchers have proposed that the hormonal differences between men and women may also contribute to this gender disparity. It has been speculated that female hormones, specifically progesterone and estradiol, could have an inhibitory effect on the growth and proliferation of the microorganisms responsible for mycetoma, potentially reducing the likelihood of infection in women. As a result, men tend to be more frequently affected by this condition (Hernández, 1995; Ménde, 1991).

The long latency period and the difficulty in recalling the initial trauma often lead to a delay in diagnosis, as the patient may not immediately associate their symptoms with a previous injury. This is particularly challenging for healthcare providers, as the condition can

develop gradually over time, making early detection difficult. Consequently, by the time the patient seeks medical advice, the infection may have progressed significantly.

Understanding these factors—such as the prolonged incubation period, the gender predisposition, and the potential hormonal influence—can aid in better recognizing the risk factors for mycetoma and contribute to more accurate and timely diagnoses. Improved awareness and a thorough medical history, including any minor injuries or exposure to high-risk environments, are crucial for managing and treating this neglected tropical disease effectively.

**Clinical Features**

Mycetoma primarily affects the lower extremities, with the foot being the most commonly involved site. The hand is the next most frequent site, typically affecting the right hand more than the left. Other areas that can be affected include the head, neck, chest, shoulders, and arms (Verma, 2019). Rare cases of eumycetoma have been observed in locations such as the abdominal wall, facial bones, paranasal sinuses, orbit, eyelids, and genital areas, including the vulva or scrotum (Fahal, 2018). Actinomycetoma, on the other hand, is more commonly found on the chest or abdominal wall compared to the limbs, and in some cases, both limbs may be affected simultaneously.

The presentation of mycetoma generally follows a classical triad: a painless, hard subcutaneous mass that feels woody, multiple discharging sinuses, and the presence of grains in the purulent or seropurulent discharge (Verma, 2019). These grains are the colonies of the causative microorganisms, and their color, size, and consistency can vary depending on the type of pathogen involved. However, in some instances, this classical triad may not be present, making diagnosis more challenging. Instead of the typical indurated swelling, a softer, lobulated, or even cystic swelling may be observed (Fahal, 2018). Rare presentations include a painless firm swelling on the sole without any discharging sinuses, even in the absence of a prior history of trauma or barefoot walking. The initial lesion is often a small papule that gradually evolves into a painless nodule. Occasionally, an abscess or an ill-defined area of induration may form as the initial lesion. As the condition progresses, pustules develop, which rupture and discharge purulent material containing grains (Grover, 2017). These pustules and nodules may grow in size and rupture, either through the skin or along fascial planes, leading to the spread of the disease. Sinuses develop as the infection penetrates deeper, and these are often interconnected. The disease alternates between active and healing phases, resulting in the simultaneous presence of both fresh and healed sinuses, which is characteristic of mycetoma. The overlying skin becomes smooth, stretched, shiny, and fixed to underlying structures, often displaying areas of hypo- or hyper-pigmentation. In rare cases, there may be an increase in local sweating and raised temperature over the lesion, likely due to sweat gland hyperplasia and increased blood flow from inflammation.

The grains present in the discharge during the active phase are composed of the microorganism colonies, which are encapsulated in a cement-like material along with melanin and other substances. This coating helps protect the microorganisms from the host's immune defenses as well as from antimicrobial and antifungal treatments (Fahal, 2018). These grains are often visible to the naked eye, and their color typically indicates the causative organism. Black or dark grains are diagnostic of eumycetoma, while red or pink grains are associated with actinomycetoma. White or pale yellow grains may be seen in both types. The consistency of the grains ranges from soft to firm, with those from *Scedosporium somaliensis* and *Madurella mycetomatis* being particularly hard (Relhan, 2017).

Despite its aggressive clinical appearance, mycetoma is usually painless, possibly due to anesthetic substances produced by the microorganisms. In the later stages, nerve damage caused by the fibrous tissue reaction or reduced blood supply leads to a lack of pain

sensation. Pain is reported in only 15% of patients and is often linked to secondary bacterial infections or the rupture of a new sinus.

In most cases, mycetoma remains localized. However, if neglected, the disease can spread along fascial planes, affecting deeper structures like ligaments, muscles, and bones. This makes the condition more resistant to treatment, and bone involvement may lead to osteomyelitis. In rare instances, vertebral compression can occur if mycetoma affects the back, resulting in neurological symptoms (Verma, 2019). Nerves and tendons are rarely involved, and when they are, it is usually at a late stage. This may be due to increased blood flow to the affected area, which limits trophic changes. In long-standing cases, tortuous veins, similar to varicose veins, may form as a compensatory mechanism to accommodate increased venous return.

**Treatment**

In evaluating the clinical cure of mycetoma, certain parameters can be assessed. These include the normal appearance of the overlying skin, an ultrasonographic examination showing the absence of grains and cavities, and a radiological assessment revealing the reappearance of a normal bone pattern along with the absence of soft tissue swelling. These factors serve as indicators that the disease may have been successfully treated.

However, there are several predictors for recurrence of mycetoma. These include poor health education, which often leads to a delayed diagnosis, as well as long-standing disease in areas with limited medical resources. Other risk factors include a positive family history, larger lesion sizes (greater than 10 cm) at the time of presentation, and patients with long-standing extra-pedal mycetoma. Additionally, elderly individuals with a shorter disease duration and those living in non-endemic areas may face increased risks due to lower immunity and the lack of exposure to low-grade subclinical infections. Patients with pedal mycetoma who have undergone previous surgeries, especially those with a family history of the disease, may experience further complications. Previous surgical excisions may spread the organisms along different tissue planes, leading to fibrosis and cavitation, making complete excision difficult. Other factors contributing to recurrence include early discontinuation of systemic antimicrobials, incomplete resection, and faulty debridement. Local excision under local anesthesia may also lead to incomplete removal, posing a higher risk of recurrence.

**Treatment of Mycetoma**

The diagnosis of mycetoma is often overlooked in its early stages, which, combined with its gradual progression, presents significant challenges for physicians. This delayed diagnosis requires a multidisciplinary approach for effective management. Recently, the treatment of mycetoma has evolved, with systemic antimicrobials and surgical debulking of larger lesions now considered essential components of the management strategy. However, since the causative agents of mycetoma belong to two different microbial families, each requiring distinct treatments, confirming the diagnosis is crucial before starting any therapy.

For eumycetoma, surgical debulking plays a vital role due to the poor drug penetration through the fibrous tissue surrounding the lesion. This procedure helps reduce the mycetoma load, improving the response to clinical therapy. Careful surgical dissection with an adequate safety margin is necessary, followed by thorough examination and irrigation of cavities and deep pockets with iodine solution and hydrogen peroxide to eliminate any remaining hyphae and grains. While ketoconazole was once a standard treatment, its use has decreased due to potential hepatotoxicity. Currently, itraconazole (400 mg/day) is considered the gold standard therapy, though treatment response can vary among patients. Terbinafine, when used alone, has limited efficacy but can be combined with itraconazole for better results.

Newer antifungal drugs such as fosravuconazole, a prodrug of ravuconazole, and Isavuconazole have shown promising in-vitro results and are currently being tested in clinical trials for eumycetoma. Despite their in-vitro effectiveness, echinocandins and amphotericin B have shown poor activity against Madurella mycetomatis and are not recommended for use in mycetoma treatment. However, a novel approach involving amphotericin B-impregnated calcium sulfate beads inserted into bony defects after surgical debulking has demonstrated good clinical outcomes with fewer side effects. Meanwhile, recommendations to improve the current treatments include using cotrimoxazole combined with amoxicillin or doxycycline for prolonged periods after the disease becomes inactive. The disappearance of swelling and healing of sinuses, along with tissue examination confirming the clearance of organisms, are signs of successful treatment.

While the search for more effective drugs continues, enhancements to existing therapies are being explored to improve clinical outcomes. For instance, an oral solution of itraconazole in a cyclodextrin vehicle has shown increased bioavailability compared to the standard capsules and may prove particularly useful in pediatric populations. Additionally, therapeutic drug monitoring (TDM) techniques like high-performance liquid chromatography (HPLC) and mass spectrometry (MS) can help maintain effective and safe drug levels, optimizing treatment. Combining systemic antifungals with NSAIDs has also shown positive results in treating refractory cases of mycetoma, with no relapses reported during long-term follow-up. Furthermore, combining oral prednisolone with antifungals and sulfamethoxazole plus trimethoprim has been reported to improve clinical outcomes without significant side effects.

Several factors contribute to the recurrence of mycetoma, including poor health education, which leads to delayed diagnosis, and long-standing disease in areas with limited medical resources. Other predictors include a positive family history, large lesions (greater than 10 cm), and patients with long-standing extra-pedal mycetoma. Additionally, elderly individuals with a shorter disease duration who live in non-endemic areas may have lower immunity and are less likely to be exposed to subclinical infections, making disease spread and surgical intervention more difficult. Patients with pedal mycetoma who have undergone previous surgeries are also at higher risk of recurrence, as surgery may cause the organisms to spread, resulting in fibrosis and cavitation that make complete excision challenging. Early discontinuation of antimicrobials, incomplete resection, and faulty debridement also contribute to recurrence, as does performing local excision under local anesthesia, which can lead to incomplete removal of the infection.

## METODE

This study employed a case report approach aimed at providing a detailed description of a neglected case of mycetoma or "Madura foot" that had not received optimal medical treatment. The subject of this report was a 35-year-old male farmer who presented with classical symptoms of mycetoma. Data were collected through direct clinical observation, thorough anamnesis, physical examination, and supporting investigations such as laboratory tests, histopathology, and radiological imaging to confirm the diagnosis. Determination of the type of mycetoma—either eumycetoma or actinomycetoma—was based on the morphology and color of the grains, as well as microbiological culture results when available. Once the diagnosis was established, the patient underwent surgical debulking followed by pharmacological therapy in accordance with established treatment protocols for either actinomycetoma or eumycetoma. All procedures adhered to medical ethical principles and were conducted with the patient's informed consent. Data analysis was carried out descriptively to illustrate the disease progression, therapeutic response, and potential risk factors contributing to the delayed diagnosis and treatment in this case.

## RESULTS AND DISCUSSION

### Case report

A 35-year-old male farmer was admitted with complaints of swelling and discharge on his right foot for the past year. Upon examination, a poorly defined nodular swelling measuring 10x10x8 cm was observed on the medial side of the right foot, involving the instep. The swelling was accompanied by multiple discharging sinuses, suggesting a chronic infection, likely mycetoma. The presence of these sinuses is characteristic of mycetoma, a condition often marked by swelling, sinuses, and discharge of grains or granules from the affected area.

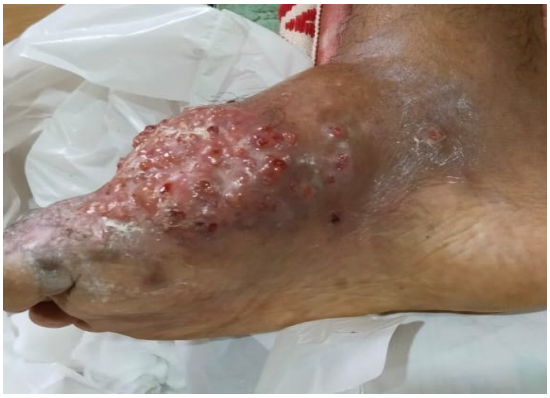

**Figure 1. Before treatment**

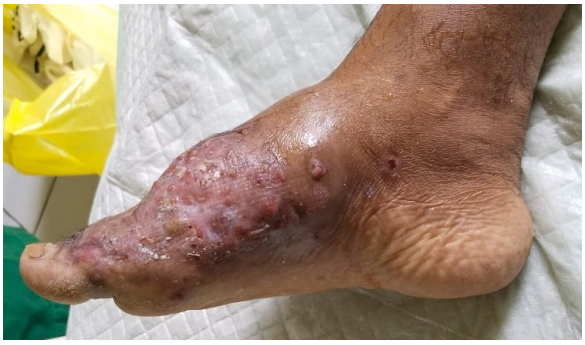

**Figure.2 after treatment 15 days**

Investigations revealed a Gram stain showing few pus cells along with Gram-positive cocci. Additionally, a potassium hydroxide mount displayed branched septate hyphae and fungal spores, indicating a fungal infection. The X-ray of the foot did not show any bony abnormalities, suggesting that the infection was localized to the soft tissues. Histopathological examination revealed a neutrophilic infiltrate surrounded by palisading histiocytes, with a mixed inflammatory infiltrate of lymphocytes, plasma cells, eosinophils, macrophages, and fibrosis, further supporting the diagnosis of mycetoma.

Based on these findings, the patient was started on a treatment regimen consisting of itraconazole (400 mg/day) divided into two doses. In addition, doxycycline (100 mg orally, twice daily) was prescribed to address the infection. This combination of antifungal and antibiotic therapy aimed to target both the fungal and bacterial components of the mycetoma. The patient had previously undergone surgical debulking to reduce the size of the lesion, which helped improve the effectiveness of the treatment.

After three months of treatment, the patient's condition showed significant improvement. The swelling reduced, and there was a noticeable decrease in discharge from the sinuses. The clinical response indicated that the combination therapy was effective in

managing the infection and facilitating recovery. This improvement was further documented through clinical follow-up and examination (Fig. 3), highlighting the positive outcome of the treatment plan.

The case emphasizes the importance of early diagnosis and appropriate therapy in managing mycetoma. The use of systemic antifungals like itraconazole, along with supportive antibiotics like doxycycline, proved to be an effective treatment strategy. Surgical intervention, such as debulking, also played a crucial role in reducing the mycetoma load and aiding in the patient's recovery.

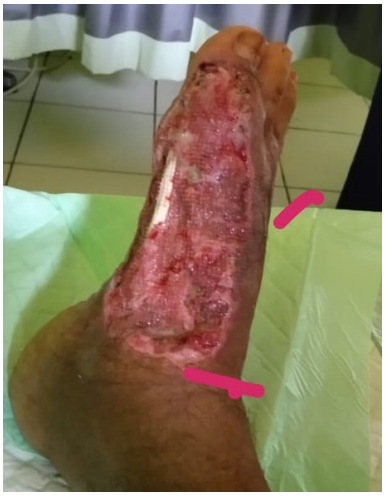

**Figure.3 after treatment (3 month)**

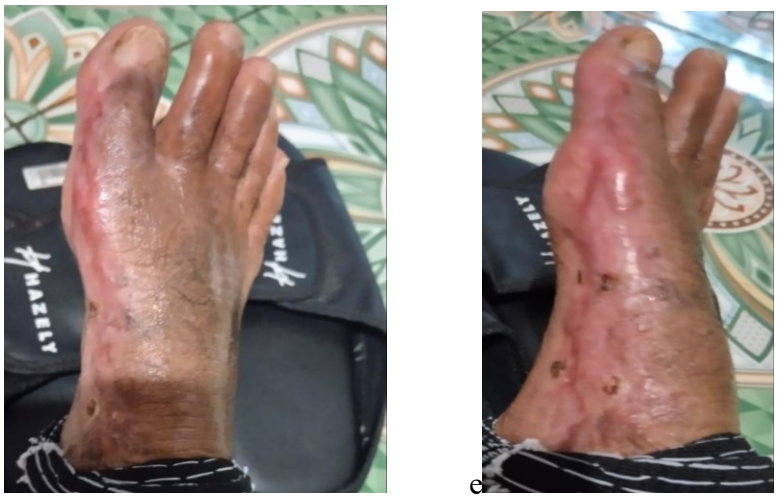

**Figure:4 after treatment (6 month)**

## Discussion

Managing eumycetoma remains one of the major challenges in the medical world, particularly in developing countries where access to health services is limited. This disease, which is often chronic and debilitating, tends to go unnoticed in its early stages due to the slow progression of symptoms. Patients frequently delay seeking medical help, either because of a lack of awareness or inadequate health infrastructure, and by the time they present to healthcare facilities, the disease is often already at an advanced stage, making treatment more difficult and costly.

A significant factor contributing to the delay in diagnosis and treatment is the limited education and poor socioeconomic status of many patients. People affected by eumycetoma often come from rural or marginalized communities where healthcare literacy is low, and the

resources required to access treatment are unavailable. These circumstances often lead to prolonged suffering, with individuals tolerating symptoms for years until the disease causes substantial discomfort or disability. At that point, the consequences can be devastating, including permanent damage to the affected limb or even the necessity for amputation.

Even in situations where early diagnosis is successfully established, patients may still choose to delay or reject treatment altogether. This decision is frequently influenced by fear, stigma, or the belief that the condition will resolve on its own. Unfortunately, such delays often worsen the prognosis, leading to greater functional impairment. For this reason, it is critical to develop a comprehensive treatment plan that not only addresses the medical aspects of the disease but also incorporates social and economic support mechanisms to encourage patient adherence.

In terms of therapeutic strategy, eumycetoma in its advanced stages typically does not respond well to pharmacological treatment alone. For optimal outcomes, a combination of antifungal medications and surgical procedures is considered the most effective. Research has shown that ketoconazole, an antifungal drug, is effective in treating eumycetoma caused by Madurella mycetomatis, with reported success rates exceeding 70%. However, this drug is optimally absorbed only under acidic gastric conditions, and its efficacy can be reduced by conditions such as achlorhydria or by the use of medications like antacids and anticholinergics.

Despite its therapeutic value, ketoconazole is associated with several serious adverse effects that limit its use. These include endocrine-related disorders, gynecomastia, and hepatotoxicity. Due to these potential risks, ketoconazole is no longer recommended as a first-line therapy and is generally reserved for cases where other antifungal agents are ineffective or contraindicated. This shift in treatment preference has led to the development and use of newer, safer antifungal agents.

Recent advances in antifungal therapy have focused on triazole-based medications, which tend to have better efficacy, fewer drug interactions, and more tolerable side effects. One such medication is itraconazole, which works by inhibiting the synthesis of ergosterol, a vital component of fungal cell membranes. This action weakens the structure and function of the fungal cells. Itraconazole is usually administered in doses ranging from 200 to 400 mg per day for a minimum period of six months. In many cases, it has been shown to produce favorable outcomes in terms of symptom resolution and infection control.

Effective treatment of eumycetoma is marked by the complete disappearance of nodules and draining sinuses, along with normal findings on ultrasonographic examination and negative results in fungal cultures or histopathological studies. However, the bioavailability of itraconazole varies depending on factors such as food intake and gastric acidity. The drug should be used with caution in patients who have ventricular dysfunction or congestive heart failure. After surgical treatment, continuing itraconazole for an additional three months is recommended to reduce the likelihood of recurrence.

Surgical management is often required, especially in severe or advanced cases. The primary goal of surgery is to remove all infected tissues, often including surrounding healthy tissue, to ensure total excision of the lesion. The types of procedures performed may include debridement, wide local excision, and, in extreme cases, limb amputation. Unfortunately, the recurrence rate following incomplete or simple resection is quite high, and this often necessitates more aggressive interventions. Thus, surgery is most successful when combined with prolonged antifungal therapy.

The highest rates of cure are typically seen in patients who receive a combination of pharmacological and surgical treatment, especially when the lesion is entirely excised. During early stages of the disease, a regimen combining terbinafine and itraconazole is commonly used. Treatment is considered complete only when all sinus tracts have healed, no

masses are visible either clinically or radiologically, and histological examination reveals no granulomatous inflammation or fungal elements. Regular monitoring throughout the treatment course is essential to ensure these criteria are met.

Given the chronic and often relapsing nature of eumycetoma, a proactive and aggressive approach is essential, even in the early stages of the disease. A combination of itraconazole (400 mg daily) and terbinafine (500–750 mg daily) for at least six months is generally recommended. This combination should be initiated before surgery and continued for 6 to 12 weeks preoperatively, and then maintained postoperatively until complete healing or the emergence of side effects. This comprehensive approach offers the best chance of recovery and helps reduce the risk of recurrence or progression to disability.

## CONCLUSION

Mycetoma is a widespread disease that significantly impacts both the economic and healthcare resources of affected regions. Uncommon presentations of the disease are increasingly being reported, which leads to delays in diagnosis. Additionally, variations in the etiological agents across different regions result in differing guidelines for the use of antimicrobials, further complicating treatment strategies. These factors highlight the need for timely recognition and effective management.

The disease's prolonged, slow-progressing nature calls for the development of new therapeutic agents that can achieve faster cures, ultimately improving patient adherence to treatment. As the disease burden continues to rise, exploring more efficient treatment options becomes essential to address both the health and economic challenges associated with mycetoma.

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