International Journal of Health Sciences and Research
Vol.13; Issue: 1; January 2023
Website: www.ijhsr.org
Case Report *ISSN: 2249-9571*

Actinomycetoma Treated with Oral Trimethoprim + Sulfamethoxazole and Amoxicillin with Clavulanic Acid: A Case Report

Pooja Shrivastava[1], Manjunatha P[2]

[1]Junior Resident, Department of Dermatology, Venereology, Leprosy, KVG Medical College and Hospital, Sullia, India
[2]Professor, Department of Dermatology, Venereology, Leprosy, KVG Medical College and Hospital, Sullia, India

Corresponding author: Pooja Shrivastava

DOI: https://doi.org/10.52403/ijhsr.20230112

ABSTRACT

Mycetoma is endemic in many developing countries. We report here a case of actinomycetoma in a 60 year old male, farmer by occupation, patient gave history of bare foot walking and patient recalls history of trivial trauma over legs who presented with diffuse multiple plaques studded with discharging sinuses and surrounding oedema over the medial aspect of left ankle. Patient is a known case of uncontrolled T2DM on insulin and altered renal parameters that posed as a therapeutic challenge where welsh/modified welsh regimen could not be planned in this patient.
Based on clinical and histological picture and Pus & culture sensitivity reports patient was treated with oral Sulfamethoxazole 800mg with Trimethoprim 160mg two tablets daily and oral amoxicillin with clavulanic acid 1gm twice daily for 4months showed marked improvement, lesions dried up after four months and healed with post inflammatory hyperpigmentation & scars.
This case is presented to demonstrate how early disease diagnosis and prompt treatment can reduce the significant morbidity associated with this devastating infection.

Keywords: *Actinomycetoma, Suppurative granuloma, Trimethoprim-sulfamethoxazole (SMX+TMP), Amoxicillin clavulanic acid*

INTRODUCTION

Mycetoma is defined as chronic progressive granulomatous exogenous infection of subcutaneous tissue which may spread contiguously to involve adjoining skin with formation of multiple sinuses, discharge of pus and granules.
It can be caused by true fungi (Eumycetes) or higher bacteria (Actinomycetes); thus, it is classified as eumycetoma and actinomycetoma, respectively. Mycetoma has a characteristic clinical triad: Firm swelling on the lesion, draining sinuses, and discharge of grains comprising either fungi or bacteria(1).

Actinomadura Madurae, Actinomadura pelletieri, Nocardia brasiliensis, Nocardia asteroides and Streptomyces are most frequently responsible for causing actinomycetoma (2).
Actinomycetoma is more common in southern India where as eumycetoma is more common in northern India (3).
This condition is seen in farmers and occupations which requires bare field walking over soil and thorny fields also seen in manual labourers and field workers.
The diagnosis can be done by both clinical features and histopathology examination, definitive diagnosis requires positive tissue

culture with identification of the specific etiologic pathogen.

This process can be cumbersome because of stringent growth requirements and frequent contamination of the specimens, as well as the small numbers of viable organisms present in a long-standing, very inflammatory lesion.[4]

Actinomycetoma is usually treated with prolonged antibiotic therapy.

We here report a case of actinomycetoma that was complicated by uncontrolled diabetes mellitus with altered renal parameters, patient was on insulin. So, we discuss our approach to such case.

CASE REPORT

A 69 years old male patient from Daksin Kannada district of Karnataka, India came with chief complaints of swelling and multiple discharging sinuses over the medial aspect of left ankle since 15days.

Initially the patient noticed a painless nodule over the left ankle that became painful and gradually developed into discharging sinuses.

Patient is also known case of type two diabetes mellitus (uncontrolled) and chronic renal failure.

Patient is farmer by occupation and past history of bare foot walking is present and patient recalls history of trivial trauma over legs.

On local examination, Multiple diffuse erythmatous plaques present over the medial aspect of left ankle with few areas of ulceration and exudation of pus and multiple discharging sinuses with surrounding oedema and desquamation of the surrounding skin was observed. (fig-1)

Gross examination of the seropurulent discharge and sinuses were done. On palpation, tenderness was present. The regional lymph nodes were not enlarged. The patient's clinical history and physical examination was highly suggestive of actinomycetoma at this point of time.

On the examination the patient vital were stable.

Laboratory investigations were done,

The Serum. Creatinine level was (2.8)mg/dl elevated , total bilirubin (T) 0.4mg/dl (D)0.2mg/dl,(ID) 0.2mg/dl, SGOT (18U/L), SGPT(11IU/L).

No bony deformities on xray.

Skin biopsy was done along with culture of the purulent discharge.

Gram stain showed moderate pus cells, plenty of gram positive cocci and. The culture and sensitivity testing reports were positive for methicillin sensitive coagulase negative staphylococci which was sensitive for cotrimoxazole (TMP/SMX) and amoxyclav.

Histologically, H and E stain showed pseudoepitheliomatous hyperplasia with suppurative granulomas (composed of neutrophils) and mixed inflammatory infiltrate comprising lymphocytes, plasma cells, eosinophils, histiocytes seen. Dermal oedema was present.

A diagnosis of actinomycetoma was made based on clinical and histopathological correlation.

Nephrology, ENT, Medicine references were given in view of uncontrolled type 2 diabetes, nephrotoxicity and ototoxicity. Patient was started on oral Sulfamethoxazole 800mg with Trimethoprim 160mg two tablets daily for 4months with oral Amoxicillin with clavulanic acid 1gm twice daily for 4months.[5]

Other IV antibiotics like rifampicin, amikacin, linezolid and Traditional welsh regimen was not given as patient had altered renal parameters and uncontrolled T2DM with high risk of nephrotoxicity & ototoxicity.

Patient showed excellent response with healing of all sinuses after two months of therapy.

He was on regular follow up and four months after treatment, marked improvement was seen as lesions resolved with post inflammatory hyper pigmentation and scarring. Patient was followed up for one year and no reoccurrence was seen.

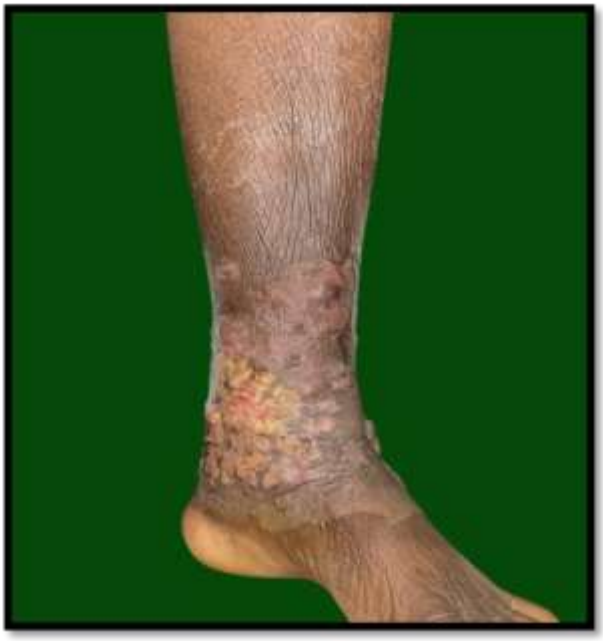


Fig-1 : Lesion at initial presentation

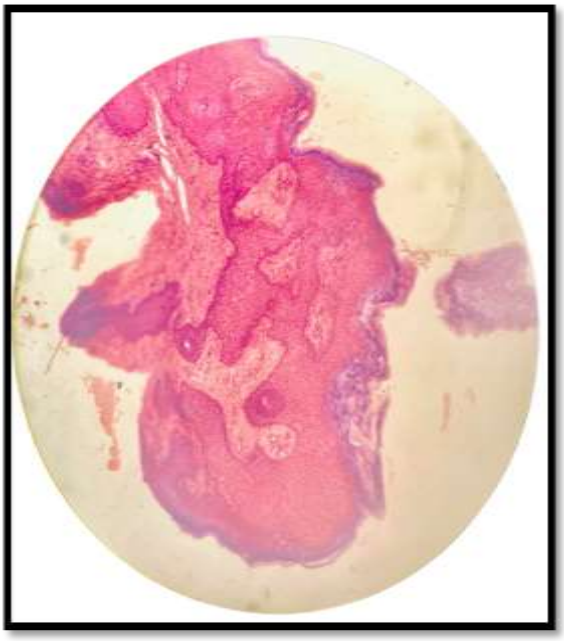


FIG 2 : H&E 10X view

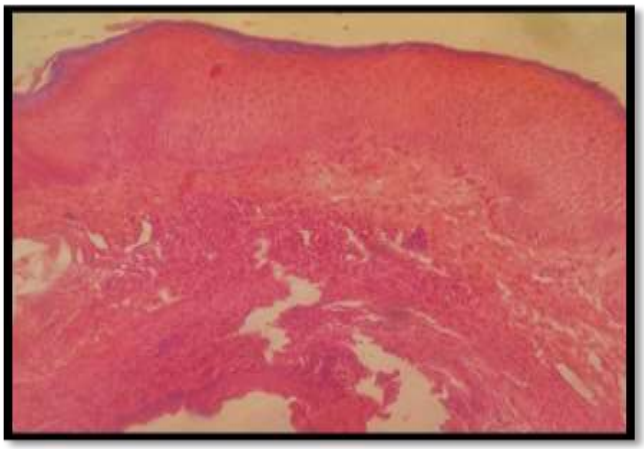


FIG 3: H&E 10X VIEW showing pseudoepithelial hyperplasia

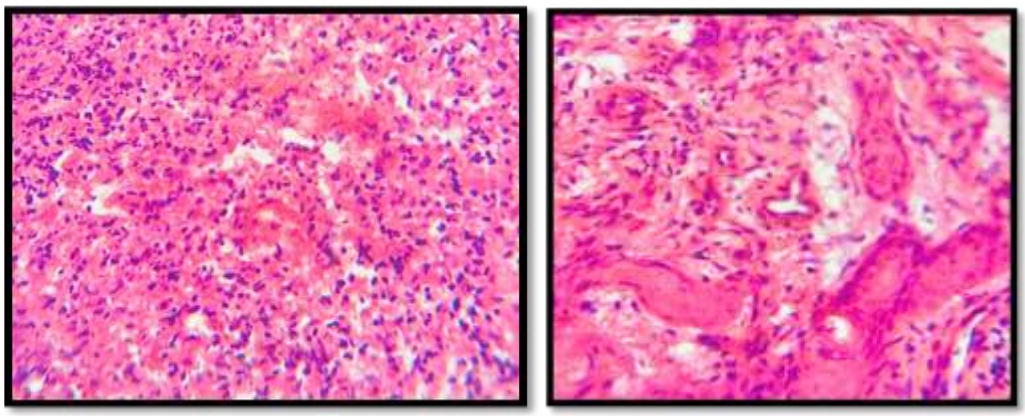
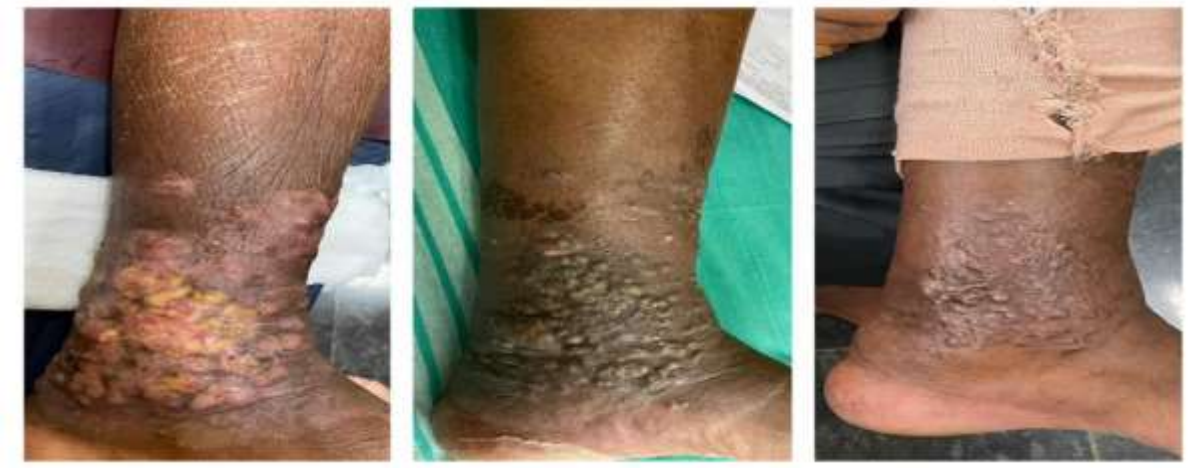


FIG 4&5: H&E 40X view showing suppurative granuloma consisting mainly of neutrophils surrounding mixed inflammatory infiltrates (lymphocytes & histiocytes and giant cells)



1st month 2nd month 3rd month

Fig-6: lesion at on subsequent follow-ups after initiation of treatment

FIG 7: 4 months after initiation of treatment showing completely resolved lesion with Post inflammatory hyperpigmentation and scarring.

DISCUSSION

The oldest description of this disease dates back to the ancient Indian Sanskrit text Atharva Veda in which reference is made to padavalmikam, meaning "anthill foot"[5] In modern times , Mycetoma was first reported in 1842 by Dr. John Gill in Madurai, India in Army medical reports and it was Colebrook in 1844 who described it as Madura foot which was what the disease was known as in those areas. This was later termed as mycetoma by Vandyke carter in 1860.It was Rustomjee in 1860 who described the two variants of disease , with black & yellow granules respectively. Later in 1894, Boyce and Surveyor established that those two variants were different and termed it as actinomycosis and maduramycosis[6]. Mycetoma is more commonly reported in males than females (3:1) because men being more commonly involved in agricultural work. The disease is characterised by numerous deformations and disabilities, high morbidity and its late stage is potential fate [7]. The most common site of occurrence is foot (approximately 70% cases), Hand is the next common site. Infection can be caused by fungi 40% cases and 60% cases by bacteria [8].

It has a worldwide distribution, with preponderance over the tropics and sub-tropics. The disease has also been reported in areas of temperate climate. It is predominantly a disease of men in rural areas, who work bare foot on land such as cultivators and daily labourers [9].

Common risk factors include poor hygiene, low socioeconomic status and poor nutrition.

Currently, over 56 taxonomically varying organisms, either of fungal (eumycetoma) or bacterial (actinomycetoma) origin have been implicated as causative agents of mycetoma. Most common among them are

actinomycetoma are Streptomyces somaliensis, Actinomadura madurae, A. pelletieri, Nocardia brasiliensis and N. asteroides[10].

Actinomyces sp. and Nocardia sp. are filamentous bacteria which have the same Class as Actinobacteria and same Order as Actinomycetales. Aerobic bacteria like Actinomyces species normally live at the respiratory, digestive, and genitourinary systems and can cause local suppurative disease by forming fistulae. The aerobic environment of Nocardia sp. and Actinomyces sp. can cause actinomycetoma [11].

Actinomcetoma is defined by triad of tumefaction of affected tissue, formation of multiple draining sinuses and presence of oozing granules. It usually affects the foot, legs and hand with tissues becoming necrosed and swollen after infection. The result is gross swelling of the affected part with deformity [12].

Actinomycetoma tends to progress more rapidly, with greater inflammation and tissue destruction and earlier invasion of bone than implantation mycosis.

Spread of the infection may also occur through the lymphatic, resembling sporotrichosis[13]. Metastatic lesions can also occur at various distant lymph nodes, which might become suppurative. These lymph node lesions are more common in actinomycetoma than in eumycetoma. Hematological spread has also been described[14].

The disease causes disfigurement but is rarely fatal. When left untreated, disease continues to progress, and bacterial superinfection leads to increased morbidity from local abscess formation, cellulitis, and bacterial osteomyelitis. In advanced cases, deformities or ankylosis may occur[15].

Mycetoma continues to pose huge public health threat in many tropical and sub-tropical countries[16].

If not detected and managed early, it causes gruesome deformity of the limbs, severe disability, premature termination of occupation, difficulty in finding jobs. Just like leprosy, in which stigma affects many dimensions of victim's life[17].

This may lead to misdiagnosis and and eventual mistreatment of patient[18] especially in places there is limitation of diagnostic tools and medical practitioners are left with little or no option but to clinically diagnose the patients[19].

The resolution and clinical outcome of actinomycetoma is associated with disease severity so, early commencement of appropriate treatment will reduce disability or disfigurement. This can be achieved through prompt diagnosis and early initiation of treatment. Also, careful consideration should be given to differential diagnosis mimicking actinomycetoma and careful differentiation between eumycetoma from actinomycetoma.

Mycetoma can be diagnosed from the culture of fungal and bacteria from the grains, exudate or from tissue or aspiration. However, the culture often does not produce satisfactory results due to various conditions such as, bacterial contamination, or cultured tissue obtained from late stage lesion containing fibrosis tissue rather than purulent exudates so in such cases clinical examination and careful history taking is more important for diagnosis [19].

Hematoxylin and eosin (H and E) stain shows suppurative granulomas (composed of neutrophils), surrounding characteristic grains which are present in the subcutaneous tissue. Grains or druses are aggregates of septated and branched, radially arranged broad hyphae, sometimes with vacuole formation. They are seen as broad, pink-stained hyphae surrounded by a sharp basophilic strand. The neutrophilic infiltrate is, in turn, surrounded by palisading histiocytes, beyond which a mixed inflammatory infiltrate comprising lymphocytes, plasma cells, eosinophils, and macrophages is seen. In long-standing cases, fibrosis may also be appreciated in the outermost layer[20].

The treatment of actinomycetoma could be done with antimicrobial agents and surgery. The recommendations of drug regimens are

based on expert experience. There are no randomized controlled trials for effective therapy regimens for mycetoma. The treatment is given in combination regimens to prevent drug resistance. The duration of therapy is 3-24 months depending on the response of the patient. The healing of the lesions can be assessed based on subcutaneous nodules and sinus, or indurations of the skin.

Combination antibiotic therapy is preferable to monotherapy to avoid development of drug resistance and to eradicate residual infection[21].

Sulfonamides, particularly trimethoprim-sulfamethoxazole (TMP/SMX), have hitherto been the mainstay therapy, often in combination with other drugs such as amoxicillin/clavulanate and amikacin[22] .

In 1987, Welsh demonstrated excellent therapeutic response with amikacin alone and in combination with TMP-SMX (Welsh regimen) in the treatment of 15 patients with poorly responsive actinomycotic mycetoma and those with systemic involvement. The regimen included cyclical dosing of amikacin 15 mg/kg/day, in two divided doses in cycles of 21 days for 1–3 cycles with intervals of 15 days between cycles while cotrimoxazole (one DS tablet BD) was administered continuously for 35–105 days. The 2-week interval of amikacin in the 5-week cycle is used for renal and audiometric monitoring. All patients achieved remission with this regimen with most patients requiring two cycles (42 days) of amikacin and 70 days of cotrimoxazole therapy[23]. Damle et al. in 2008 introduced the modified Welsh regimen in unresponsive patients by adding rifampicin as the third drug[24].

Combined antibiotic therapy is preferable to monotherapy to avoid drug resistance and to eradicate residual infection.

As actinomycetoma has potential morbidities prompt treatment based on clinical and histological findings alone should be initiated, even if specific microbiologic confirmation cannot be obtained.

CONCLUSION

This case is reported for its rare occurrence and to highlight the importance of awareness among the clinicians for the early diagnosis of the disease and initiation of early & prompt treatment as to reduce the associated substantial morbidity with this devastating infection.

As of now there no one fixed treatment protocols or guidelines for actinomycetoma which is accepted worldwide and the availability of treatment options are based on personal experience, preference drug availability and associated co morbidities as seen in our case. The complexity our case with uncontrolled T2DM and chronic renal failure lead us to use oral trimethoprim with sulfamethoxazole and amoxicillin with clavulanic acid combination as a first line treatment modality instead of other IV regimen and welsh regimen.

Patient showed excellent response to the treatment and on follow up for one year no reoccurrence was seen.

Declaration by Authors

Ethical Approval: Not Applicable

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Fahal AH, Suliman SH, Hay R. Mycetoma: The spectrum of clinical presentation. Trop Med Infect Dis 2018;3:97.
2. Singh H. Mycetoma in India. Indian J Surg 1979;41:577-97
3. Tilak R et al. A case of Actinomycotic mycetoma involving the right foot. J Infect Developing Countries 2009;3(1):71-73.
4. Liu A, Maender JL, Coleman N, Hsu S, Rosen T. Actinomycetoma with negative culture: a therapeutic challenge. Dermatol Online J. 2008;14(4).http://dx.doi.org/10.5070/d319m6r34k

5. Musa EA, Abdoon IH, Bakhiet SM, Osman B, Abdalla SA, Fahal AH. Mycetoma management and clinical outcomes: the Mycetoma Research Center experience. Trans R Soc Trop Med Hyg. 2022; http://dx.doi.org/10.1093/trstmh/trac069
6. Ghosh LM, Dey NC, Panja D. Madura foot (mycetoma). Ind Med Gaz. 1950;85(7):288–91.
7. Amit MS, Namitha S. Non-Invasive Management of Madura Foot with Oral Posaconazole and Ciprofloxacin. The American Journal of Tropical Medicine and Hygeine. 2014
8. Kiran A, Veena M. Histological Diagnosis of Madura Foot: A Must for Definitive Treatment. Journal of Global Infectious Disease. 2009
9. Turiansky GW1, Benson PM, Sperling LC, Sau P, Salkin IF, et al. (1995) Phialophora verrucosa: A new cause of mycetoma. J Am Acad Dermatol 32: 311–315 .
10. Branscomb, R., 2003. Mycetoma: an overview. Laboratory Medicine. 11, pp. 803-808
11. Bravo, F.G., Arenas, R., Sigall, D.A. 2012. Actinomycosis, nocardiosis, and actinomycetoma. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffel DA, Wolff K, editor. Fitzpatrick's dermatology in general medicine. 8th edition. New York: McGraw-Hill. Page:2241-52
12. Malti PK, Ray A, Soma B. Bilateral eumycetoma:A rare presentation. Case report.Indian J Medical Microbiol 2000;18 (3):135-36.
13. el Hassan AM, Mahgoub ES. Lymph node involvement in mycetoma. Trans R Soc Trop Med Hyg. 1972;66:165–9.
14. Agarwal P, Relhan V, Mahajan K, Garg V. Mycetoma: An update. Indian J Dermatol. 2017;62(4):332. http://dx.doi.org/10.4103/ijd.ijd_476_16
15. Zijlstra EE, van de Sande WWJ, Welsh O, Mahgoub ES, Goodfellow M, Fahal AH. Mycetoma: a unique neglected tropical disease. Lancet Infect Dis. 2016;16(1):100–12.http://dx.doi.org/10.1016/s1473-3099(15)00359-x
16. Fahal AH. Mycetoma: a thorn in the flesh. Trans R Soc Trop Med Hyg. 2004;98(1):3–11.http://dx.doi.org/10.1016/s0035-9203(03)00009-9
17. Van't Noordende AT, Van Brakel WH, Banstola N, Dhakal KP. The impact of leprosy on marital relationships and sexual health among married women in Eastern Nepal. J Trop Med. 2016;
18. Efared B, Tahiri L, Boubacar MS, Atsam-Ebang G, Hammas N, Hinde EF, et al. Mycetoma in a non-endemic area: a diagnostic challenge. BMC Clin Pathol . 2017;17(1):1. http://dx.doi.org/10.1186/s12907-017-0040-5
19. van de Sande WWJ, Fahal AH, Goodfellow M, Mahgoub ES, Welsh O, Zijlstra EE. Merits and pitfalls of currently used diagnostic tools in mycetoma. PLoS Negl Trop Dis.2014;8(7):e2918.
20. http://dx.doi.org/10.1371/journal.pntd.0002918
21. Agarwal P, Relhan V, Mahajan K, Garg V. Mycetoma: An update. Indian J Dermatol.2017;62(4):332. http://dx.doi.org/10.4103/ijd.ijd_476_16
22. Fahal AH. Mycetoma: a thorn in the flesh. Trans R Soc Trop Med Hyg. 2004;98(1):3–11.http://dx.doi.org/10.1016/s0035-9203(03)00009-9
23. Welsh O, Al-Abdely HM, Salinas-Carmona MC, Fahal AH. Mycetoma medical therapy. PLoS Negl Trop Dis. 2014;8(10):e3218. http://dx.doi.org/10.1371/journal.pntd.0003218
24. Agarwal P, Relhan V, Mahajan K, Garg V. Mycetoma: An update. Indian J Dermatol . 2017;62(4):332.http://dx.doi.org/10.4103/ijd.ijd_476_16
25. Damle DK, Mahajan PM, Pradhan SN, Belgaumkar VA, Gosavi AP, Tolat SN, et al. Modified Welsh regimen: A promising therapy for actinomycetoma. J Drugs Dermatol. 2008;7:853–6.

How to cite this article: Pooja Shrivastava, Manjunatha P. Actinomycetoma treated with oral trimethoprim + sulfamethoxazole and amoxicillin with clavulanic acid: a case report. *Int J Health Sci Res.* 2023; 13(1):90-96. DOI: *https://doi.org/10.52403/ijhsr.20230112*

******