

A CASE OF ACTINOMYCETOMA TREATED WITH CO-TRIMOXAZOLE (TRIMETHOPRIM + SULFAMETHOXAZOLE)

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ABSTRACT

A 32-year-old man presented with a history of progressive, painful nodular growths with discharge consisting granules over the right thigh, inguinal area and right foot. Histopathological examination of the tissue biopsy was actinomycotic mycetoma. The patient showed improvement with trimethoprim-sulfamethoxazole. The novelty of our case is to use Co-trimoxazole as a first line treatment modality for all case diagnosed or suspected as actinomycetoma.

KEYWORDS: actinomycetoma, trimethoprim-sulfamethoxazole, cotrimoxazole

INTRODUCTION

Actinomycetoma is a chronic suppurative and or granulomatous infectious process caused by aerobic filamentous bacteria. Actinomycetomas are caused by members of genera *Nocardia*, *Streptomyces*, *Nocardiosis*, and *Actinomadura*.

The term mycetoma, coined by Vandyke Carter in 1860, suggests a fungal growth; however, aerobic filamentous bacteria cause most cases worldwide¹. We report an advanced stage of actinomycetoma. To the best of our knowledge cure is possible, although a prolonged period is needed. Recurrence is common after an incomplete or irregular course of medical treatment.

There are no existing acceptable treatment protocols or guidelines for mycetoma. The available treatment options are based on personal experience, preference and drug availability.

CASE

A 32-year-old Filipino male who worked as a farmer and a food-vendor, from Tondo, Manila presented with a history of progressive multiple nodules over the right lower limb associated with seropurulent discharge.

Eight years PTC, patient had penetrating injury by a bamboo stick over the right foot, after which he developed a solitary mass measuring approximately 1x1cm gradually increasing in number and size. Surgical

consultation was done and underwent tumor excision and split thickness skin graft from the right thigh. I.V. antibiotics was given post-surgically for a week and oral-antibiotics continued for a week later. He was asymptomatic for 8 years after which he sought medical consult, when there was difficulty in breathing, progressive multiple nodules over the right-foot, right-thigh and right-inguinal area associated with seropurulent discharge. He was confined in Internal Medicine and co-managed with Orthopedics with assessment to consider Osteosarcoma R.

Laboratory investigations revealed a decrease in hemoglobin 104g/dL (n.v 135-180g/dL) and hematocrit 0.40-0.54% (n.v 0.25%), leucopenia 21.05 (n.v 5-10 X 10⁹). Urinalysis revealed normal results.

His Chest X-ray PA and Lateral view revealed pleural effusion vs pleural thickening right, PTB R.upper lobe, pleurodiaphragmatic adhesion bilateral. X-ray of the pelvis suggested arthritic hip, probably infectious in origin and R.foot revealed soft tissue masses in the 1st & 2nd intradigital space, beginning osteomyelitis 2ndmetatarsal right.



Fig.1 Chest X-ray PA view: Pleural effusion vs pleural thickening right



Fig.2 Chest X-ray Lateral view: PTB R. upper lobe, Pleurodiaphragmatic adhesion bilateral

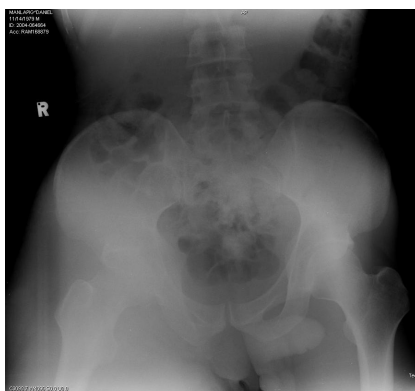


Fig. 3 X-ray Pelvis: Consider arthritic hip, probably infectious in origin



Fig.4 X-ray R.foot : Soft tissue masses in the 1st & 2nd intradigital space, Beginning osteomyelitis 2nd metatarsal right

Patient was also referred to our service for further evaluation and management, hence; this consultation.

The system review revealed pallor and weight loss. Patient was non-hypertensive and non-diabetic, but history of pulmonary tuberculosis four-years back for which he was treated with Anti-Koch's drugs for 1 year. Past history of penetrating injury by a bamboo stick over the right foot. He is smoker with four-pack years, occasionally drinks alcoholic beverages and admits to have only one-sexual partner (wife). Lives with nine-other family members in a crowded environment. No similar illness in his family. He had been working as a farmer in the province until he moved to Manila and became a food-vendor. He admitted to being a habitual barefoot walker.

The patient had Blood pressure of 100/70mm Hg, heart rate 89bpm, respiratory rate of 28/min and temperature of 36.5°C. He had pale palpebral conjunctiva.

On dermatological examination, he was found to have multiple, ill-defined, soft to firm, confluent erythematous nodules productive of seropurulent discharge associated with tenderness and swelling over the anterior right thigh and right foot



Fig.5 Lesions over the Right-Thigh spreading towards the inguinal area



Fig.6 Lesions over the Right-foot

The findings on an incision biopsy on the right-thigh revealed Actinomycetoma. The epidermis showed presence of pseudocarcinomatous hyperplasia, parakeratosis, and presence of sulfur granules. Dermis showed: dilated capillaries along with sulfur granules, neutrophils, lymphocytes and plasma cells. Periodic Acid Schiff Stain of the sulfur-granules was suggested which was Positive. Fungal culture however suggested and done showed no growth after incubation for 4days.

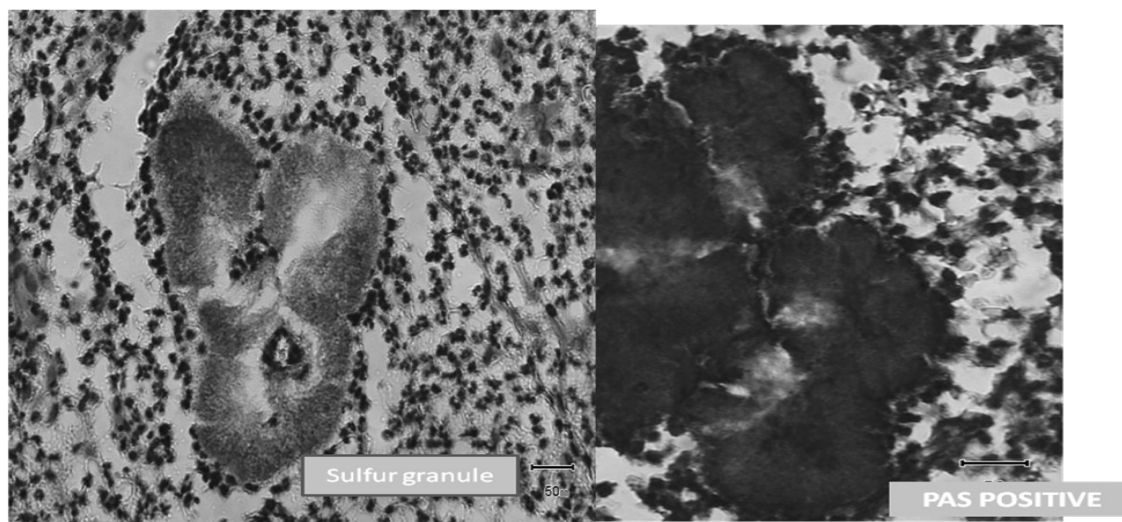


Fig.7 Characteristic sulfur granules which stained positive for Periodic Acid Schiff Stain

DISCUSSION

Actinomycetoma is a non-contagious chronic infection, characterized by the triad of localized lesions, tumefactions, and multiple draining sinuses. Involves the cutaneous, sub-cutaneous tissues, fascia and bone. The exudates contain grains, which may be yellow, white, red, brown, or black depending on the causative agent.

Mycetoma is classified as Eumycetoma or true-mycetoma caused by fungi and Actinomycetoma caused by aerobic filamentous bacteria. Actinomycetomas are caused by members of genera *Nocardia*, *Streptomyces*, *Nocardiosis*, and *Actinomadura*.

The term mycetoma, coined by Vandyke Carter in 1860, suggests a fungal growth; however, aerobic filamentous bacteria cause most cases worldwide.² 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 laborers.³ Poor hygiene, low socioeconomic status and low nutrition are suggested risk factors.⁴

The causative organism is usually found in the soil and enters the host through a breach in the skin or the mucosal membrane by sharp objects. The legs and feet are most commonly affected sites. Organisms gain entry into the skin through traumatic inoculation causing localized infection that is focally aggressive but does not typically disseminate.

Early diagnosis and treatment can affect morbidity associated with this condition. Thus, it is important for clinicians to be aware of this disorder's clinical presentation and methods available for confirming the diagnosis.^{5, 10}

Clinically, patients experience formation of erythematous papulonodules with drainage of purulent material and sinus tract formation. Ultimately, fibrosis and destruction of underlying soft tissue and bone will ensue. Severe edema and regional lymphadenopathy are common as the disease progresses.

Beyond the clinical appearance, histopathological analysis of affected skin is a critical step. A reaction pattern of granulomatous inflammation, abscess formation and fibrosis is typical.^{6, 8} Presence of the sulfur granules, on examination of smears of the discharge or tissue biopsy confirms the diagnosis of mycetoma.

Treatment regimens vary according to the organism causing the infection. The duration of treatment is dictated by the clinical response to medication, but reported cure rates are 60-90 percent with a mean duration of therapy greater than one year. Second-line agents include minocycline, co-amoxiclav, amikacin, cefuroxime, ceftriaxone, quinolones, imipenem, and linezolid. Involvement of underlying bone often requires more aggressive measures, including surgical debridement or even amputation of the affected areas.^{7, 9, 11}

Actinomycetoma lesions involving soft tissues are only mildly painful; those affecting

bones or joints are more so. Systemic symptoms are absent or minimal.

“Since there are no existing acceptable treatment protocols or guidelines for mycetoma, and the available treatment options are based on personal experience, preference and drug availability. **The novelty of our case is to use Co-trimoxazole as a first line treatment modality for all case diagnosed or suspected as actinomycetoma.** Because of the associated potential morbidities, empiric treatment based on clinical and histological findings alone should be initiated, even if specific microbiologic confirmation cannot be obtained. Also because studies have stated that; actinomycetomas are more responsive to antibiotics.”

Our patient's incision biopsy showed the presence of sulfur grains, positive PAS stain. Fungal culture was negative. These features were consistent with actinomycetoma. Incision and Trochar biopsy as suggested by the department of Orthopedics was done to rule out Osteosarcoma. Results revealed soft tissue mass, epidermal inclusion cyst, infected acute and chronic inflammation and granulation tissue formation; final result ruled out osteosarcoma.

As suggested in Basilio J Anía, MD et al; Staging of actinomycetoma according to bone involvement

Based on the radiological findings and the staging according to bone involvement, our patient is Stage4 i.e. longitudinal spreading along a single ray.¹²

The patient was then started on Co-trimoxazole (SMX-TMP) 800/160mg one tablet three times a day together with supportive therapy consisting of Multivitamin 1 capsule two times a day, Ferrous sulfate 1 capsule twice a day, and Tramadol + Paracetamol 500mg one tablet as needed for pain. Wound care was with Potassium permanganate (kmno4) compress two times a day for ten minutes followed by application of tetracycline ointment.

He was on regular follow up every two weeks. Four months after treatment, marked improvement was seen with decreased discharge, drying up of lesion, ease of pain on ambulation.

Although compliant with medications, new lesions, discharge and painful ambulation observed on his third-month of follow-up. As revealed by the patient there was shift of the medication from a branded to a generic brand due to economic constraints.

However, when Cotrimoxazole was shifted back to the previous brand, good response regarding decrease in the discharge, drying up of lesions with no new lesions was observed.



Fig.8 New lesions over the right thigh with discharge



Fig.10 Improvement of lesions over right thigh and inguinal area, 3weeks after restarting Co-trimoxazole to the original brand



Fig.9 Discharge from the lesions over the right foot



Fig.11 Improvement of lesions over right foot, 3weeks after restarting Co-trimoxazole to the original brand

Unfortunately, two weeks later; patient died while at home. He was still being treated with Cotrimoxazole for past 6 months. According to the death certificate death due to cardiopulmonary arrest 2^o to hypovolemic shock and underlying chronic anemia.

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