

## Case 26

A 25-year old Thai man from Bangkok

**Chief complaint:** A painful red plaque on left sole for 8 months



(Fig. 26.1)

### Present illness:

The patient noticed an indurated, painful, dull-red papule on his left plantar surface that gradually enlarged in the past 8 months with some extruded whitish grains and punctums.

He was afebrile and otherwise healthy.

### Past history:

- He had no any underlying diseases.

- He had a previous history of penetrating wound on the affected foot.

### Physical examination:

V/S: T 36.8°C, P 90/min, RR 20/min, BP 121/74 mmHg

HEENT: no pale conjunctivae, anicteric sclerae

Lymph node: no lymph node enlargement

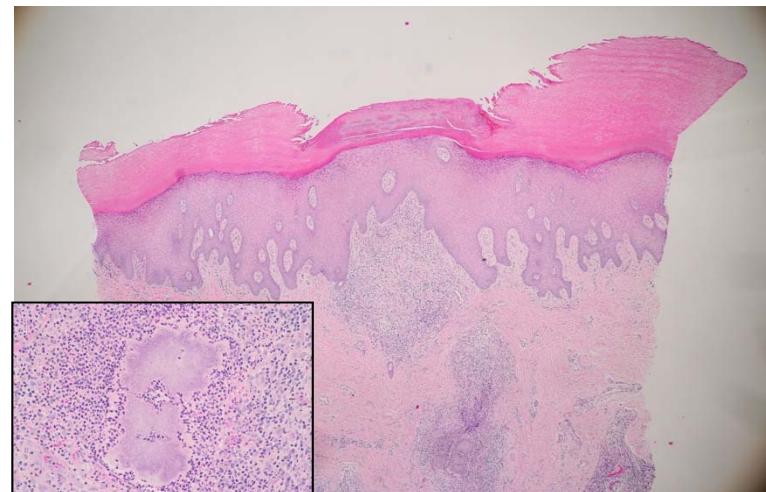
Other systems: unremarkable

### Dermatological examination:

(Fig. 26.1)  
Solitary ill-defined purplish indurated plaque on left sole with some whitish papules and sinuses

### Histopathology:

(S17-27643A, Left sole) (Fig. 26.2)



(Fig.26.2)

- Pseudocarcinomatous epidermal hyperplasia associated with

- nodular cell infiltrate of lymphocytes, histiocytes, plasma cells, and numerous neutrophils forming microabscess with central grain-like material
- Brown-Brenn and Fite stain reveal gram positive filamentous bacteria

**Laboratory investigations:**

- CBC: Hb 14.1 g/dL, Hct 43.6%, WBC 5,000 cells/ $\mu$ L (N 54%, L 30%, Mo 9%, Eo 6%, B 1%), Platelets 137,000 cells/ $\mu$ L
- Tissue imprint for gram stain, AFB, mAFB, GMS: no organisms
- Tissue PCR for 16s RNA: *Nocardia nova* complex
- Tissue culture for aerobe: *Nocardia nova* complex
- Tissue PCR for 18s RNA, TB: negative
- Tissue culture for TB and fungus: no growth
- Film Lt foot AP: no osteolytic lesion on the adjacent bone

**Diagnosis:** Nocardial mycetoma

**Treatment:** Trimethoprim-sulfamethoxazole (80/400) 1 tab PO bid

**Presenter:** Thiraphong Mekwilaiphan, MD

**Consultant:** Penpun Wattanakrai, MD

**Discussion:**

Mycetoma is a chronic suppurative infection affecting skin, subcutaneous tissue, and bones prevalent in tropical and subtropical regions.<sup>1</sup> Mycetoma is caused by several true fungi and bacteria, and hence it is classified as eumycetoma and actinomycetoma, respectively.<sup>2</sup> The predilection site is mainly foot. The typical clinical manifestation is a triad of localized swelling, underlying sinus tracts, and production of grains or granules<sup>1</sup> that could grossly characterize

the causative organisms (Table 1).<sup>2</sup>

Actinomycotic mycetoma is caused by aerobic species of actinomycetes belonging to the genera *Nocardia*, *Streptomyces* and *Actinomadura* with *Nocardia brasiliensis*, *Actinomadura madurae*, *Actinomadura pelletieri*, and *Streptomyces somaliensis* being most common.<sup>1</sup>

Nocardiosis is an infection caused by different species of *Nocardia* spp. *Nocardia asteroides* complex, *N. brasiliensis*, *N. farcinica*, and *N. nova* are commonly implicated for infection in humans. They are gram-positive, aerobic, acid-fast, filamentous saprophytic bacteria found in soil, decaying wood, water, and air.<sup>3</sup> Cutaneous nocardiosis may present as primary infection in immunocompetent individuals with history of trauma or may present as a part of disseminated infection secondary to pulmonary focus in immunocompromised individuals. Primary cutaneous nocardiosis clinically presents as acute infection (abscess or cellulitis), sporotrichoid infection or mycetoma<sup>4</sup> which bone involvement occurs infrequently. Notable bony changes include periosteal thickening, osteoporosis and osteolysis.<sup>3</sup>

**Table 1. The common different mycetoma causative organisms.**

Grain color	Causative organisms
<b>Eumycetoma</b>	
Black grains	<i>Madurella</i> spp. <i>Leptosphaeria</i> spp. <i>Curvularia</i> spp. <i>Exophiala</i> spp. <i>Phaeoacremonium</i> spp. <i>Phialophora verrucosa</i> <i>Pyrenophaeta mackinnonii</i> <i>P. romeroi</i>
Pale, white, yellow grains	<i>Pseudallescheria boydii</i> ( <i>Scedosporium apiospermum</i> ) <i>Acremonium</i> spp. <i>Aspergillus</i> spp.
<b>Actinomycetoma</b>	
Pale, white, yellow grains	<i>Actinomadura madurae</i> , <i>Nocardia</i> spp.
Yellow to brown grains	<i>Streptomyces</i> spp.
Red to pink grains	<i>A. pelletieri</i>

Adapted from Ahmed AA et al. Mycetoma laboratory diagnosis: Review article. PLoS Negl Trop Dis 2017;11:e0005638

The hallmark for diagnosis is based on microbiological evidence. *Nocardia* spp. can be stained with gram stain, modified Kinyoun stain, the Ziehl-Nielsen stain, and Brown-Brenn stain in tissue section.<sup>5</sup> Histopathology shows abscess (collection of neutrophils) and granules (grains). Grains are closely aggregated with a peripheral radial deposition of intensely eosinophilic material – a Splendore-Hoepli reaction.<sup>6</sup> Selective media including Thayer-Martin media, and charcoal-buffered yeast extract media may be necessary to enhance recovery of *Nocardia* spp. and minimize the growth of contaminating organisms. Genus identification could be performed by biochemical, chemotaxonomic, serological, and molecular methods in which DNA sequencing provides rapid and usually reliable identifications for most *Nocardia* spp. isolates.<sup>7</sup>

Drug susceptibility test for *Nocardia* spp. are showed in Table 2.

**Table 2 Comparison of the antimicrobial susceptibility of *Nocardia* species isolated from patients with different infection sites.**

	Susceptible percentage of isolates (%)			
	Skin	Lung	Disseminated	Lung+disseminated
Amikacin	97	100	94	86
TMP/SMZ	94	97	95	75
Minocycline	79	81	78	71
Cefotaxime	79	86	67	75
Gentamicin	80	97	57	63
Ampicillin	17	17	16	22
Ciprofloxacin	12	8	20	11
Erythromycin	0	0	0	0

Adapted from Wang HK et al. Clinical characteristics, microbiology, and outcomes for patients with lung and disseminated nocardiosis in a tertiary hospital. J Formos Med Assoc 2015;114:742-9.

The treatment of choice for actinomycetoma is a combination of

dapsone 100 to 200 mg once daily and trimethoprim-sulfamethoxazole (TMP-SMX) 80/400 to 160/800 mg once daily for 2 to 3 years. Intramuscular amikacin 15 mg/kg or 500 mg twice daily for 3 weeks is recommended only in disseminated nocardiosis or resistant cases, because of its high cost and toxicity (nephrotoxicity and ototoxicity).<sup>8</sup> Surgical treatment is indicated for small, limited lesions and in cases with bone destruction. Amputation is indicated in cases lacking a satisfactory antimicrobial response associated with severe bone destruction of the affected segment.<sup>9</sup>

For this patient's treatment; according to drug susceptibility test results, Trimethoprim-sulfamethoxazole was prescribed at dose of 160/800 mg daily. After one month pain and size of the indurated area decreased.

**References:**

1. Relhan V, Mahajan K, Agarwal P, Garg VK. Mycetoma: An Update. Indian J Dermatol 2017;62:332-40.
2. Ahmed AA, van de Sande W, Fahal AH. Mycetoma laboratory diagnosis: Review article. PLoS Negl Trop Dis 2017;11:e0005638.
3. Sharma NL, Mahajan VK, Agarwal S, Katoch VM, Das R, Kashyap M et al. Nocardial mycetoma: diverse clinical presentations. Indian J Dermatol Venereol Leprol 2008;74:635-40.
4. Banashankari GS, Rudresh HK, Sreeja S; Beena. Nocardial mycetoma: re-infection with a different species at an unusual site--a rare case. Indian J Pathol Microbiol 2013;56:333-4.
5. Chedid MB, Chedid MF, Porto NS, Severo CB, Severo LC. Nocardial infections: report of 22 cases. Rev Inst Med Trop Sao Paulo 2007;49:239-46.
6. Sharmila P. Patil, Nitin J. Nadkarni, Nidhi R. Sharma. Nocardiosis: Clinical and Pathological Aspects, Histopathology - Reviews and Recent Advances 2012.
7. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. Clin Microbiol Rev 2006;19:259-82.
8. Arenas R, Fernandez Martinez RF, Torres-Guerrero E, Garcia C. Actinomycetoma: an update on diagnosis and treatment. Cutis 2017;99:E11-E15.
9. Sampaio FM, Wanke B, Freitas DF, Coelho JM, Galhardo MC, Lyra MR et al. Review of 21 cases of mycetoma from 1991 to 2014 in Rio de Janeiro, Brazil. PLoS Negl Trop Dis 2017;11:e0005301.