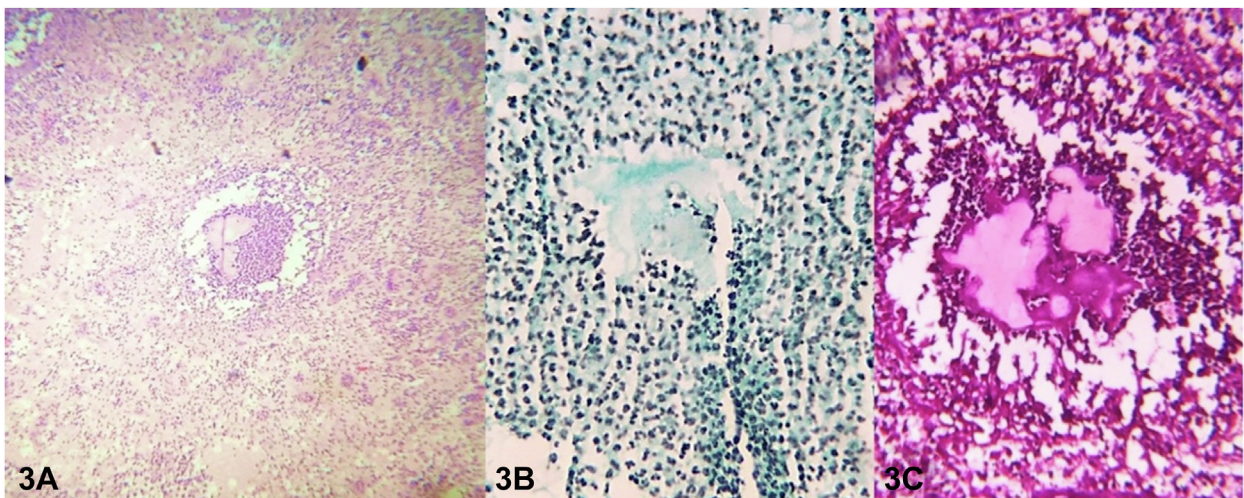
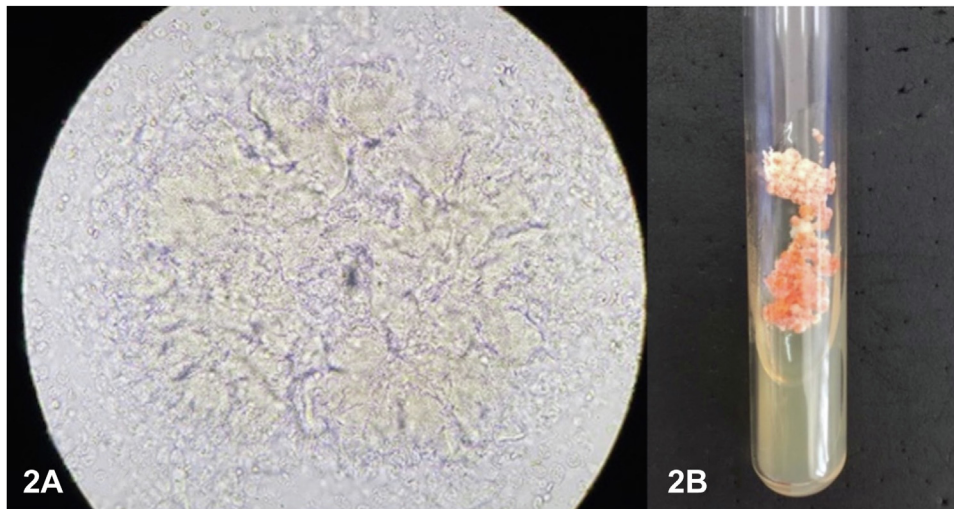


Deforming vegetative nodules in a woman from Amazon



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A 37-year-old female from Western Amazon, Brazil, presenting with a 13-year history of vegetating, friable and painful nodules, and fistulas that drained whitish grains on the right foot, with no history of local trauma and no improvement after surgical drainages (Fig 1). Direct microscopy of the grains culture, and skin biopsy were performed (Figs 2 and 3). After 2 months with no improvement with sulfamethoxazole/trimethoprim (SMX/TMP) 800/40 mg twice daily, imipenem 2 g/daily was added in the third month, which also showed unsatisfactory results. Transtibial amputation of the right leg was performed to control the disease due to chronic osteomyelitis that extended from the foot bones to the tibia on radiography.

Question 1: What is the most likely diagnosis based on the history, clinical presentation, and histology?

- A. Actinomycetoma
- B. Eumycetoma
- C. Botryomycosis
- D. Verrucous carcinoma
- E. Lobomycosis

Answers:

A. Actinomycetoma — Correct. Considered a neglected tropical disease, mycetoma is a chronic granulomatous infection caused by filamentous fungus (eumycetoma) or filamentous aerobic bacteria (actinomycetoma).¹ Actinomycetoma by *Nocardia spp.* is common in regions with high humidity, while low humidity regions have a higher prevalence of *Actinomadura spp.* and *Streptomyces spp.*² It is common in South America, with higher incidence in Brazil.^{3,4} Generally, actinomycetoma is more aggressive than eumycetoma. Due to direct dissemination, it can affect bones, causing mutilating injury that leads to limb amputation.⁵

B. Eumycetoma — Incorrect. Clinically, eumycetoma is indistinguishable from actinomycetoma, and differentiation is possible through grain analysis by microscopy. Eumycetoma grains are composed of larger mycotic filaments. Black grains are produced by *Madurella mycetomatis*, *Trematosphaeria grisea*, and *Leptosphaeria senegalensis*, while *Fusarium spp.*, *Acremonium spp.*, and *Aspergillus nidulans* produce

white grains. Actinomycetoma grains are smaller, composed of actinomycetes. *Nocardia spp.* and *Actinomadura spp.* produce yellow-white grains, while *Streptomyces spp.* produces yellow-brown grains.¹

C. Botryomycosis — Incorrect. Botryomycosis is a chronic, granulomatous, and suppurative infection caused mainly by *Staphylococcus aureus*, with the formation of nodules, fistulas, and yellowish-white grains very similar to mycetoma. The diagnosis occurs through the culture showing *S. aureus*.

D. Verrucous carcinoma — Incorrect. Verrucous carcinoma is a well-differentiated variant of squamous cell carcinoma. It presents as a slow growing, exophytic tumor that commonly appears in burn scars, and the presence of fistulas and grains are not characteristic.

E. Lobomycosis — Incorrect. Lobomycosis is a chronic granulomatous infection caused by *Lacazia loboi*, common in the Amazon region, and presents as keloid-like nodules or vegetating lesions, mainly on the lower limbs, which may ulcerate or undergo carcinomatous degeneration.

Question 2: What is expected in the exams performed to confirm the correct diagnosis?

A. Septate hyphae on direct examination and microabscess with grains surrounded by hyphae on the periphery on histology

B. Grain formed by coccoid cells or bacilli among an amorphous substance on direct examination or histology

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C. Filaments without septa on direct examination and microabscesses containing grain formed by filamentous bacteria

D. Round or oval yeast cells with a birefringent membrane on direct examination or histology

E. Papillomatous acanthosis with invasive growth of ridges in the dermis

Answers:

A. Septate hyphae on direct examination and microabscess with grains surrounded by hyphae on the periphery on histology – Incorrect. This description is from eumycetoma. The hyphae are large, with a diameter between 2 and 6 μm , septate and may be hyaline or dematia, depending on the pathogenic fungus, with grouped chlamydospores. In the histology of mycetomas, a granulomatous process with specific individual characteristics and formation of microabscesses are visualized. In eumycetoma, microabscess is composed of grains surrounded by hyphae on the periphery forming clubs.^{1,2}

B. Grain formed by coccoid cells or bacilli among an amorphous substance on direct examination or histology – Incorrect. This description is of botryomycosis. Histologically, the Splendore-Hoeppli phenomenon may also be present, with the presence of a lobulated grain formed by non-filamentous bacteria grouped in an amorphous, basophilic material and surrounded by radiated eosinophilic substance.

C. Filaments without septa on direct examination and microabscesses containing grain formed by filamentous bacteria – Correct. The presence of fine and delicate filaments, measuring 0.5 to 1.0 μm , grouped and without septa on direct examination and on histological examination, microabscesses containing grains formed by small actinomycetes and absence of fungal structures in Grocott's and periodic acid Schiff's special stains conclude the diagnosis. The cerebriform and orange colored colony are characteristic of *Nocardia spp.*^{1,2}

D. Round or oval yeast cells with a birefringent membrane on direct examination or histology – Incorrect. This description corresponds to lobomycosis. Yeast cells can be found singly or forming a chain. They reproduce by simple budding, forming cells of similar sizes.¹

E. Papillomatous acanthosis with invasive growth of ridges in the dermis – Incorrect. Histological

description of verrucous carcinoma, a well-differentiated keratinocytic neoplasm with minimal cell atypia and very low mitotic rate.

Question 3: What is the first-line therapy indicated for the disease?

A. Wide surgical excision associated with anti-fungal agents

B. Traditional surgical excision or Mohs micrographic surgery

C. Cephalosporin

D. Itraconazole

E. SMX/TMP

Answers:

A. Wide surgical excision associated with anti-fungal agents – Incorrect. The surgical approach is the best therapy for isolated and well-defined lesions of lobomycosis. For disseminated lesions, antifungal agents may be used with unsatisfactory results. As an adjuvant therapy to prevent the recurrence of surgically removed lesions, Itraconazole has been shown to be partially effective.¹

B. Traditional surgical excision or Mohs micrographic surgery – Incorrect. They are first-line treatment options for verrucous carcinoma, depending on the size and location of the tumor.

C. Cephalosporin – Incorrect. Cephalosporins, as well as SMX/TMP and doxycycline, are therapeutic options for the treatment of botryomycosis, which should be guided by an antibiogram.

D. Itraconazole – Incorrect. The first-line treatment for eumycetoma is itraconazole, however, as the result is unsatisfactory in most cases, it is necessary to combine it with surgical treatment.¹

E. SMX/TMP – Correct. SMX/TMP is considered the gold standard for actinomycetoma. For moderate to severe forms, with or without bone involvement, or after failure of SMX/TMP monotherapy, the therapy of choice is the combination with amikacin or carbapenems, as in the case reported. However, the patient did not respond satisfactorily to the combined therapy with carbapenem and underwent transtibial amputation of the right leg for disease control.^{1,5}

Abbreviation used:

SMX/TMP: sulfamethoxazole/trimethoprim

Conflicts of interest

None disclosed.

REFERENCES

1. Carrasco-Zuber JE, Navarrete-Dechent C, Bonifaz A, Fich F, Vial-Letelier V, Barroeta-Mauriziano D. Afectación cutánea en las micosis profundas: una revisión de la literatura. Parte 1: micosis subcutáneas. *Actas Dermosifiliogr*. 2016;107(10):806-815.
2. Bonifaz A, Tirado-Sánchez A, Calderón L, Saúl A, Araiza J, Hernández M, et al. Mycetoma: experience of 482 cases in a single center in Mexico. *PLoS Negl Trop Dis*. 2014;8(8):e3102. <https://doi.org/10.1371/journal.pntd.0003102>
3. van de Sande WWJ. Global burden of human mycetoma: a systematic review with meta-analysis. *PLoS Negl Trop Dis*. 2013;7(11):e2550. <https://doi.org/10.371/journal.pntd.0002550>
4. Emergy D, Denning DW. The global distribution of actinomycetoma and eumycetoma. *PLoS Negl Trop Dis*. 2020;14(9):e0008397. <https://doi.org/10.371/journal.pntd.0008397>
5. Sampaio FMS, Wanke B, Freitas DFS, et al. Review of 21 cases of mycetoma from 1991 to 2014 in Rio de Janeiro, Brazil. *PLoS Negl Trop Dis*. 2017;11(2):e0005301. <https://doi.org/10.371/journal.pntd.0005301>