Facial ulcerations and neurologic symptoms in a farmer

Ricardo Luconi, MD, a Paula Hitomi Sakiyama, MD, b Carlos Floriano de Morais, PhD, a Julio Cesar Empinotti, PhD, a and Hirofumi Uyeda, MD a
Cascavel and Curitiba, Brazil

Key words: central nervous system fungal infections; mycoses; neurologic manifestations; paracoccidioidomycosis; skin ulcer.

A 47-year-old immunocompetent man presented with a 2-month history of ulcers on the face (Fig 1). He worked in a rural area in the state of Pará, northern Brazil, was a smoker, and had an alcohol use disorder. He had a 3-month history of weight loss, tetraparesis, reduced visual acuity, and vertical nystagmus. Magnetic resonance imaging showed multiple bilateral brain lesions with marginal contrast enhancement (Fig 2). Cerebrospinal fluid findings were nonspecific. Skin samples were collected for culture and histopathologic examination and stained with hematoxylin-eosin and Grocott methenamine silver (Fig 3). The skin culture results were negative.

From the Department of Dermatology, Western Paraná State University, Cascavel; Department of Dermatology, Hospital Santa Casa de Curitiba.b
Funding sources: None.
Conflicts of interest: None disclosed.
IRB approval status: Not applicable.
Correspondence to: Ricardo Luconi, MD, Av. Tancredo Neves, 3224, Cascavel, Paraná, Brazil, 85806-470. E-mail: ricardoluconi@gmail.com.

JAAD Case Reports 2021;7:95-7.
2352-5126
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https://doi.org/10.1016/j.jdcr.2020.11.005
Question 1: What is the most likely diagnosis?

A. Tuberculosis
B. Sporotrichosis
C. North American blastomycosis
D. Paracoccidioidomycosis (PCM)
E. American cutaneous leishmaniasis

Answers:

A. Tuberculosis—Incorrect. Tuberculosis can cause ulcerated, verrucous lesions and affect the central nervous system (CNS). However, the biopsy would show formation of caseating tuberculoid granulomas.
B. Sporotrichosis—Incorrect. Sporotrichosis causes ulcers, but the biopsy would reveal small cigar-shaped spores and asteroid bodies.
C. North American blastomycosis—Incorrect. North American blastomycosis is a lung infection that can cause verrucous and ulcerative lesions on the skin; however, it is endemic to the southeast and Great Lakes regions of the United States. Its histopathology is characterized by intraepidermal abscesses and small round spores, with double contour, thick walls, and a broad-based single bud, usually within giant cells.
D. PCM—Correct. PCM, also called south American blastomycosis, is endemic to Latin America, especially Brazil. The acute-subacute form affects mainly young subjects, being more serious due to intense involvement of the mononuclear phagocyte system; the chronic form, reported in this case, is the most common and can be mild to severe, depending on the clinical and the patient’s general condition. The chronic form classically affects the mouth, skin, and lungs but can involve other organs, like CNS. The chronic form predominates in men who work outdoors as farmers or hunters as Paracoccidioides is found in soil; there is also an association with smoking, alcohol use, and malnutrition.1-4 The biopsy revealed large, thick-walled yeasts, with a narrow-based single bud, distributed in a chain or concentrically covering the entire surface of the yeasts like a “rudder wheel” or “Mickey Mouse ears.”
E. American cutaneous leishmaniasis—Incorrect. Leishmaniasis also causes ulcers in exposed areas, but its histopathology would reveal Leishmania bodies in histiocytes.

Question 2: Which of the following statements is correct regarding the diagnosis of the disease presented?

A. Serology testing is the gold standard for diagnosis
B. False-negative results in serological tests can occur in patients with very localized lesions or associated immunosuppression
C. Culture is a highly sensitive and specific method
D. Histopathologic examination of a skin biopsy has a secondary role in the diagnosis
E. Diagnostic confirmation can be made based solely on the presence of characteristic clinical findings

Answers:

A. Serology testing is the gold standard for diagnosis—Incorrect. The gold standard for the diagnosis of PCM is the identification of fungal elements suggestive of Paracoccidioides spp. in a biopsy fragment of organs supposedly affected and/or in a fresh examination of sputum or another clinical specimen (scraped from the lesion or aspirated from lymph nodes).1
B. False-negative results in serological tests can occur in patients with very localized lesions or associated immunosuppression—Correct. False-negative results can occur in individuals with very localized lesions or in those with immunosuppressive conditions. On the other hand, false-positive reactions may occur in sera from patients with histoplasmosis and eventually in the sera of those with leishmaniasis and aspergillosis.1
C. Culture is a highly sensitive and specific method—Incorrect. Culture is a specific but not a highly sensitive method.2
D. Histopathologic examination of a skin biopsy has a secondary role in the diagnosis—Incorrect. The identification of the fungus in the affected organ, including the skin, is the gold standard for diagnosis. Thus, a dermatologist has an important role in confirming PCM since obtaining samples from other organs is often risky and/or difficult, as in the case presented here, in which CNS was affected.1,2,5
E. Diagnostic confirmation can be made based solely on the presence of characteristic clinical findings—Incorrect. PCM cases can be defined as
suggested, probable, or confirmed. In situations where there are only compatible clinical findings, the case is considered suspected. Probable cases are those with suggestive clinical manifestations and anti-Paracoccidioides spp. serum antibody titers. Finally, confirmed cases are those with compatible clinical manifestations, in which it is possible to detect the presence of fungal elements suggestive of Paracoccidioides spp., as in the patient presented here.1

**Question 3: What is the best treatment option for the case presented?**

A. Itraconazole
B. Amphotericin B
C. Trimethoprim sulfamethoxazole
D. Echinocandins
E. N-methylglucamine antimoniate

**Answers:**

A. Itraconazole—Incorrect. Itraconazole is the treatment of choice for patients with mild-to-moderate disease.1 Mild cases are those with a satisfactory nutritional status, good health, and involvement of 1 or a few organs or tissues without dysfunction; moderate cases are those with an intermediate form, which generally does not affect organs other than the skin, mouth, and lungs.5 In the case presented, itraconazole does not represent the best choice due to CNS involvement.1,5

B. Amphotericin B—Incorrect. Amphotericin B is indicated in severe and disseminated forms, pregnant women, and patients with liver disease.1 Severe cases are defined by 3 or more of the following criteria: a) weight loss greater than 10% of the normal weight; b) intense pulmonary involvement; c) involvement of other organs, such as adrenal glands, CNS, and bones; d) lymph nodes affected in multiple chains (pseudotumoral form or suppurrative form); and e) high antibody titers.3

C. Trimethoprim sulfamethoxazole—Correct. Trimethoprim sulfamethoxazole is an option for mild, moderate, and severe forms of the disease; however, it is the best drug for neuroparacoccidiomycosis, as in the case presented here, and in situations of concomitant treatment for tuberculosis. An oral suspension is a good alternative for children who cannot tolerate pills and adults with difficulty in swallowing, which may be due to esophageal and tracheal strictures associated with the progression of the disease; a venous solution, on the other hand, can be used in patients with disabsorptive disorders.1,5

D. Echinocandins—Incorrect. Echinocandins have not shown efficacy in the treatment of PCM.

E. N-methylglucamine antimoniate—Incorrect. N-methylglucamine antimoniate is used to treat leishmaniasis and is ineffective for PCM.

The authors would like to thank everyone who collaborated in managing the case, especially the infection and neurosurgery teams at the hospital.

**Abbreviations used:**
CNS: central nervous system
PCM: paracoccidioidomycosis

**REFERENCES**