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Isolated cutaneous lesions in paracoccidioidomycosis: a suggestive case of acquisition through cutaneous inoculation

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Dear Editor

Paracoccidioidomycosis, an infection caused by the dimorphic fungus of the species *Paracoccidioides brasiliensis* and *P. lutzii*, is endemic in the American continent, with a high number of reports in South America. It is believed that its incidence in endemic areas ranges from three to four new cases per million each year[1]. The lung is the major "gateway" to PCM infections, and direct cutaneous inoculation is extremely rare[2]. We report a rare case of paracoccidioidomycosis with isolated cutaneous involvement, with no evidence of primary pulmonary complex or infection in other organs.

A 66-year-old male patient, reported a previous history of hypertension, smoking and skin lesions that appeared one year before on the left lower limb, after stepping on an anthill in the municipality of Sao Sebastiao do Cai, Rio Grande do Sul State, Southern Brazil, where he has worked as a farmer and has always lived. The patient reported that the lesions appeared after some time at the site of the ant bites, at most three months after the injuries. The physical examination revealed hyperkeratotic erythematous plaques with hemorrhagic areas and ulcerations, with a linear ascending pattern on the left lower limb affecting the sole, dorsum of the foot, knee and thigh (Figure 1). Cervical, axillary and inguinal lymph nodes were examined, and no abnormalities were detected. Two skin biopsies were performed. The first histopathological exam was suggestive of a squamous cell carcinoma. Due to the incompatible clinical presentation, a fresh biopsy was performed which showed the presence of epithelial hyperplasia, intraepithelial microabscesses (Figure 2A) and multiple budding yeasts in Grocott's staining (Figure 2B). Culture of the biopsy tissue revealed typical findings with appearance of "popcorn popped" (Figure 3), compatible with *Paracoccidioides* spp., ruling out the previous diagnosis of squamous cell carcinoma. No serological test was performed. Magnetic resonance imaging of the abdomen and pelvis and two chest X-ray (performedtwice , in 2018 and 2019) were normal. The first 2018 X-ray was performed when the patient had already had the confirmed diagnosis through the second biopsy and the direct mycological examination. The second one, performed in 2019, was a follow-up chest X-ray. Hepatic and renal functions were also normal, and the patient had no associated symptoms related to PCM. The treatment was performed with itraconazole 200 mg/day for six months, until complete remission of lesions.

Paracoccidioidomycosis most commonly affects adult males between 30 and 50 years of age and can be classified into two clinical forms: the acute-subacute form and the chronic form[1]. The adult chronic form is subdivided into the unifocal form, with involvement of a single organ or system, usually the lungs, and the multiple form, with more than one affected organ and system, usually the skin and lungs. Cutaneous lesions are present in more than half of the patients[3]. The causative fungus is present in the soil of high humidity environments[2]. Agricultural activity is the major risk factor for the infection. Smoking and alcoholism are also associated with an increased risk of contracting the disease. Paracoccidioidomycosis is endemic in Rio Grande do Sul State, mainly in the Northern region and around the metropolitan region of Porto Alegre, the State capital, where is located the municipality of Sao

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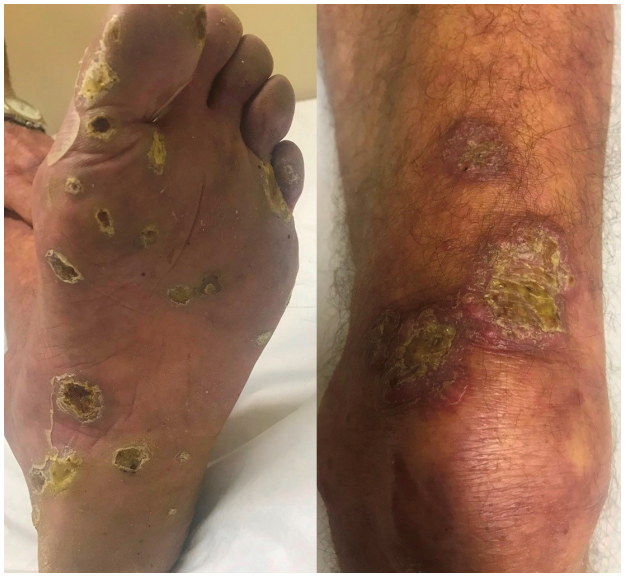

Figure 1 - Ulcerated hyperkeratotic plaques on the foot and left thigh.

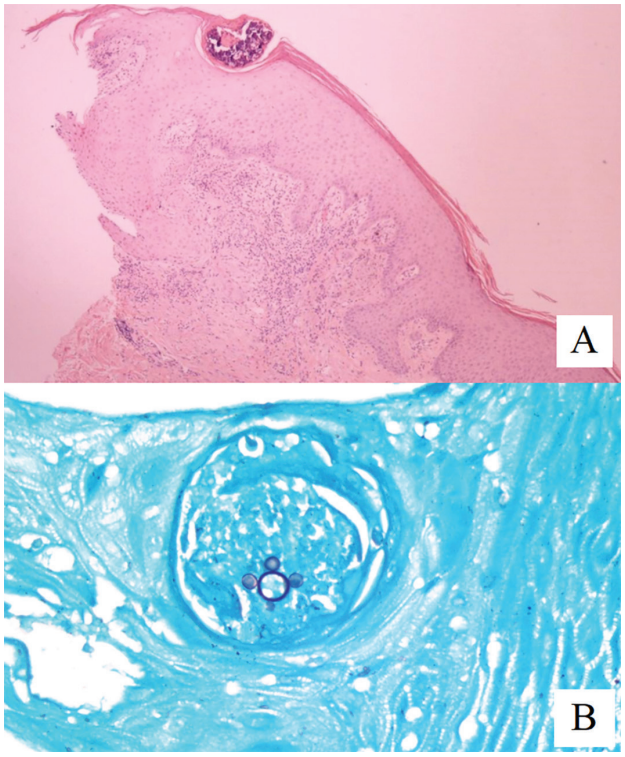

Figure 2 - Pseudoepitheliomatous hyperplasia with intraepithelial microabscesses; HE staining, 4x magnification (A). Yeast with multiple buds; Grocott's staining, 40x magnification (B).

Sebastiao do Cai[4-6]. However, we did not find any other case report in this specific municipality in the literature.

The main source of infection is inhalation, controlled by the cellular immune response, which may or may not progress to other organs involvement through hematogenous dissemination[1]. There are few reports of infections caused by direct fungal inoculation, which is questionable due

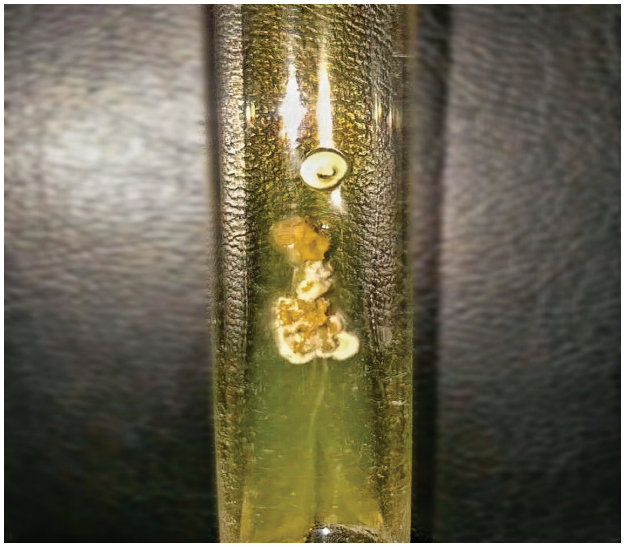

Figure 3 - White, wrinkled, slow growing filamentous colonies, with appearance of "popcorn popped". Mycosel cultivation at 25 °C.

to the small inoculum of subcutaneous fungal particles following minor trauma[7-9]. In our case report, the first and only clinical manifestation were the cutaneous lesions occurring after a history of stepping on an anthill. However, it is important to note that the chest X-ray may not have shown subtle pulmonary injuries, making it difficult to exclude a pulmonary involvement. Nevertheless, in recently published guidelines for the clinical management of paracoccidioidomycosis in Brazil, the X-ray was indicated as an exam to be performed for the diagnosis of PCM[1].

The absence of pulmonary injuries, according to the X-ray, and other related symptoms of PCM, led us to consider the possibility of a direct inoculation as the mode of transmission. Infections with fungus-contaminated material, such as branches and plants, have also been suggested in other studies[8,10,11]. However, isolating *Paracoccidioides* species directly from the environment is not simple[1], making it difficult to confirm the presence of the fungus in a certain place or object, such as the anthill in our case report.

The clinical presentation of the patient did not differ from the polymorphic lesions described in the literature, characterized by papules, ulcers and hyperkeratotic lesions[12]. In addition, the farming and the smoking habits were relevant aspects for suspecting this diagnosis. An initial confounding factor was the first histopathological examination results compatible with squamous cell carcinoma, which may have occurred due to the finding of pseudoepitheliomatous hyperplasia, common in both pathologies. The last biopsy showed epithelial hyperplasia and intraepithelial microabscesses and the microbiological culture revealed the presence of white wrinkled and filamentous colonies, characteristic of *Paracoccidioides* spp.

Therefore, we emphasize the importance of considering this differential diagnosis, since the patient could have been subjected to an unnecessary surgical intervention. This case highlights the fact that although there is little evidence in favor of an infection acquired by direct inoculation, this possibility cannot be ruled out[7,8,10]. Finally, it is important to note that our case report has limitations, such as the lack of a CT scan and other specific exams. The approach should be individualized, as the clinical manifestations of paracoccidioidomycosis are diverse and can represent diagnostic challenges.

AUTHORS' CONTRIBUTIONS

FBP, NABV, ALB, ALA and LM were involved in the case and wrote the article; AK, DMP and MLS critically revised the article; all authors approved the article submission.

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