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Enlarged, painful cervical and axillary lymph nodes in chronic paracoccidioidomycosis

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Abstract

Background: Paracoccidioidomycosis is an important medical and social problem mainly in rural areas of Brazil, because of the high incidence of the diseases, its long clinical evolution, frequent recurrences and sequels leading to anatomical and functional incapacities.

Main observation: We present a 73-year-old patient with paracoccidioidomycosis showing significant lymph node manifestations, which are only common in children and teenagers.

Conclusions: Paracoccidioidomycosis may have a long incubation period, and it can be diagnosed outside of the endemic regions, where it was acquired. Thus, all dermatologists should maintain a high index of suspicion, especially in unusual cases of extensive lymph node enlargement in the elderly patients. (*J Dermatol Case Rep*. 2014; 8(2): 50-54)

Introduction

Paracoccidioidomycosis is a systemic mycosis endemic in Latin America caused by the fungus *Paracoccidioides brasiliensis*.[1,2] It is estimated that 80% of the cases occur in Brazil.[3] The main form of contamination is by inhalation, which leads to a transitory pulmonary infection that can progress to the acute form, or, more frequently, reactivate later to the chronic form of the disease.[1,2] Due to its endemicity in Brazil and frequent involvement of skin and mucosa, besides other organs in the chronic phase of the disease, it is vital that the dermatologist be aware for its diagnosis, aiming at early treatment and prevention of sequels.

Case report

A male patient, 73-years-old, born in the state of Pará, north of Brazil, with a history of farm labor for several years, developed 8 months before painful cervical and axillary lymphadenomegalies, which fistulized, besides an ulcerated lesion on the mentum and non-measured weight loss. The patient denied other symptoms and also denied smoking or drinking alcoholic beverages. At examination he presented linear ulcer of approximately 10 cm with irregular borders, granular and clean surface in the right cervical region (Fig. 1), two rounded ulcers of 1.5 cm in diameter, raised borders and clean surface, with one in the back cervical region (Fig. 2) and the other in the left axilla (Fig. 3). He also had an ulcerative-vegetative lesion of 1.5 cm on the right side of the mentum (Fig. 4), besides increased and painful lymph nodes in the cervical and axillary chains (Fig. 5). The lab tests presented blood cell count, liver enzymes and biochemistry without alterations and blood sedimentation rate of 37 mm. Direct mycological examination of the mentonian lesion showed yeast-like cells with multiple gemulation and refringent double membrane; fungi culture was

positive for *Paracoccidioides brasiliensis* and histopathology (Figs. 6 to 8) evidenced chronic diffuse granulomatous dermatitis, which with silver impregnation revealed numerous rounded fungi structures with multiple budding, typical of *P. brasiliensis* (Fig. 9).

He was treated with sulfamethoxazole/trimethoprim at 400/80 mg/day, in the dosage of three tablets every 12 hours with good response. This medication had to be withdrawn because a probable interstitial nephritis caused by sulphonamide and it was changed to itraconazole at 200 mg/day with follow up every 6 months.

The otorhinolaryngologic examination did not reveal lesions in the mucosa. Despite asymptomatic clinical presentation from the respiratory point of view, the X-ray and CT scan of the thorax suggested lung involvement by the disease. Tuberculin test was negative and *P. brasiliensis* was not demonstrated in induced sputum. Endocrinologic evaluation excluded adrenal insufficiency.

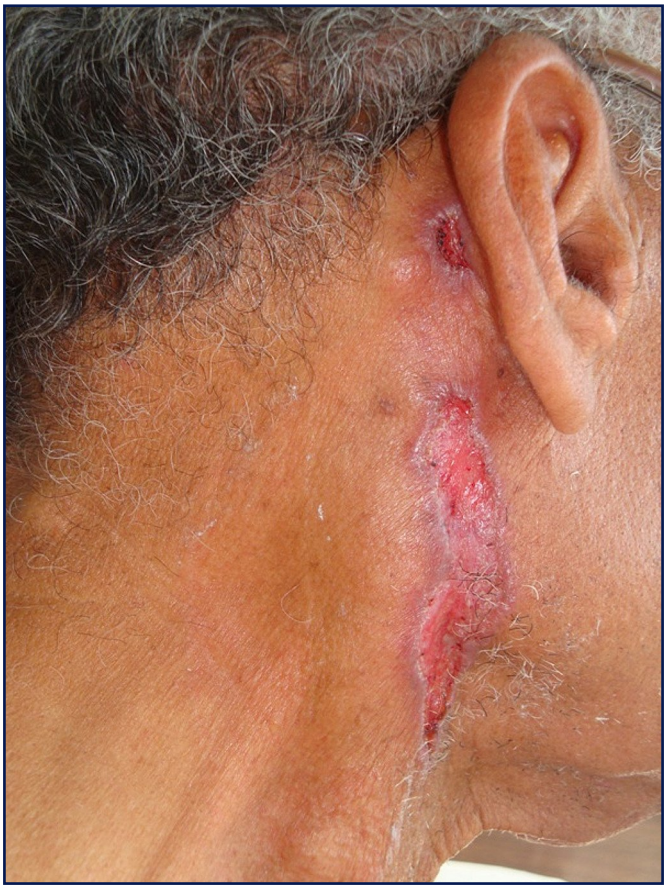

Figure 1
Linear ulcer of approximately 10 cm with regular borders, granular and clean surface, in the right cervical region.

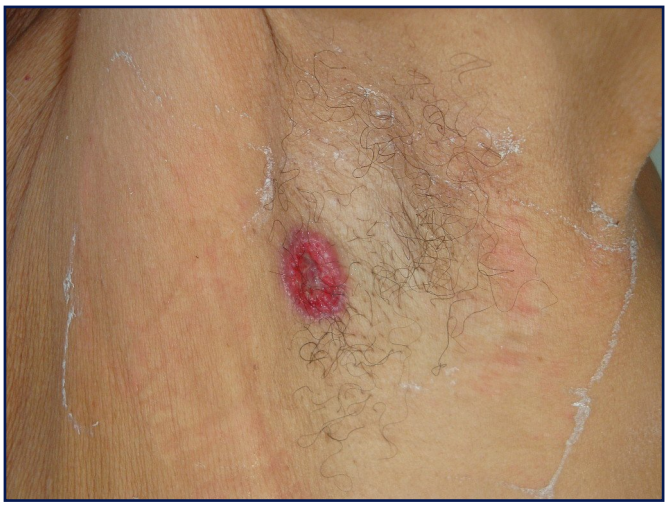

Figure 3
Round ulcer of 1.5 cm, with raised border and clean surface in the left axilla region.

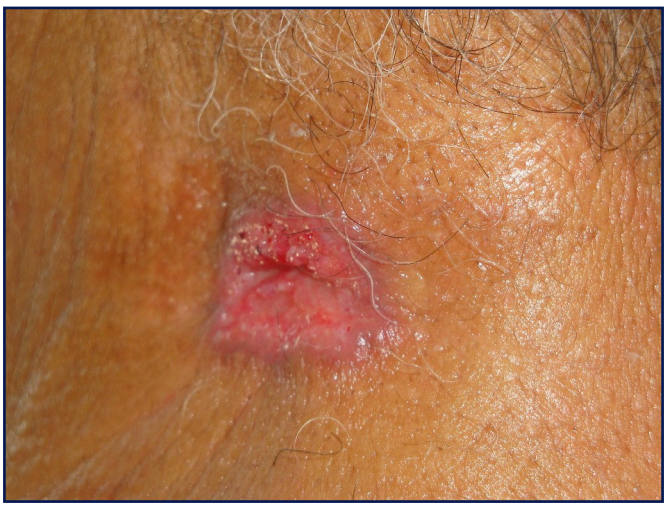

Figure 2
Round ulcer of 1.5 cm, with raised border and clean surface in the left back cervical region.

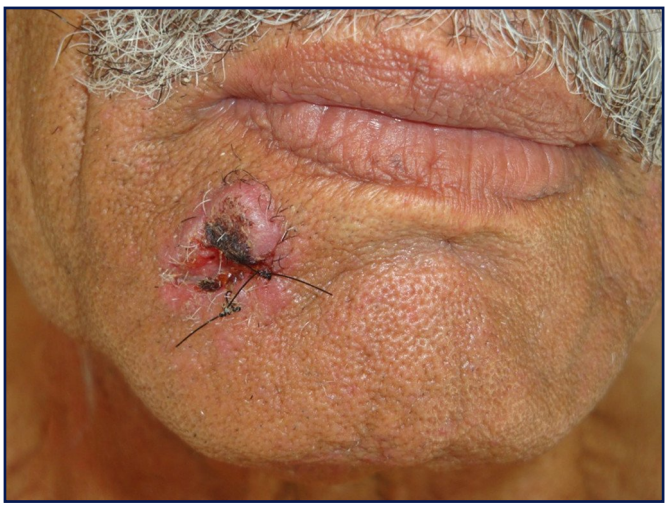

Figure 4
Ulcerative-vegetative lesion of 1.5 cm on right mentum, where biopsy was performed.

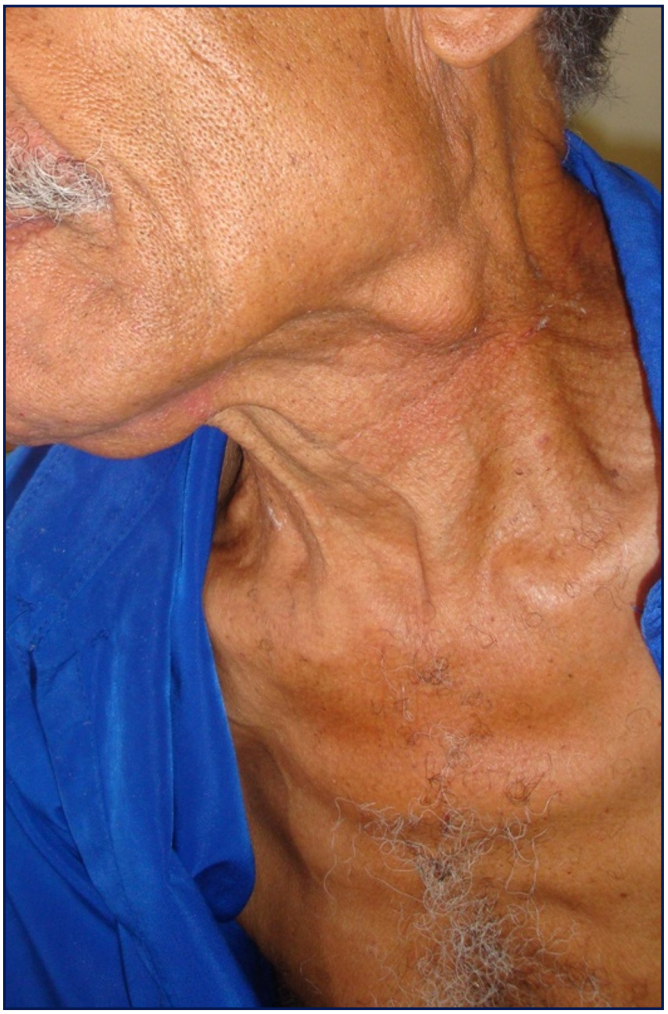

Figure 5
Weight loss, submentonian and submandibular lymphadenomegalies at the left.

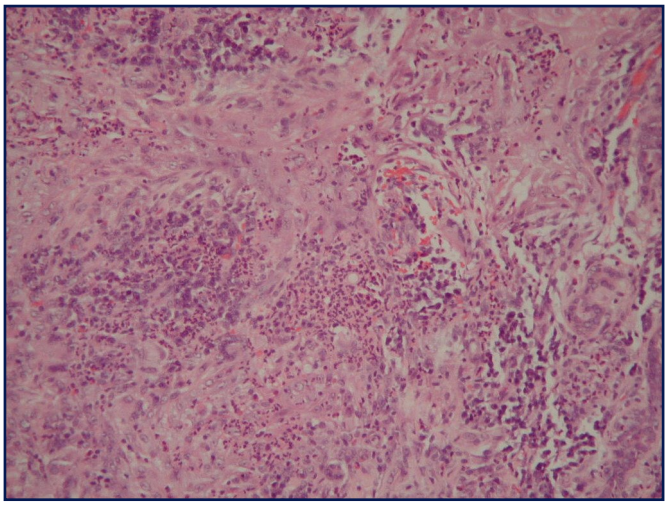

Figure 7
Abscesses and giant cells. (H&E, 100X).

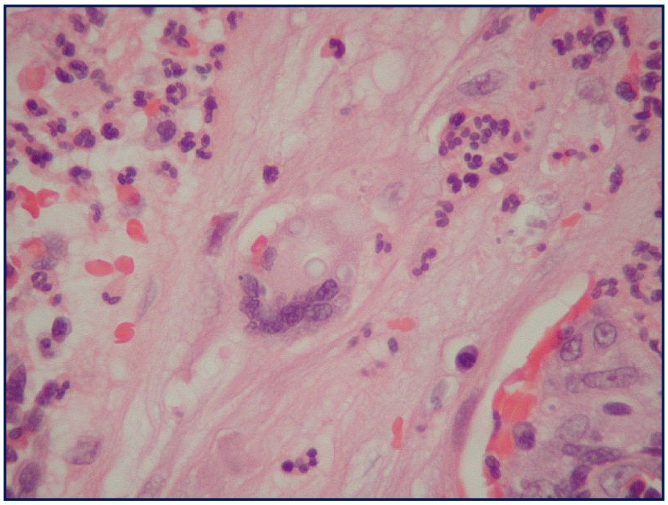

Figure 8
Giant cell containing three fungal cells in the midst of squamous epithelium (H&E, 400X).

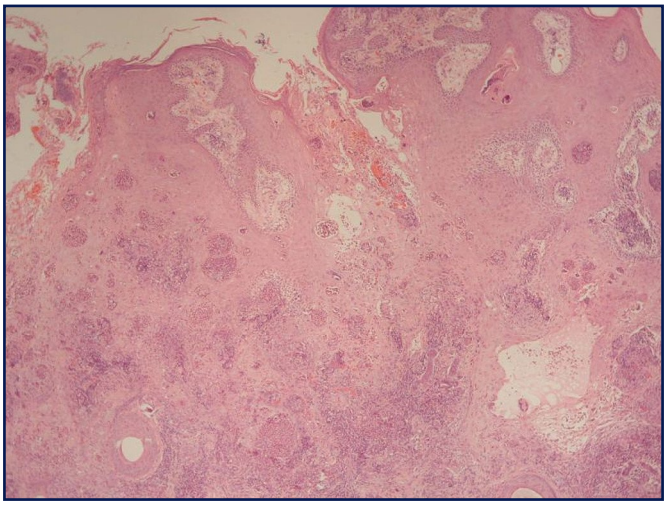

Figure 6
Squamous pseudo-epitheliomatous hyperplasia, abscesses and giant cells (H&E, 40X).

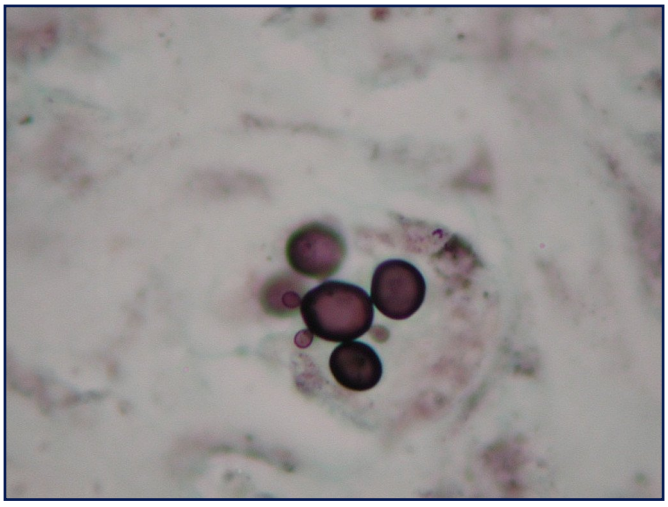

Figure 9
Giant cell containing rounded fungal structures with multiple budding of several sizes and directions (Grocott, 1000X).

Discussion

Paracoccidioidomycosis, caused by *Paracoccidioides brasiliensis*, a thermodimorph fungus, is the most prevalent systemic mycosis in Brazil.

Since it is not a disease of mandatory notification, there is no data regarding its incidence and prevalence in the country. An incidence of 1 to 3 new cases per 100,000 inhabitants per year is estimated, and, in general, it affects individuals that have or had contact with rural environments.[3]

Inhalation of conidia is the main contamination form by humans, which usually occurs in the first two life decades.[1,2,3,4] The paracoccidioidomycosis-infection corresponds to patients with reactivity in cutaneous test for paracoccioidin or other antigens of the fungus and it is believed that 50% of the inhabitants of endemic regions were already exposed to the fungus.[3] Only a small portion of those individuals develop paracoccidioidomycosis-disease which may present in two forms: 1. Acute/sub-acute form (juvenile type) — which occurs in children and adolescents, with equal distribution between both sexes. It is characteristic especially for compromising the reticuloendothelial system, entailing enlargement of lymph nodes, hepatosplenomegaly, osteoarticular and cutaneous lesions; and 2. Chronic form (adult type) — which is the most common form with over 90% of the cases,[3] of slow evolution, and prevailing in males in age ranging from 30 to 60 years. Clinical manifestations are varied, and can occur as a single focus, when compromising only a single organ or system, with the lung being the most affected organ, or multifocal with several systems affected, in most cases lungs, skin and mucous membranes, but also lymph nodes, adrenals, nervous system and others. The cutaneous lesions are polymorphic[5] and oral lesions occur in over 50% of cases, usually by contamination of the oral mucosa by pulmonary secretions. In cases of mucocutaneous involvement of the mouth and face there is frequent association with cervical and submandibular lymphadenopathy, and lymph nodes may become fistulized.[6]

In Brazil, paracoccidioidomycosis is the main infectious cause of Addison's disease.[7] Some authors call attention[3,8,9] to the importance of the evaluation of adrenals, since non-diagnosed cases of their insufficiency may result in death.

Due to the possibility of varied clinical manifestations, the differential diagnosis will depend on the presentation of the disease; the reported case had cutaneous lesion with intense fistulized lymph adenomegalies, and absence of oropharyngeal lesions and respiratory symptoms, common in the chronic phase. Ganglionar tuberculosis, histoplasmosis and lymphoma were important differential diagnoses, with tuberculosis frequently appearing in association with paracoccidioidomycosis.

Proof of diagnosis consists in identification of the fungus by histopathologic examination, direct mycological examination and/or culture. Serologies help to confirm the diagnosis and are relevant for the follow-up and after treatment. Several techniques are used, with immunodiffusion the most relevant.[1] At direct mycological examination, *Paracoccidioides brasiliensis* is observed in its yeast form as a rounded structure, with a double contour and thick wall, isolated or in small aggregations, presenting a single or multiple budding with the aspect of a "pilot wheel". Those fungal structures can also be visualized at histopathologic examination. Impregnation by silver and the use of periodic acid-Schiff stain help to demonstrate the organisms.

Colony microscopy varies with the temperature in which the culture is maintained. At 37˚C, yeast colonies are easily distinguishable by their cerebrifom aspect and cream color. At temperatures near 20 to 25˚C, there is a growth of the colony of mycelia of cotton-like aspect; under the microscope, there are fine septated hyphae with terminal and interspersed clamidospores.[4]

Comorbidities are frequent in patients with paracoccidioidomycosis. Among the infectious comorbidities, tuberculosis is present in 5 to 10% of cases[3] and should always be investigated. Parasitoses, such as strongyloidiasis, are also common.[8] Tobacco and alcohol addiction are frequently associated and some authors observed that the intensity of smoking may have a relation with the age of disease onset.[10]

Several antifungals may be used in the treatment, among which sulfamidics (sulfadiazine, sulfamethoxazole/trimethoprim association), amphotericin B and azole derivatives (ketoconazole, fluconazole, itraconazole). New therapeutical options are being studied and there is a report case of good response with the use of terbinafine.[11] Therapeutical schemes and duration of treatment vary according to the disease severity. In mild to moderate forms, the most frequently used medications are oral sulfamethoxazole/trimethoprim and itraconazole. In more severe cases the indications are for amphotericin B or venous sulfamethoxazole/trimethoprim, until disappearance of clinical signs is reached, followed by oral antifungal therapy. Immunotherapy with vaccines containing fungus' antigens, in the attempt to stimulate the immune response, has been studied as a proposal of adjuvant therapy.[6] The time for the treatment and follow-up are long, requiring great adhesion by the patient in attendance to the consultations and performance of examinations. To infer the cure, clinical, radiologic and serological criteria are used, however there are cases of recurrence.[3]

Conclusion

The great number of cases, long clinical evolution, frequent recurrence and disability due to anatomic and functional sequels make paracoccidioidomycosis an important medical and social problem. Even unusual cases, as the one presented, since extensive lymph node enlargement is not frequent in the elderly as it is in children and adolescents, must be promptly recognized so the correct therapy can be prescribed avoiding these important sequels.

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