RESUMO
Paciente feminina, 47 anos, hipertensa e tabagista, em uso crônico de corticoide, apresentou lesões em pele e mucosa nasal, com dor local; tratado empiricamente como sinusite. Houve piora das lesões, com ulceração. Após nove meses do início dos sintomas, foi realizada biópsia da lesão, revelando o anatomopatológico uma micose cutânea sugestiva de criptococo. A paciente foi diagnosticada com infecção pelo vírus da imunodeficiência humana (HIV) e, então, internada em hospital de referência, tendo recebido tratamento com fluconazol 800mg/dia endovenoso, a seguir, fluconazol 800mg/dia oral até completar 12 semanas de tratamento. Houve resolução da lesão ulcerada e posterior fibrose da narina esquerda.

Palavras-chave: Criptococo; Vírus da imunodeficiência humana (HIV); Síndrome de imunodeficiência adquirida (Aids)

ABSTRACT
A 47-year-old woman, carrier systemic hypertension, tobacco user, and chronic user of corticosteroids, showed skin and nasal mucosa lesions, with local pain; treated empirically as sinusitis. The lesions evolved with increased ulceration. After nine months of symptoms onset, the lesion was biopsied, revealing fungal skin pathology suggestive of cryptococcosis. The patient was diagnosed with an HIV infection. The patient was then hospitalized in a specialized hospital and treated with intravenous fluconazole 800mg/day, followed by fluconazole 800mg daily orally up to 12 weeks of treatment. There was resolution of the ulcerated lesion and subsequent fibrosis of the left nostril.

Keywords: Cryptococcosis; Human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (Aids)
INTRODUCTION

*Cryptococcus* spp is a fungus commonly found in the ground and which can cause diseases in humans\(^1\)\(^-\)\(^3\). It is the second most prevalent opportunistic fungus, present only in a lower number of infection cases than those caused by *Candida albicans*\(^4\). The microorganism presents a cell wall that produces a protection factor, which allows it to survive within the macrophages\(^5\). In immunocompetent persons, a granulomatous wall is formed to prevent the microorganism from disseminating, and therefore it is a rare cause of disease in patients whose immune response is adequate\(^5\). Hence, the *Cryptococcus* spp is most commonly found in immunosuppressed patients (e.g. acquired immunodeficiency syndrome [AIDS], immunosuppressant therapy, decompensated liver cirrhosis), and the airways are usually its gateway. It is not transmitted by direct human contact but by environmental exposure. The most commonly affected organs are the lungs and the central nervous system, but it can also occur in the skin, eyes, and genitourinary tract\(^2\)\(^,\)\(^6\). Considering HIV-positive patients, the infection is most prevalent in cases that the CD4+ lymphocyte count is less than 100 cells/mm\(^3\), and it can be classified as an AIDS-defining disease\(^5\).

This is the case report of a patient who is unusually presenting a fungal disease by *Cryptococcus* spp. According to the report, the patient’s medical records were reviewed by the health services where the patient is being treated.

CASE REPORT

A 47-year-old woman, with controlled systemic arterial hypertension, tobacco user, and chronic user of corticosteroids for three years due to low platelet count, showed lesions in the skin and left nostril mucosa, along with local pain and fatigue. She was empirically treated for sinusitis with amoxicillin and amoxicillin-clavulanate, with no improvement. The lesions progressed, increased in volume, and ulcerated. After nine months experiencing the symptoms, the lesion was biopsied, and the anatomopathologic exam revealed it was an ulcerated skin mycosis suggestive of Cryptococcosis (figure 1: anatomopathologic exam of the lesion using silver staining and figure 2: aspect of the lesion before treatment started). The patient was referred to her city’s infectious disease services where she tested positive for HIV in two samples using different methods (Enzyme Imunnoassay [ELISA] and Western Blot). At that time, the patient was admitted to the specialized hospital, where she was treated for a week with intravenous fluconazole 800mg/day and then with fluconazole 800mg/day orally until the end of the 12-week treatment. Concurrently, she started taking the antiretroviral drugs lamivudine, zidovudine, and lopinavir/ ritonavir. Before starting the antiretroviral therapy, her T CD4+ lymphocyte count was 180 cells/mm\(^3\), T CD8+ lymphocyte at 1.219 cells/mm\(^3\), and a CD4+/CD8+ ratio of 0.14; her viral load was 435.447 copies/ml. Additionally, directly research was done for *Cryptococcus* spp in CSF and urine of patients whose results were negative. The patient reported having had the same sexual partner for 15 years, and they didn’t use condoms. The partner was tested for HIV, and the result was negative. Approximately four weeks after the antifungal treatment, the patient showed improvements to the aspect of the lesion, as well as to the associated symptoms. There was local tissue retraction and today the patient uses nighttime spacers in the affected nostril, having reported a significant expansion after she started using it. The excessive adverse gastrointestinal effects made the
patient quit lopinavir/ ritonavir for efavirenz. The patient is still taking antiretroviral regularly and is undergoing maintenance treatment with fluconazole 200 mg/day orally. She is currently asymptomatic, and even her low platelet count has disappeared. The prednisone was suspended soon after the diagnosis of infection by the HIV virus. The latest exams carried out, CD4+ 285 cells/mm³, CD8+ 3180 cells/mm³; CD4+/CD8+ ratio: 0.09; HIV viral load below the minimum limit.

DISCUSSION

Cryptococcus spp infection is a disease which the diagnosis is increasing in the clinical practice, being more prevalent in immunocompromised patients although they may not show signs of immunosuppression. It is three times more prevalent in men than women, especially transplant patients, once that the advances in aids antiretroviral therapy decrease the rates of opportunistic infections (6-7). In a study reported in Cuiabá/MT with 1300 HIV-positive patients, Cryptococcus spp was the most found fungus (50%) in those who presented systemic mycosis (8). Besides, other clinical conditions may be associated to it such as diabetes, neoplasias, lymphomas, sarcoidosis, and the use of corticosteroids (9). The main sources of contact with the fungus are environmental, such as contact with soil contaminated by pigeon feces, eucalyptus trees, and decomposing hollow tree stumps (3,10). In a recent study in Pelotas/RS, 26.9% of the pigeon’s feces in public places were contaminated with Cryptococcus spp. That’s the reason fungus isolation in urban areas becomes a public health risk, particularly for immunocompromised ones (11). The primary site of infection by Cryptococcus spp is the respiratory tract or the central nervous system; however, skin-adjacent mucosa, the eyes, or the genitourinary tract may be affected (3) as well. As for skin Cryptococcosis, according to Neuville et al in a 15-year retrospective cohort study, only 28 cases of primary Cryptococcosis and 80 cases of its secondary form were reported, showing how rare the case is (11).

Mucocutaneous involvement by Cryptococcus may take place only in the skin form or along with the disseminated form, which is more common in Aids patients. Lesions usually occur in the body's upper extremities and are characterized by multiple lesions similar to the molluscum contagiosum. They can be seen as the first clinical manifestation of the disease. There may or may not be regional lymphadenomegaly (8). As a result of that, differential diagnosis should be carried out with acne, syphilis, skin tuberculosis, lipoma, squamous cell carcinoma, and other types of ulcers (9). Therefore, skin biopsy is recommended for the diagnosis. Since the skin lesion is not pathognomonic but more usually presents itself as nodules, ulcers, and paronychia. However, using direct fungus investigation, collecting specific cultures, or using immunological methods (latex agglutination, direct immunofluorescence, and agglutination reaction in a tube) will also help diagnose this pathology (9). In cytology, smear findings range from a cellulitic granulomatous response to a mixed inflammatory response. Although it is important to collect a culture to identify the responsible pathogen, Cryptococcus is faster obtained in cytology by looking at the mucopolysaccharide capsule in special colors (10). Additionally, secondary to the identification of the responsible agent, patients with isolated skin lesions by Cryptococcus must be investigated in all cases for underlying causes of immunodeficiency. That includes blood, urine and mucus samples, chest x-rays, full skin examination looking for similar lesions elsewhere, test to detect HIV antibodies, CD4+, immunoglobulins, and glycemia (11).

According to the Center of Disease Control and Prevention (CDC), the standard treatment for cryptococcosis is Amphotericin B deoxycholate associated to Fluocytosine for two weeks or more. As an alternative, fluconazole can be used at 400 to 800 mg/day for two weeks or more. The treatment makes mortality to decrease up to 80% in case the disease has spread (6,12).

Immunosuppressed patients by AIDS must get maintenance treatment with Fluconazole 200 mg/day for life or until their immune system recovers, which may occur as a consequence of the antiretroviral treatment (12).

Therefore, skin cryptococcosis can be present without any evidence of immunosuppression. Hence, it is advisable to monitor skin lesions in the long run, along with investigating the patient’s immunological status in order to advance the diagnosis of the disease. Nevertheless, the clinical presentation can oftentimes be misleading, with varied presentations. However, histopathological and microbiological exams will help reach the definitive diagnosis.

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REFERENCES


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