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Case Report

Cardiac beriberi and malnutrition: rare complication of paracoccidioidomycosis

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ABSTRACT

Paracoccidioidomycosis is an endemic systemic mycosis that predominates in southern Mexico, parts of Central America, and South America. It is caused by a dimorphic fungus and is generally acquired through the lungs, from where it disseminates. Paracoccidioidomycosis has different clinical manifestations that require differentiation with tuberculosis, Hodgkin disease, several systemic and subcutaneous mycoses, and squamous cell carcinoma. Radiologic abnormalities in the lung fields may be seen. Mucous membrane lesions occasionally occur. The diagnosis is confirmed by finding yeast-like elements of P. brasiliensis in microscopic examinations of wet preparations of specimens submitted for mycologic studies. The occurrence of malnutrition and particularly beri beri conditions concomitant with paracoccidioidomycosis is uncommon. We report a case of a patient of low socio-economic status, without permanent employment , possibly carrying out work as a bricklayer or working on small farms during the harvest season, with a five-year history of oral cavity lesions, which resulted in difficulty eating and thus weight loss. A diagnosis of paracoccidioidomycosis was made through direct microscopy examination, culture and multisystem involvement was confirmed through imaging tests, including dilatation and dysfunction of the right ventricle. The hypothesis of Cardiac Beri-Beri related to thiamine deficiency was raised. The treatment was carried out with thiamine supplementation and liposomal amphotericin B, with excellent clinical evolution of the patient. This case highlights the importance of early recognition of paracoccidioidomycosis in its early stages and the adoption of proactive measures in the search for possible organic complications caused by nutritional deficiencies in prolonged cases.

Keywords: Paracoccidioidomycosis, Beriberi, Thiamine deficiency, Malnourishment

INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic mycosis caused by a thermodimorphic fungi from the Paracoccidioides genus, that was first described in 1908 by Adolpho Lutz. [1,2]

Paracoccidioidomycosis is a systemic granulomatous disease that can affect any organ in the body, predominantly the lungs, organs rich in mononuclear phagocyte system cells, the mucous membrane of the upper aerodigestive tract, the skin and adrenal glands. This condition is caused by thermally dimorphic fungi of the *Paracoccidioides brasiliensis* complex- *P. brasiliensis, P. lutzii*. It is an endemic disease limited to Latin America, from Mexico to Argentina, but its impact on public health has not been fully evaluated because of a lack of available data.[3,4] PCM affects current or former rural workers who are exposed to intense and continued contact with the soil. The disease predominates among

males due to the protection conferred by estrogen, which inhibits or hinders the transformation of conidia and mycelial fragments into the yeast-like form, which is pathogenic.[5-7] PCM predominates among individuals aged 30 to 59 years of age and also among those of mixed race and the lung involvement is particularly relevant due to its high frequency and occurrence of residual fibrosis as well as because the lungs are the portal of entry for *P. brasiliensis* in almost all of the patients.

In patients with systemic mycosis, such as PCM, the presence of cutaneous and mucosal lesions are initiators of specific diagnoses. Taken together, the characteristics of these lesions, including their number, clinical morphology and accessibility for biopsy and collection of material for direct examination and culture, provide valuable indicators that may enable early diagnosis.[8]

Mucosal lesions in PCM patients are characterized by superficial ulcers with microgranulation and haemorrhagic pinpoints, often referred to as mulberry-like stomatitis. These mucosal lesions also exhibit infiltrated borders or infiltrative tissue at their base. This clinical feature is often observed in patients with lesions of the buccal, ocular or genital mucosa. The histological features of mucosal lesions are similar to those of ulcerated cutaneous lesions.[3]

Adrenal involvement by *P. brasiliensis* was first reported by Viana in 1913 during the autopsy of a patient with disseminated disease; it was subsequently reported in a patient with areas of pulmonary fibrosis.[9,10]

The main signs and symptoms of chronic adrenal insufficiency in patients with PCM are malaise, fatigue, anorexia, weight loss, arterial hypotension, orthostatic hypotension, hyperpigmentation of the skin and mucous membranes, nausea, vomiting, and reduced libido and sexual potency. Hyperpigmentation is usually reported or confirmed by patients and is most evident on the oral mucosa

Diagnostic imaging is a significant contribution to the identification of adrenal involvement in PCM. On computerized tomography, the adrenals exhibit irregular contours, as well as volume and density abnormalities. Ultrasound allows for assessing the shape, contours, density and size of the adrenal glands.[3]

The adrenal function seldom recovers after antifungal treatment for PCM, but persistence of residual adrenal insufficiency is much more frequent.[11] The clinical picture and symptoms of beriberi secondary to thiamine deficiency are nonspecific, often being over shadowed by clinical manifestations of concomitant systemic diseases. We reported a case of a patient of low socio-economic status, with a five-year history of oral cavity lesions, which resulted in difficulty eating and thus weight loss. Specific laboratory tests confirmed the diagnosis of paracoccidioidomycosis and thoracic radiological tests indicated probable BeriBeri due to thiamine deficiency.

CASE REPORT

A 51-year-old man coming from the south east region of the state of São Paulo, working as a bricklayer and small farmer, former smoker for a period of 20 years and a history of large alcohol intake. Presented with a five-year history of oral cavity lesions that progressively led to partial loss of some teeth, excessive salivation (sialorrhea), pain during chewing, resulting in difficulties in both eating solid and liquid foods, and a weight loss of approximately 13 kg during this period. The patient also reported experiencing a persistent dry cough in the last two years, informing that during this period he did not seek medical assistance due to economic difficulties He appeared emaciated and in relatively good general condition. He also had notable bilateral submandibular lymphadenopathy, which was painful on palpation. Dermatological examination revealed infiltrated plaques and ulcers covered by serohemorrhagic crusts on the tongue, oral and gingival mucosa (Figure 1). A direct microscopy examination of the oral lesions was performed, revealing a pattern of multiple budding around the mother cell (Figure 2). The chest X-ray showed diffuse and bilateral symmetrical reticulonodular opacities (Figure 3).

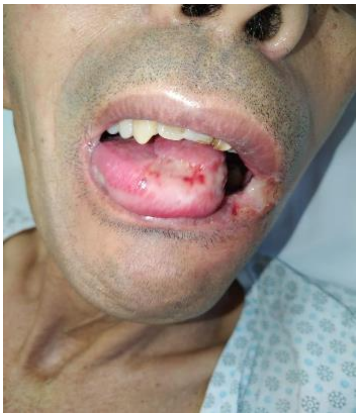

Figure 1: Ulcers covered by serohemorrhagic crusts on the tongue and lip.

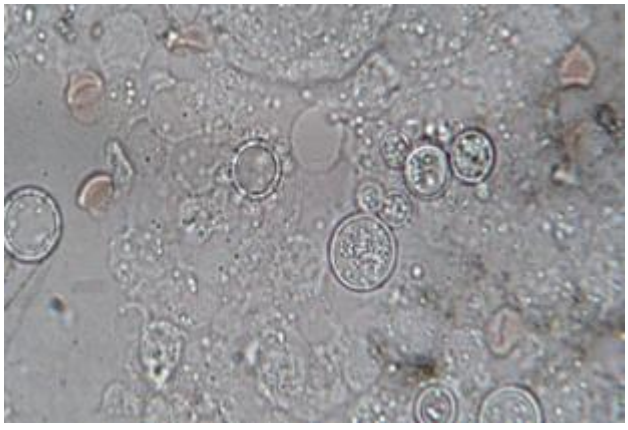

Figure 2: Direct microscopy with rounded, double-walled, refracting cells, with and without budding.

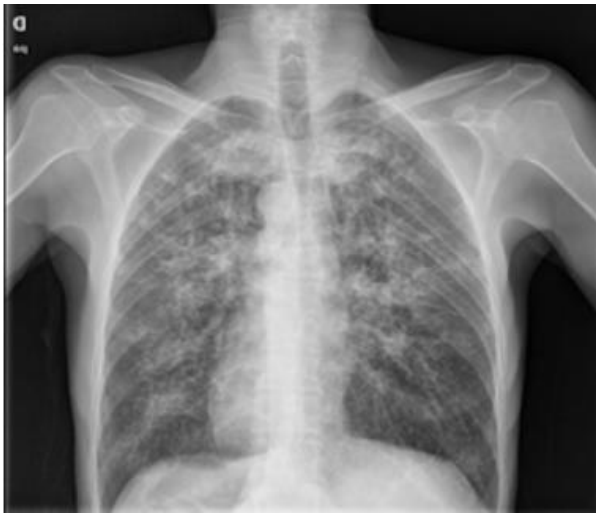

Figure 3: Chest X-ray with diffuse and bilateral symmetrical reticulo-nodular opacities.

Additionally, body tomographies were performed of the thorax and abdomen, which revealed suggestive images of adrenal gland involvement in the abdominal region. In the thoracic area, perilymphatic micronodules, irregular nodular thickening of the interlobular septa, and peribronchovascular interstitial confluence in a consolidative focus were observed, suggestive of a granulomatous infectious process. Bronchiectasis and areas of architectural distortion were also noted, suggesting a subacute/chronic component. Culture was carried out on sabouraud agar medium of the material collected from the mucosal lesion, which identified the growth of *Paracoccidioides brasiliensis*.

The initial immunoelectrophoresis result for paracoccidioidomycosis was 1/128. A subsequent echocardiogram demonstrated dilatation and dysfunction of the right ventricle. Due to the patient's nutritional status and the cardiac changes identified, a thiamine pyrophosphate (TPP) measurement was performed, which revealed a result below normal (10 ng/ml, normal= 20-60 ng/ml). The blood count revealed mild iron deficiency anemia. Other biochemical tests showed no changes. Serology for hepatitis, syphilis and HIV were negative. Despite low levels of thiamine and nutritional deficiencies, the patient did not present with peripheral neuropathy or ocular motility disorder, with mild mental confusion.

Therapy began with intravenous infusion of liposomal amphotericin B at a dose of 3 mg/kg/day, with a total cumulative dose of 3 g. Simultaneously, thiamine supplementation was introduced at a dose of 15 mg every 12 hours orally, administered for 15 days, in addition to adapting the daily diet. The patient progressed extremely satisfactorily with these associated medications, with improvement of the heart function and reverse remodeling of the right ventricle even during hospitalization. Furthermore, there was notable enhancement in the patient's general condition and resolution of mucocutaneous lesions. There was also a marked improvement in dyspnea and coughing episodes practically disappeared.

DISCUSSION

Paracoccidioidomycosis is a systemic fungal disease that continues to be a public health issue in Latin America and Brazil, with an underestimated prevalence based on reports and case series.[12] Although this mycosis primarily affects economically active middle-aged rural workers, to date, it is still not a notifiable disease in Brazil.[13]

The most aggressive manifestations are recorded for the acute/subacute forms, whereas in patients with the chronic form, progression is slow and is accompanied by residual scarring. Patients with either progressive form usually complain of fever and constitutional symptoms such as malaise, asthenia, adynamia, anorexia, and weight loss, all of which are complemented by a wide variety of symptoms related to the afflicted organs.[14,15]

Oral mucosa lesions are regularly observed and localized preferentially in the gums and the hard palate but also in the oropharynx and the larynx. More infrequently, the nasal and the anal mucosa may become involved. Lesions are single or multiple and progressive and with time become destructive; they appear as tumor-like outgrowths covered by hemorrhagic dots (mulberry-like stomatitis) that may ulcerate and are accompanied by prominent edema. Dysphonia, dysphagia, and sialorrhea, as well as a loosening of teeth, are regularly observed. Lymph nodes located around the afflicted mucosal area become hypertrophied, with spontaneous rupturing resulting in fistula formation.[15]

The oral lesions are typically described as painful lesions and can lead to difficulty of feeding resulting in decreased ingestion of micro and macronutrients. Deficiency in thiamine, a water-soluble vitamin, can lead to congestive heart failure, also known as wet beri beri. Usually patients with heart failure present normal or low cardiac output, but a minority can present a high-output heart failure. . Some patients can present non- specific manifestations that can lead to delay of treatment and diagnosis. A few days after the initiation of treatment the cardiac dysfunction can be expected to improve.[16,17]

Depending on the affected organ, scars and other sequels can incapacitate patients for life, forcing young subjects into early retirement, with socio-economic consequences. In Brazil, paracoccidioidomycosis represents the eighth most frequent cause of death due to chronic or recurrent infectious and parasitic diseases and presents the highest mortality rate among the systemic mycoses.[19,20]

Dissemination to the adrenal glands occurs commonly and is as frequent as 90% in autopsy cases; in vivo, however, adrenal involvement is diagnosed in 48% of the cases if cortisol is measured after adrenocorticotropic hormone

(ACTH) stimulation. Adrenal function may become normal upon the completion of antifungal treatment in some patients, although damage to the glands may be permanent in others.[18] Not-withstanding its 'epidemiological invisibility', paracoccidioidomycosis is a serious cause of disease and death and especially affects rural young men. Treatment usually begins late, when the disease has already spread to several organs.

Our patient had no specific cardiac symptoms, the wet beri beri diagnosis was made due to alterations on an electrocardiogram performed to monitor during drug infusion for treatment of the fungi. As for patients with common risk factors for thiamine deficiency or history of new onset heart failure of unknown etiology, vitamin B1 deficiency should be considered and further investigated.[21,22]

In the present case, after the diagnosis, the introduction of specific treatment with liposomal amphotericin B and supplementation with thiamine, the patient showed significant clinical improvement, the skin-mucosal lesions regressed, the clinical picture related to the onset of malnutrition completely regressed, with the patient returning to eating properly, without any further complaints of diarrhoea and pain when swallowing.[23,24] The patient is undergoing monthly outpatient follow-up and has no clinical complications to date. It is also being monitored in the dentistry sector for tooth care.

CONCLUSION

Over the years, paracoccidioidomycosis has undergone epidemiological changes, but has maintained an important impact on public health. This case underscores the importance of early recognition and appropriate management of paracoccidioidomycosis, particularly when it manifests with multisystem involvement. Our aim was to alert clinicians, especially those working in endemic regions, to conduct investigations into possible organic complications induced by nutritional deficiencies. This proactive approach not only aims to prevent the inexorable progression of these conditions, but also has the potential to instigate a reversal of their harmful effects, ultimately leading to improved morbidity and mortality outcomes.

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