Multifocal paracoccidiodomycosis: a diagnostic challenge due to late cutaneous manifestation

Paracoccidiodomicose sistêmica multifocal - desafio diagnóstico por manifestação cutânea tardia

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Abstract: Paracoccidiodomycosis is an endemic systemic mycosis in Brazil, frequent in the rural areas and often in adult men. It is reported the case of a farmer, who is an illicit drugs' user, with insidious manifestations affecting kidneys, lungs, lymphonodes, bones and lately, the skin, with a delay of more than one year in the diagnosis and effective therapy. It is important to include paracoccidiodomycosis as differential diagnosis, even in the absence of cutaneous lesions, for early recognition and treatment, given the high mortality of this entity.

Keywords: Diagnosis; Paracoccidiodomycosis; Skin manifestations

INTRODUCTION
Paracoccidiodomycosis (or South American blastomucosis, or Lutz-Splendore-de Almeida disease) is a systemic mycosis of high prevalence in Brazil, native of the Americas, caused by Paracoccidioides brasiliensis, a dimorphic fungus.1,2 It was originally described in Brazil, by Adolfo Lutz, in 1908.2,3 It is endemic in the country predominantly in the south, south-east and midwest regions of Brazil.3,4 The main source of infection is inhalational and the pulmonary complex can be eliminated becoming a quiescent focus or progressing to internal organs.3,5 In most cases (70-80%), paracoccidiodomycosis (PCM) is multifocal.2

CASE REPORT
Twenty year-old male patient, born as a farmer and raised in Santarém-Pará. Two years before he had shown high fever, axillary and cervical lymphadenopathy, weight loss, dry cough, backache and asthenia. Has a background history of alcoholism, smoking and chronic cocaine user. The patient presented nephritic proteinuria and right pleural effusion. After comprehensive clinical investigation it was introduced as a treatment for lymphadenopathy and tuberculosis. After 6 months, while still undergoing regular treatment for tuberculosis, returns maintaining of the previous condition and with a generalized microand polyadenopathy besides erythematous nodules on...
dorsum of the thorax, abdomen and the neck, with a pleuritic pain, hepatomegaly and ascites. During hospitalization it was carried out tomography of the chest that revealed a right pleural effusion, hypodense lesions and osteolytic lesions in the sternum and right rib (Figures 1 and 2). Doctors suspected of sarcoidosis and the medication for tuberculosis was suspended. Evolved with worsening of the dermatological condition and growth of new nodular-tumor lesions with signs of suppuration and flogose (Figure 3) requiring a dermatological evaluation. The first skin biopsy showed chronic granulomatous dermatitis, subepidermal, nonspecific, with absence of alcohol-acid resistant bacilli and a negative Grocott staining for fungi. It was carried out a new skin biopsy and a swab of a ganglion exudate. On direct microscopic examination it was observed the presence of roundish cells, birefringent, with multiple buddings, compatible with Paracoccidioides brasiliensis (Figure 4), that were confirmed by culture. Histopathology revealed granulomas with fungal yeast cells with a double membrane wall in multiple budding that is best seen when stained by silver. Amphotericin B was used for the treatment, with clinical improvement after a cumulative dose of 1g (Figure 5). The patient was discharged after 2 months with sulfamethoxazole and trimethoprim for maintenance and he had regular dermatological and pulmonary monitoring, without presenting new lesions for 1 year.

DISCUSSION

PCM occurs mainly in men (9-13:1), from 30-60 years of age, in the rural area, being rare in children and young adults. It presents acute, subacute or chronic evolution that can affect one (unifocal) or more organs (multifocal). In this case the profession, origin and the chronicity of the condition were relevant aspects in clinical suspicion of this mycosis. However, the systemic onset presented itself gradually and slowly, hampering the definitive diagnosis.

Mechanisms related either to the resistance or to the susceptibility of males to Paracoccidioides brasiliensis are still unknown. Factors linked mainly to the host are nutritional and socioeconomical factors, co-infections, immunosuppressive therapeutic, alcoholism and smoking. Airways and lungs are the most common sites of inoculation and initial location of the disease, ranging from 50 to more than 90% of the cases. Usually, respiratory symptoms are non-specific such as fever, chest pain, cough, expectoration, hemoptysis and dyspnea in extensive forms and chest X-ray shows in 80-90% of the cases, bilateral images, macro and micronodular, infiltrative or inter-
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Stitch, associated to fibrosis or opacification, usually in the medial and inferior third of the lobes. Miliaria, pneumatic and cavitory lesions are also found. It is rare the occurrence of ascites and pleural infusion, that was seen on the very beginning of the clinical condition of this patient. This association with lymphadenopathy led to the initial hypothesis of tuberculosis which was only discharged after therapeutic trial, showing the importance of concomitant tuberculosis investigation, that occurs in 12% of the cases.

PCM can take various clinical forms, depending on the affected organ. Frequency, number and morphology of skin lesions are consequence of the agent/host interaction. Purely cutaneous disease incidence ranges between 12-15% and originates from hematogenous dissemination of the fungus; of contiguous pre-existing lesion; or rarely, from direct inoculation. The hematogenous pathway is predominant and, in general, with multiple lesions, as reported here. Skin lesions following contiguous bone injury is rare. The skin alterations are polymorphic ranging from acneiform lesions to exudative and/or ulcerative-vegetative nodules. Except for anthrax, there is no pathognomonic skin condition.

Lymph nodes are affected secondarily to skin and/or visceral involvement, being predominant at the cervical or submandibular, supracavicular and abdominal lesions, simulating lymphadenopathic tuberculosis. Adenopathies can be regional or generalized, with fluctuation and fistulization.

The cutaneous-ganglionic and hepatosplenic involvement is classically demonstrated in the acute-subacute form, typical of young people and heavily immunosuppressed patients. Bone alterations can be seeing as osteolytic lesions mainly of the clavicles, the ribs and the humerus with a tendency towards symmetry. In this case, the sternum was affected and reports or citations of this fact were not found in other patients. Ocular involvement is rare, affecting mainly eyelids and conjunctiva.

Gastrointestinal and genitourinary tracts, nervous system and suprarenals can be occasionally affected specially in severe cases, as our patient, who presented nephritic proteinuria, that was the reason for his hospitalization.

The association of PCM and AIDS is varied, being predominant the acute-subacute form, expressing itself by cervical or generalized ganglia infarction, hepatosplenomegaly, frequent atypical skin lesions, bone lesions, tendency towards systemic dissemination and, occasionally, association with TB. So, it is recommended to exclude retrovirus in disseminated multifocal cases besides immunosuppressive factors such as the use of illicit drugs which were investigated in this case. The effective drugs against PCM comprise three groups: amphotericin B, sulfadiazine, and other sulfonamides compounds and azoles with systemic action. Classic amphotericin B a is drug of choice in the serious or multifocal cases. Its choice was made possible by hospital apparatus, which allowed quick clinical remission of the serious and lagged condition of this case.

PCM in Brazil should be considered mainly in men exposed to occupational or non-occupational rural activities or from endemic areas. The approach should be individualized and multidisciplinary since both diagnosis and the treatment of disseminated cases are a challenge similarly to this case that was diagnosed with a delay of more than one year.
REFERENCES

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