Case Report/Relato de Caso

Clinical and evolutionary characteristics of four patients with pulmonary histoplasmosis reported in the Paraíba Paulista Valley Region

Características clínicas evolutivas de quatro pacientes com histoplasmose pulmonar encontrado na Região do Vale do Paraíba

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ABSTRACT

The type of pulmonary histoplasmosis presents limited lesions to the lungs, with symptoms that are clinically and radiological similar to chronic pulmonary tuberculosis. This paper describes the clinical features of four cases of pulmonary histoplasmosis. Aspects of diagnostic and clinical, epidemiological, laboratorial and imaging exams are discussed, in addition to the clinical status of the individuals five years after disease onset. The treatment of choice was oral medication, following which all the patients improved. It is important to understand the clinical status and the difficulties concerning the differential diagnosis of histoplasmosis, to assist the proper indication of cases, thus reducing potential confusion with other diseases.

Key-words: Histoplasmosis. Epidemiology. Pulmonary fungal disease.

RESUMO

A histoplasmose do tipo pulmonar apresenta lesões limitadas aos pulmões, cujos sintomas são clínica e radiologicamente similares à tuberculose pulmonar crônica. Esse trabalho descreve as características clínicas de quatro casos de histoplasmose. Os aspectos do diagnósticos clínicos, epidemiológicos, laboratoriais e exames de imagem são relacionados, além da situação clínica dos indivíduos, 5 após o início da doença. O tratamento de escolha foi através de medicação oral, aonde todos os pacientes evoluíram bem. É importante conhecer o quadro clínico e da dificuldade em diagnosticar a histoplasmose para ajudar a conduzir as boas indicações dos casos, reduzindo assim o mal-entendido com outras entidades patológicas.

Palavras-chaves: Histoplasmose. Epidemiologia. Doenças fúngicas pulmonares.

INTRODUCTION

Histoplasmosis is caused by the fungus *Histoplasma capsulatum*, developing as an acute pulmonary infection of controlled seriousness in healthy individuals and can develop in immunocompromised patients in chronic, progressive or disseminated forms[1]. It is acquired through the inhalation of soil dust particles contaminated by birds and bats feces, containing microconidia (infectious form). When it penetrates the pulmonary alveoli and the hilar and mediastinal lymph nodes, it can spread to several parts of the body through the blood flow, permitting the agent to sponge on tissues of the monocytic-histiocytic system, the host's response against the infection, which determines the extension of the disease[2,3].

Fungal pulmonary infections occur due to climatic conditions favorable to their development and are controlled by the protection of natural barriers (mountains, seas and deserts)[4].

Most infections caused by *Histoplasma capsulatum* are asymptomatic or subclinical, symptomatic cases usually manifest as self-limiting respiratory tract infections. Massive aspiration of conidia of the fungus can lead to the emergence of an acute pulmonary form after an incubation period of one to three weeks. The most common symptoms consist of fever, chills, headache, myalgia, appetite loss, cough, dyspnea and chest pain[5].

In order to broaden the understanding of the occurrence of the disease, its consequences and environmental implications, four clinical cases which occurred in the Paraíba Valley are presented, including their main manifestations, treatment and evolution over 5 years. The cases are summarized in **Table 1**.

CASE REPORTS

CASE 1

A 13 year-old male complained of continuous high temperature, holocraniad headache and myalgia. He had been inside a cave for 12 hours 15 days prior to examination. Alteration was verified in the hemosedimentation rate in the first hour, 31mm, and in C reactive protein (CPR 8.05mg/dL). Positive serology for *H. capsulatum* was obtained on day 35 of evolution. The thorax computed tomography (CT) showed small areas of parenchymal densifications, of unspecific aspect, in upper and lower lobes of the right lung. In the chest CT taken on day 50, small parenchymal densifications, of vague limits, were identified in the upper lobe and apical segment of the lower lobe of the left lung. Four months after initial exposure, the same exam revealed a nodule. A year after the initial event, the chest CT presented a small subpleural calcified nodule on the right lower lobe, which could still be identified in the exam three years later.

CASE 2

A 45 year-old man presented high continuous fever, intense adynamia, holocraniad headache and myalgia for 7 days. He reported

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TABLE 1 - Summary of patients's symptoms.

	Image tests			
	Case 1	**Case 2**	**Case 3**	**Case 4**
Thorax CT	35th day small densifications inferior and superior lobes D	32nd day lungs nodule (9 to D, 8 to E) 1 nodule of 1.9cm superior lobe E		41st day nodule condensations pulmonary basis
	50th day small densifications inferior and superior lobes D	62nd day bilateral densifications superior, medium lobes and basis D		
	4 months nodule 1cm superior lobe 4 nodules < 0.5mm inferior lobe D	5 months small nodules medium and inferior D lobes		
	1 year small nodule calcified subpleural inferior lobe D	1 year 2 nodules <1cm superior and inferior lobes D		
Thorax X-rays	16th and 35th days normal	12nd day obliteration in costophrenic sinus tenuous opacity third superior E basis D 49th day normal	normal 5th day 7th day	

having been to the same cave 15 days prior to examination. He presented erythematous micropapules on his skin, light tachycardia and dyspnea, cervical ganglia palpable. Following a chest X-ray, obliteration of the costophrenic sinus and poorly defined tenuous opacity in the upper third of the left lung and at the base of the right lung was observed. The hemosedimentation rate for the first hour was 69mm and PCR was 20.08. On day 2 following admission, the patient had fever, and ceftriaxone, chloramphenicol and itraconazole were introduced due to suspicion of histoplasmosis. A Chest CT (day 31) showed multiple nodules in both lungs and a larger nodule (1.9cm). The patient presented positive serology for Lyme disease and no medication was administered, since he was already receiving intravenous ceftriaxone. By day 33, he showed reagent serology for *H. capsulatum*. The CT of observation day 62 showed small dense areas of unspecific aspect in the upper lobe of the left lung and in the middle lobe and at the base of the right lung. After 5 months, the patient presented small pulmonary nodes of residual aspect in the middle and lower lobes of the right lung in a thorax CT. A year after the onset of symptoms, 2 nodes smaller than 1 cm could be seen in the upper and lower lobes of the right lung.

CASE 3

A 32 year-old man, with a history of systemic arterial hypertension, coronary spasm and tobacco addiction, took part in shootings carried out 15 and 7 days earlier in the bat-inhabited cave. After 10 days, the patient complained of an intense, continuous and pulsatile holocraniad headache, with discrete icterus, palpable liver, fever, snoring under pulmonary auscultation and morbilliform cutaneous eruption on the torso, face, neck and upper limbs. Laboratorial exams showed alterations in hemosedimentation rates (47mm in the first hour; 97 mm in the second hour). The patient evolved slowly. On day 60, patient had left thoracic pain and asthenia, was diagnosed with histoplasmosis and received itraconazole for 6 months.

On observation day 75, he had pain in the left lumbar region and palpable spleen. The patient showed good evolution, using medication for 6 months, as prescribed.

CASE 4

A 23 year-old man, with a tobacco addiction, complained of continuous epigastric pain for 5 days with progressive worsening, with no relation to feeding. He also reported to have continuous fever and headache for four days, preceded by agues and dark urine

for the last three days. The patient had been in the same cave about 15 days earlier. On day 32, he presented light myalgia, conjunctive heartburn, important asthenia and palpable spleen. A chest CT showed parenchymatous nodular condensations in the pulmonary bases.

DISCUSSION

Infection with Histoplasmose capsulatum results in varied and occasionally unusual clinical syndromes[6] caused by agent inhalation, with primary infection in the lungs, mostly benign, which can pass unnoticed or manifest as a light flu and result in small calcifications in the lung, without severe compromise of the organ.

Among a group of six individuals described here, who were exposed to a cave environment for several hours, four people got ill. High fever, followed by holocraniad headache and cervical lymphadenomegaly marked the onset of the disease for all the patients described in current work, associated with myalgia complaint. Important prostration was a relevant event for two individuals. A clinical picture of probable pulmonary histoplasmosis can be established by uniting the findings of the present work and that of reviewed authors: persistent high fever, relevant headache, respiratory symptoms (cough, dyspnea, and thoracic pain), asthenia, anorexia, prostration, hepatomegaly, proteinuria and hematuria[7-9].

The Grocott-Gomori methenamine silver method revealed intracellular yeast forms and cultures of sputum samples and bronchoalveolar lavage in Sabouraud dextrose agar revealed the presence of *Histoplasma capsulatum*.

After disease evolution for a month, it was possible to identify nodular imaging in all lungs. This period of time is perfectly compatible with the evolution of a granulomatous fungal pulmonary disease[8,9].

The chest CT of the patients studied here showed sequential involution of pulmonary lesions, denoting calcification documented in two patients performing such controls. However, chest radiography was a less efficient resource in case follow-up, since it did not show the existing lesions, demonstrated at that time by chest CT (Case 1, on day 35 of evolution).

Unis, Oliveira and Severo[10] highlighted the difficulty of establishing clinical and radiological diagnosis for histoplasmosis, considering exams with a specific stain (Gomori-Grocott) as the best option for diagnosis confirmation[4,5,7,8]. Once the diagnosis of histoplasmosis was established, all the patients received antifungal treatment (itraconazole)[9], though only two of them accepted the use of medication for six months; the other two patients followed other medical advice.

All the patients reported in this work evolved slowly, but are healed, have been under observation and are clinically well five years after the onset of the disease.

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