

Case Report

An outbreak of histoplasmosis in the city of Blumenau, Santa Catarina*

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ABSTRACT

Acute pulmonary histoplasmosis is rarely diagnosed and is often confused with tuberculosis. Most knowledge of the disease has been derived from descriptions of epidemics in which a number of individuals were exposed to the same source of infection. Isolation of *Histoplasma capsulatum* var. *capsulatum* from soil samples is conclusive evidence of an epidemic focus. This is the first report of an outbreak of histoplasmosis, in which two cases were reported and the fungus was isolated at the focus of the epidemic, in the state of Santa Catarina. Further epidemiological studies are needed in order to determine the prevalence of the infection statewide.

Keywords: Histoplasmosis/diagnosis; Histoplasmosis/epidemiology; *Histoplasma*/isolation & purification; Lung diseases, fungal; Disease outbreaks; Case reports [publication type]

INTRODUCTION

The thermal dimorphic fungus *Histoplasma capsulatum* var. *capsulatum* causes various clinical manifestations, depending on the anatomical and immunological status of the host and on the quantity of fungal inoculum. Acute pulmonary histoplasmosis occurs when an otherwise healthy individual inhales a large quantity of fungal propagules.⁽¹⁾

In previously healthy individuals, acute pulmonary histoplasmosis manifests as cough, fever, dyspnea, and asthenia. In primary infections, these symptoms appear three weeks after exposure to the

fungus, whereas they appear more rapidly (within one week after exposure) in cases of re-infection. The course of the disease is self-limited, with spontaneous regression of the symptoms. Clinical and laboratory findings vary depending on whether or not the host has been previously infected and on the quantity of inoculum.⁽²⁾ The fungus is found in the upper layers of the soil and is propagated through airborne dispersion.⁽³⁾ Length of exposure determines disease severity.⁽⁴⁾

Most knowledge of the disease has been

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derived from descriptions of epidemics in which a number of individuals were exposed to the same source of infection,⁽²⁾ such epidemics being more easily recognized, since they affected an entire group of people simultaneously. The simultaneous onset of symptoms in more than one patient should raise the suspicion of histoplasmosis and can be used to rule out the possibility of tuberculosis. Histoplasmosis mimics tuberculosis in its clinical, radiological, and histopathological aspects. It is therefore necessary to carry out specific tests, using cultures to identify the etiologic agent.

Since 1958, 26 outbreaks of histoplasmosis have been reported, all occurring in one of eight Brazilian states (Rio de Janeiro, Rio Grande do Sul, São Paulo, Distrito Federal, Minas Gerais, Paraíba, Amazonas and Bahia), and the fungus was isolated from soil in five of those states (Rio de Janeiro, Rio Grande do Sul, São Paulo, Distrito Federal and Paraíba).⁽⁵⁾ Herein we describe the first outbreak of acute pulmonary histoplasmosis in which *H. capsulatum* was isolated at the focus of the epidemic in the state of Santa Catarina.

CASE REPORT

Case 1

A 67-year-old white male, resident of the city of Blumenau, in the state of Santa Catarina, and a sales representative, presented with dyspnea, asthenia, chest pain, and sweats ten days after having cleaned his attic, where there are water tanks. He was in contact with bat guano for a limited period of time when the area was being swept.

The presence of pulmonary nodules on the chest X-ray and tomography of the chest (Figures 1A and 1B), together with the absence of expectoration, justified the performance of a biopsy to evaluate the pulmonary nodule.

The microbiological evaluation revealed negative double-immunodiffusion for *H. capsulatum*. Hematoxylin and eosin staining of the lung biopsy revealed tuberculous granuloma with caseous necrosis, sputum smear microscopy was negative, and the results of the Grocott-Gomori methenamine silver (GMS) staining of the sections were negative. In view of these findings, empirical treatment for tuberculosis was initiated.

Due to the knowledge that the disease is related to contact with bat guano, the material was sent to the Santa Casa Hospital Mycology Laboratory, in the city of Porto Alegre, in the state of Rio Grande do Sul, for mycological re-evaluation. This re-evaluation revealed small, single-budding yeast-like organisms suggestive of *H. capsulatum* in the GMS staining of new tissue sections. The patient was started on itraconazole (200 mg/day) and presented favorable evolution.

Case 2

A 50-year-old white male, resident of the city of Blumenau and a stonemason, presented a clinical profile similar and simultaneous to that described in Case 1 ten days after the cleaning of the same area, in which there was bat guano. The patient was exposed to a large quantity of dust in an enclosed space. The patient was hospitalized for seven days. Two chest X-rays, one presenting

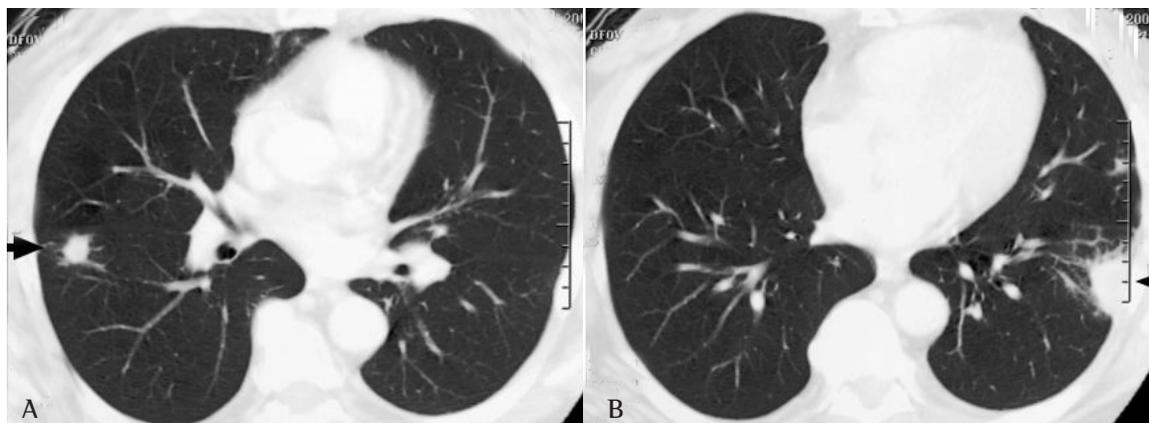


Figure 1 - A and B: Computed tomography of the chest revealing a right-sided pulmonary nodule and a triangular opacity in the lower left lobe with its base angled toward the pleura



Figure 2 - A and B: Chest X-ray revealing diffusely disseminated micronodules in both lungs and subsequent control of the condition with regression of the lesions

diffusely disseminated micronodules in both lungs and one showing the subsequent control of the condition, are shown in Figures 2A and 2B.

The microbiological evaluation revealed negative double-immunodiffusion for *H. capsulatum*. Hematoxylin and eosin staining of the transbronchial biopsy sample revealed a granulomatous chronic inflammatory process, sputum smear microscopy was negative, and the results of the GMS staining of the section were negative. In view of these results, empirical treatment for tuberculosis was initiated.

Mycological re-evaluation of the material was carried out in the same laboratory used for the Case 1 samples, and the GMS staining of new sections also revealed small, single-budding yeast-like organisms suggestive of *H. capsulatum*. The patient was started on itraconazole (200 mg/day) and presented clinical improvement one month after the onset of symptoms.

DISCUSSION

In Brazil, 26 outbreaks of histoplasmosis, involving 184 patients, have been reported since 1958⁽⁵⁾ (Table 1). The number of cases per outbreak ranged from two to thirteen. The main sources of infection were visits to caves where there was bat guano (ten outbreaks), followed by visits to abandoned mines (five), and contact with droppings

from chicken coops (three outbreaks). In 11 of those outbreaks, *H. capsulatum* was isolated from soil.

Epidemiological history can raise diagnostic suspicion. Knowledge of clinical syndromes, together with clinical suspicion, can avoid the use of empirical treatment. Radiological findings, negative test results, and the high frequency of tuberculosis in Brazil were the motivations for prescribing tuberculosis treatment for both patients. Immunodiffusion test results, although negative for these two patients, have high sensitivity and

TABLE 1

Outbreaks of histoplasmosis reported in Brazilian states

State	Isolation from soil	Histoplasmin skin test*	APH n
RJ	+	93	15
RS	+	89	3
SP	+	86	3
MG	-	64	1
AM	-	50	1
PB	+	32	1
BA	-	32	1
GO	+	22	1
SC	+	6,3	1**

*Maximum value found (%); **Present study

RJ: Rio de Janeiro; RS: Rio Grande do Sul; SP: São Paulo; MG: Minas Gerais; AM: Amazonas; PB: Paraíba; BA: Bahia; GO: Goiás; SC: Santa Catarina. APH: acute pulmonary histoplasmosis

are positive in approximately 75% of cases.⁽⁶⁾ Length of exposure determines disease severity. This explains the fact that the second patient, who was the one who swept the area, presented a more severe form of the disease, with diffuse pulmonary alterations on the chest X-ray, and required hospitalization. However, a short exposure time results in focal pulmonary lesions, as in Case 1.

The diagnosis is confirmed by the presence of *H. capsulatum* in the lung tissue biopsy. The tissue section must be stained according to the GMS technique.⁽⁶⁾ In both cases, the diagnosis of the outbreak was made through GMS staining of lung biopsy samples, which revealed small, oval-shaped, single-budding yeast-like organisms suggestive of *H. capsulatum*.

Treatment is not usually indicated for immunocompromised patients with acute pulmonary histoplasmosis, since the disease is self-limiting and presents minimal morbidity. Treatment should be considered for those who remain symptomatic for more than a month or who present diffuse radiological alterations or hypoxemia.⁽⁷⁾ When amphotericin B was the only antifungal drug available, treatment was not indicated due to the toxicity of the drug.⁽⁸⁾ With the advent of the azole antifungals, which have the advantage of easy oral administration and good tolerability, the indications increased. The treatment of choice is the use of itraconazole (200 mg/day) from six to twelve weeks.⁽⁷⁾ In the cases described herein, we opted for treatment because the patients had been symptomatic for more than a month, and because, in Case 2, hospitalization was required.

Isolation of the fungus from soil demands meticulous work and collection of various samples from multiple locations, since *H. capsulatum* concentrates in small microfoci presenting ideal growth conditions, such as temperature between 22°C and 29°C and relative humidity between 67% and 87% or more, at certain times of year.⁽³⁾ The technique used to identify the fungus is intraperitoneal

inoculation in mice, which are killed four weeks later.⁽⁹⁾ The present study represents the first time that it was possible to isolate *H. capsulatum* from soil in the state of Santa Catarina, this being conclusive evidence of an epidemic focus.⁽⁴⁾ The only epidemiologic survey in the state of Santa Catarina was carried out in 1955, involving 110 soldiers in several cities and employing various dilutions of histoplasmin (1:10, 1:100, 1:1000). The rate of positivity was found to be 6.3%, which does not reflect the current situation.⁽¹⁰⁾ Outbreaks of histoplasmosis are usually more frequent in areas of higher endemicity. Further epidemiological studies are needed in order to determine the prevalence of the infection statewide.

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