


# Histoplasmosis in the Anal Canal: Case Report and Literature Review

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## Abstract

### Keywords

- ▶ histoplasmosis
- ▶ anal canal
- ▶ condyloma acuminatum
- ▶ digestive system abnormalities

We herein present the case of a patient with anal condylomatosis concomitant with histoplasmosis, whose diagnosis was only possible through the collection of material and the subsequent evidence of a primary pulmonary focus. Histoplasmosis is a fungal disease whose contamination occurs through the respiratory route, and it can spread to the digestive tract, but the anus is rarely affected. It is important to have a high degree of suspicion to make the diagnosis, especially in immunosuppressed patients.

## Introduction

Histoplasmosis is a fungal disease caused by dimorphic agents of the species *Histoplasma capsulatum*, and its clinical manifestations range from asymptomatic infection to a form of disseminated disease, in which the components of the respiratory system become the main target of the opportunistic fungus. Histoplasmosis has become an endemic disease in most parts of the world, especially in warm regions of Central and South America, Africa, Asia and Australia.<sup>1</sup>

The first contact of the pathological agent with the body is established through the airways, with the inhalation of the infective form of this fungus, the microconidia, which reaches the alveoli and stimulate the development of an inflammatory response in the lung tissue. In more severe cases, however, the etiologic agent can reach the lymphatic system, spreading to other organs and peripheral tissues, affecting the digestive system (in 30% of the cases) and, within this group, affecting the anal canal in 2% of the cases.<sup>2</sup>

The present case report depicts the history of a patient with a rare manifestation of anal histoplasmosis. The study aims to elucidate the main manifestations of this mycosis in the digestive system, as well as the forms of investigation that led to the correct diagnosis, conduct and treatment of the patient.

## Case Report

In 2019, a 34-year-old male patient, HIV-positive since 2006 and under regular treatment with an infectious disease specialist, presented a perianal lesion that led him to a consultation at the Coloproctology Service of hospital Universitário Maria Aparecida Pedrossian, in the city of Campo Grande, Midwestern Brazil, where perianal verrucous lesions compatible with condylomatosis were observed (→ Fig. 1). Treatment with topical podophyllin was administered during four weeks without response, indicating need for surgical treatment, which was performed only in early 2022 due to the suspension of elective surgical procedures in

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**Fig. 1** Perianal ulcerative lesion on the right buttock.



**Fig. 2** Computed tomography scan of the thorax.

the context of the coronavirus disease 2019 (COVID-19) pandemic. Electrocauterization of the verrucous lesions was performed with the resection of some lesions directed for histopathological study and cultures, both of them showing a positive result for *Histoplasma sp.*. Considering that histoplasmosis can present systemic forms of infection, we examined the patient for the involvement of other organs and, due to the time elapsed since the diagnosis. A computed tomography (CT) scan of the thorax showed changes characteristic of pulmonary involvement (► **Fig. 2**). A CT scan of the abdomen and biopsies of other similar lesions in the chest (which appeared later) confirmed the diagnosis of disseminated histoplasmosis – involvement of epithelial and lung tissues. Treatment with amphotericin lipid complex was administered under the care of the infectious diseases team and outpatient follow-up, with complete resolution of the condition in eight weeks.

## Discussion

The case herein reported is of great importance for several reasons. First, it provides awareness of this rare disseminated

form of histoplasmosis, due to the affection of the gastrointestinal system, more specifically the anal form of the disease, so that in the face of uncharacteristic perianal lesions, this becomes another diagnosis to be considered.<sup>2–4</sup> Involvement of the gastrointestinal system in histoplasmosis is rare, but in the disseminated form the ileum is the most frequently affected segment (in 56% to 79% of the cases), followed by the large intestine (55% to 65%), stomach (14% to 17%), esophagus (8% to 18%), rectum (13%), pancreas (6%), gallbladder (6%), and anus (2%). In the case herein presented, the initial involvement was exclusively anal, since there were no clinical manifestations of pulmonary involvement, which is uncommon in this disease, which usually presents with ulcerative lesions disseminated by other organs and structures.<sup>4</sup>

Another important piece of data is the form of presentation of the disease. In the case herein reported, a perianal nodule was observed, which caught the attention of the authors and led to the investigation of the disease, but this is not the most common presentation in the medical routine. Ulcers are the most common form of lesions in disseminated histoplasmosis, appearing in 49% of the cases, followed by nodules in up to 21% of the patients, isolated hemorrhages in 13%, and obstructive masses in 6% of the cases.<sup>4</sup> In addition, the patient had associated perianal condylomatosis, which is not common according to reports of disease in the anal canal.

Cases similar to the one herein present have already been reported in previous articles. The first report of perianal histoplasmosis was made in 1952 by Weiss and Haskell,<sup>5</sup> who described the case of a 62-year-old male patient with significant systemic and gastrointestinal complaints of weight loss, fever, dysphagia, and pain during defecation. Proctoscopy was performed for screening, in which polyps were located in the anal and rectal canals. The anal polyp biopsy showed the presence of *Histoplasma sp.*. The case herein reported differs in that the patient did not present the typical systemic manifestations of the disease as reported by Weiss and Haskell.<sup>5</sup>

Just as the current case, in which histoplasmosis was not the initial diagnostic hypothesis and only by the examination of the collected material was it possible to establish the diagnosis, Hong et al.<sup>6</sup> also established the diagnosis by biopsy based on another diagnostic hypothesis. They<sup>6</sup> presented the case of a 72-year-old male patient with a single painless lesion in the left gluteal region, with a central and raised-edge ulcer, which led to the initial hypothesis of neoplasia. In the evolution of the history, the patient presented only dry cough as an associated symptom. Subsequently, large amounts of DNA of *Histoplasma sp.* were evidenced, confirming the diagnosis of disseminated histoplasmosis.

In the investigation of disseminated histoplasmosis, it has been observed that most patients have persistent and/or recurrent symptoms (25%).<sup>7</sup> Therefore, in view of these cases, we suggest the evaluation of certain parameters, such as: reviewing the patient's adherence to the previously established treatment, carrying out relevant investigations for other possible concomitant diseases (tuberculosis) – especially in patients with a CD4 cell count below 200 cells/mm<sup>3</sup>–, monitoring patient progress by using *Histoplasma sp.* antigen detection tests, and ensuring adequate

serum levels of the drugs proposed for the treatment.<sup>8</sup> In the case herein presented, once the initial difficulty in diagnosis was overcome, the patient had complete resolution of the condition and remained asymptomatic.

For the diagnosis of the case herein reported, a direct mycological examination was performed with a fresh skin fragment treated with 10% potassium hydroxide, which showed the presence of suggestive yeasts from *Histoplasma sp.*. In addition, an anatomopathological examination was performed, from a biopsy of a thoracic skin lesion, which showed granulomatous dermatitis with the presence of numerous ovoid structures inside macrophages with morphological characteristics suggestive of *Histoplasma sp.*

Currently, the possibility of diagnosing the disseminated form of histoplasmosis has been studied through several techniques based on urine tests, a faster and less invasive method, capable of guaranteeing good conditions for the patient submitted to it.<sup>1,7</sup> One of the main works in this regard was the prospective cohort study conducted by Hoffman et al.,<sup>7</sup> with 78 HIV-positive patients with suspected disseminated histoplasmosis in hospitals in the city of Porto Alegre, Southern Brazil. The authors<sup>7</sup> showed that the classic methods (culture/histopathological study) were responsible for 8 diagnoses (10.3%). On the other hand, the detection of antigens through urine samples using enzyme-linked immunosorbent assay (ELISA) was responsible for the diagnosis of 13 patients (overall prevalence of 16.7%). In addition, the use of home ELISA was related to the diagnosis of 14 patients (17.9%).

Given the rarity of the manifestation of histoplasmosis in the anal canal, there is little evidence regarding the best diagnostic method, and the collection of material for culture and histopathology is probably the best alternative. However, the alert for this diagnostic possibility remains in situations such as the one herein reported, in which the diagnosis begins with the disseminated lesion and later the primary focus is found, especially in immunosuppressed patients.

As for the treatment of this pathology, historically the best drug available is amphotericin B. However, nowadays, triazole derivatives have been shown to be very effective in combating the disease, so the choice of therapy is based on the clinical form presented by the patient.

Thus, acute pulmonary histoplasmosis and its complications usually resolve spontaneously within a certain period. Pharmacological treatment is indicated in those patients

with no resolution of symptoms within two to three weeks or with early systemic involvement. In these cases, the treatment of choice is oral itraconazole at a dose of 200 mg every 8 hours for 3 days, followed by 200 mg to 400 mg a day for another 6 to 12 weeks.<sup>1-4</sup>

In the disseminated form of the disease, as in the case herein reported, amphotericin B becomes the drug of choice, especially in HIV-positive patients, being administered in a total dose of 35 mg/Kg. It is usually necessary to use maintenance doses of therapy to avoid relapses, composed of amphotericin B at a dose of 1 mg/Kg twice a week or itraconazole 200 mg/day, orally. Still in this group of patients, there are also several studies<sup>1,7,8</sup> demonstrating that the primary treatment for one year with itraconazole is of great benefit, with a very low remission rate. Furthermore, it is worth mentioning that in HIV-positive patients, early antiretroviral therapy is essential to improve the cellular immunity.

#### Conflict of Interests

The authors have no conflict of interests to declare.

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