



Endobronchial histoplasmosis mimicking primary bronchogenic carcinoma during the COVID-19 pandemic

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TO THE EDITOR,

During the Coronavirus pandemic, the number of chest computed tomography (CT) scans increased, a fact that has benefited several patients on account of the incidental radiologic findings.⁽¹⁾ Chest CT scans play a crucial role in determining the severity of infection, particularly in hospitalized patients.⁽²⁾ Naturally, with the increased use of CT scanning in the current scenario, higher rates of endobronchial lesion detection have also been expected.⁽³⁾

Endobronchial lesions often represent malignancy even in young adult patients, and carcinoid tumors are the most common.⁽⁴⁾ Nevertheless, a large and heterogeneous group of possible etiologies have been reported, mimicking primary bronchogenic carcinoma.⁽⁵⁾ Those include: lymphoma, broncholithiasis, metastatic disease, and fungal infections.⁽⁵⁾ Although rare, a distinctive form of endobronchial granulomatous disease is that caused by *Histoplasma capsulatum*.

A 35-year-old non-smoking female patient presented with mild symptoms of cough and sore throat, diagnosed with COVID-19 based on PCR detection on initial nasopharyngeal/oropharyngeal swabs, and was admitted for a work-up. She had no comorbidities, and her physical examination was unremarkable. The patient underwent a chest CT, which was performed according to the institution's protocol to determine the severity of the infection. The CT did not reveal interstitial lung disease, although an 8-mm incidental pulmonary nodule was detected. This non-calcified, solid endobronchial nodule was situated in the anterior segmental bronchus of the left upper lobe, as shown in Figure 1A. The patient denied household or work exposure to tuberculosis (TB); however, she had had contact with bat guano during childhood for a limited period of time. This CT finding in the young woman led to a primary hypothesis of carcinoid tumor, as well as the findings upon bronchoscopy, as shown in Figure 1B. After complete resolution of COVID-19, we performed endobronchial biopsies with histopathological analysis and microbiological studies. The pathological findings revealed a non-caseous granuloma, and the results obtained by Grocott-Gomori methenamine silver (GMS) staining confirmed typical yeast forms of *Histoplasma capsulatum*, as shown in Figure 1C. The patient was then referred for standard follow-up with CT scans without antifungal treatment. After 6 months of follow-up, the patient had an uneventful evolution, and the imaging control showed

a significant decrease in the endobronchial lesion, with no appearance of new lung lesions, as shown in Figure 1D.

Here, we report the case of an asymptomatic young female patient with an incidental radiologic finding during work-up for COVID-19. Although imaging suggested a solid endobronchial lesion mimicking either a benign or malignant pulmonary tumor, the bronchoscopy biopsies revealed endobronchial histoplasmosis infection.

Histoplasmosis is a fungal infection caused by a dimorphic fungus predominately found in soils enriched with bird and/or bat excreta and usually occurs by inhalation of the fungal organism. In endemic areas of pulmonary histoplasmosis, such as the United States, up to 500,000 new infections occur each year. This diagnosis is naturally listed as a differential diagnosis of endobronchial lesions, however not in Southeast Brazil.⁽⁶⁾

While the clinical features may vary, most people infected by *Histoplasma capsulatum* remain asymptomatic; however, approximately 10–40% can develop pulmonary or systemic disease.⁽³⁾ In contrast, the direct endobronchial presentation is the least common. Only eleven cases of endobronchial histoplasmosis have been reported in the literature.⁽⁶⁾ Despite improvements in imaging studies and serological procedures, accurate diagnosis remains challenging.

The radiologic findings of endobronchial histoplasmosis are not considered sufficient for diagnosis since they often mimic other granulomatous infections, such as tuberculosis, and neoplastic processes.⁽³⁾ The diagnosis is confirmed by the presence of *H. capsulatum* in the tissue, obtained by endobronchial biopsy in most cases. The tissue sample must be stained using the GMS technique to reveal small, oval-shaped, single-budding, yeast-like organisms.⁽⁷⁾

A variety of tests, including the urine enzyme immunoassay for *Histoplasma* antigen, complement fixation, and culture, can help establish the diagnosis. However, the sensitivity of detection depends on clinical presentation and the host's status.⁽⁸⁾ In the present case report, the patient was only tested for the *Histoplasma* antigen, with a negative result; other serum antigen tests were not available at our institution.

The treatment of histoplasmosis depends on the severity of the illness. While conservative management is adopted in immunocompetent asymptomatic patients, specific antifungal therapy should be offered in symptomatic

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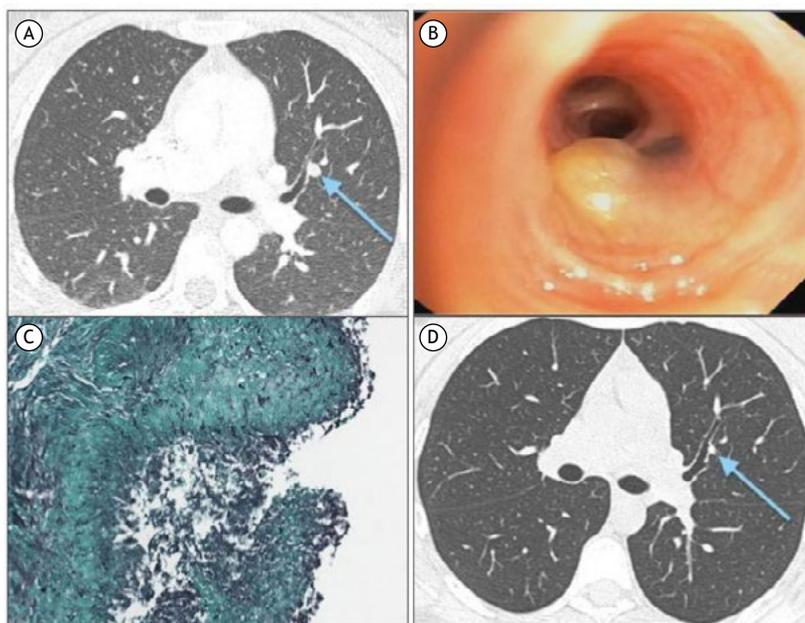


Figure 1. Radiological and histopathological findings of the endobronchial lesion. (A) Chest CT showing a non-calcified 8-mm endobronchial fungal lesion beside the anterior segmental bronchus of the left upper lobe (arrow). (B) Endobronchial nodular lesion seen by bronchoscopy mimicking a lung carcinoid tumor. (C) Histopathological analysis with Grocott staining showing bronchial wall fragments with respiratory epithelium and alveolar prolongation with chronic granulomatous inflammatory process with central caseous necrosis and small regular yeast-like structures (black stain), suggesting *Histoplasma* sp. (original magnification $\times 20$). (D) Chest CT indicating 5-mm endobronchial histoplasmosis (arrow).

patients with diffuse infiltrative lesions.⁽⁹⁾ The treatment of choice is oral itraconazole (200 mg/day) for six to twelve weeks.⁽¹⁰⁾

In conclusion, we believe endobronchial histoplasmosis should be considered part of the differential diagnosis of endobronchial lesions in young patients, even in non-endemic areas.

AUTHOR CONTRIBUTIONS

PDD: writing main content of text, editing, referencing. ANC and PRS: study conceptualization, editing, image selection. RMT: writing first draft of the case presentation, editing, study conceptualization, image selection.

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