

## An unusual infection in an immunocompetent male from a non-endemic area: Lessons from a vacation

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### Abstract

Primary pulmonary histoplasmosis is found worldwide, and is particularly endemic in some areas of North America, usually those surrounding the Ohio and Mississippi river valleys. It is not common in the East Coast of the United States, and is in fact reportable in Pennsylvania. It has been rarely described in immunocompetent individuals residing in a non-endemic region. We present a case of a previously healthy middle-aged male, a Pennsylvania resident, who presented with mid-sternal chest discomfort, fatigue, chills and mild shortness of breath, and was diagnosed with primary pulmonary histoplasmosis.

### Introduction

*Histoplasma capsulatum* is a thermally dimorphic fungus that is particularly found in environments with soil containing the droppings of birds or bats that are often decaying or decayed. When there is any disruption, it can cause the release of the fungal particles with subsequent inhalation by a potential host. Thus, it primarily affects the lungs, but other organs can also be affected. Primary pulmonary histoplasmosis is found worldwide, and is particularly endemic in some areas of the North America, usually those surrounding the Ohio and Mississippi river valleys.<sup>1</sup> Baddley *et al.* found that per 100,000 populations in the United States, 3.4 cases of histoplasmosis were present in older adults more than 65 years of age.<sup>2</sup> It is a problem in patients who have compromised immunity from infections like HIV/AIDS and is more prevalent in areas where anti-retroviral treatment is not widely available.<sup>3</sup> Histoplasmosis is not common in the East

Coast of the US. In Pennsylvania, it is in fact a reportable disease. We present an infrequent occurrence of pulmonary histoplasmosis in a middle-aged immunocompetent male living in a non-endemic area.

### Case Report

A 50-year-old physically active man presented to our hospital with mid-sternal chest discomfort, fatigue, chills and mild shortness of breath that started about a week prior and became progressively worse. He also complained of extreme diaphoresis. Vital signs showed temperature of 99.1°F, heart rate 67 bpm/regular, respiratory rate 18/m, blood pressure 144/90 mmHg and saturation 98% on room air. He was awake, alert and oriented to time, place and person. His neck was supple with no carotid bruits noted. Lung exam revealed occasional bibasilar coarse crackles, cardiac examination revealed normal rate and rhythm, normal S1 and S2 with no murmurs/rubs or gallops. Abdomen, skin, extremities and neurology examination were normal.

Three sets of troponin I were negative and electrocardiogram showed normal sinus rhythm with no significant ST-T segment changes. Chest x-ray on admission showed multiple nodules with a shaggy and therefore inflammatory appearance mainly in the upper and mid lung fields bilaterally (Figure 1). D-dimers were elevated at 1190 nanograms/milliliter (normal range 0-399). Patient underwent a Computed Tomography Angiography of the chest which was negative for pulmonary embolus. Numerous bilateral pulmonary nodules with index largest left lung nodule sized 1.3×0.8 centimeter was reported along with a peri-carinal lymph node measuring 1.5×1.2 cm (Figure 1). Concern was raised for metastatic disease of the lung especially in view of smoking history of more than 20 pack years. On further detailed evaluation by a pulmonologist, it was revealed that he had recently visited a cave in Puerto Rico that was inhabited by bats with the floor covered with the bat guano. Patient apparently also had to remove that material from his shoes. This visit was approximately 3 weeks before this presentation. Patient's chest pain was not clearly pleuritic in nature and his nuclear stress test and two-dimensional transthoracic echocardiography were normal. *Histoplasma* antigen from blood and urine were positive. We did not order for antibody to *Histoplasma* antigen as it takes around two months to develop antibodies. Patient was treated with Itraconazole orally with a loading dose of 200 mg three times a day for three days fol-

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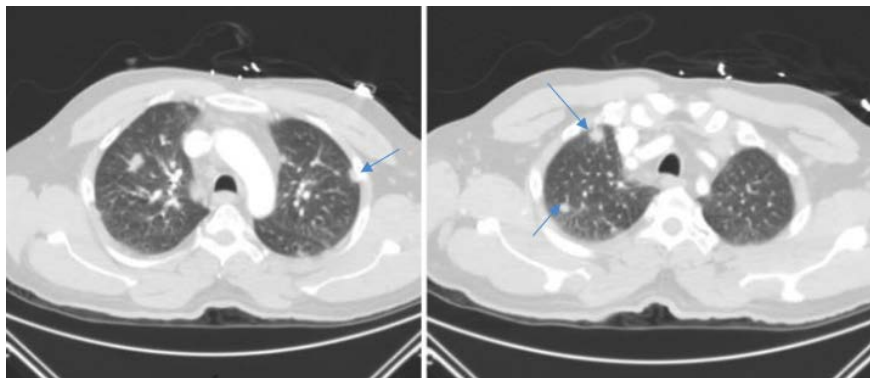
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lowed by 200 mg once daily for three months. Standard dosing recommendation was used. Therapeutic drug monitoring was not done. Patient reported significant improvement in his symptoms after the treatment.

### Discussion

Returning travelers from endemic areas require a high degree of clinical suspicion in case of development of new symptoms consistent with pulmonary histoplasmosis. The disease in itself has a very wide spectrum of presentation making clinical diagnosis equally challenging. There is a high likelihood of missed or delayed diagnosis, especially, in immunocompetent patients living in non-endemic areas. In those with an acute febrile lung illness, it is imperative to question the activities they were involved



**Figure 1. Computed tomography of the chest showing multiple bilateral pulmonary nodules (blue arrows) at different levels of cross-section.**

in and the places they visited during their stay. According to the Centers for Disease Control and Prevention, histoplasmosis is reportable in the following states and US territories: Arkansas, Delaware, Illinois, Indiana, Kentucky, Michigan, Minnesota, Nebraska, Pennsylvania, Puerto Rico, and Wisconsin. So, in an area like Pennsylvania, the diagnosis can be easily missed or delayed.<sup>2,4</sup> As it was observed in our case study, the initial plan was to move ahead with a lung biopsy or a Positron Emission Tomography scan, due to concern for malignancy because of the pulmonary nodules. A second-look and further detailed history regarding patient's travel and visit of specific sites helped to clinch the diagnosis. A very high index of clinical suspicion was thus necessary. It changed the management moving forward tremendously.

Various modalities of diagnosing histoplasmosis are available including stains for fungi, cultures, antigen detection, and serologic tests for *Histoplasma*-specific antibodies. Diagnosing histoplasmosis with methods that do not involve culturing the organism is still very accurate. As shown by Wheat *et al.*, the polysaccharide antigen of *Histoplasma* can be detected in bodily fluids.<sup>5,6</sup> Presence of the antigen in both the serum and the urine increases the diagnostic accuracy.<sup>5,6</sup>

There are many sporadic case reports that have shown the disease mimicking primary lung cancer, lymphoma, head and

neck cancer, and pulmonary metastases with patients undergoing unnecessary extensive invasive work-up. Delaying treatment for histoplasmosis has shown cases resulting in very severe disease manifestations.<sup>7,8</sup> If these cases go on to become chronic, there can be severe progressive loss of pulmonary function with mortality as high 30 percent.<sup>9</sup>

The treatment should be tailored to the clinical manifestations of the disease. Most cases are self-limiting, but, those with severe or persistent symptoms lasting more than four weeks, require treatment. Itraconazole is the initial drug of choice for mild to moderate disease while amphotericin B is reserved for moderately severe to severe infections.<sup>10,11</sup>

## Conclusions

Timely and accurate diagnosis of primary pulmonary histoplasmosis is imperative to avoid disastrous sequelae. Such cases can be easily missed in residents of non-endemic areas with intact immunity as primary clinical suspicion becomes low. Detailed history of recent exposure to *Histoplasma* antigen is important. Serum and urine antigen testing are simple, quick and accurate diagnostic modalities. Instituting prompt treatment helps to achieve complete recovery.

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