CASE REPORT

Histoplasmosis presenting with solitary pulmonary nodule: Two cases mimicking pulmonary metastases

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Abstract

Pulmonary histoplasmosis is a granulomatous disease, whose diagnosis is not always easy, as it may simulate metastatic lesions due to similar radiographic findings. We herein report two cases of histoplasmosis with solitary pulmonary nodule in asymptomatic patients with histories of cancer surgeries, whose diagnoses were confirmed by postoperative pathological examinations. Doctors must pay attention to risk factors for immunosuppression such as the histories of chemotherapy, radiotherapy, or malignancy, which may increase chances of developing histoplasmosis. Limited surgical intervention is the treatment of choice for these localized lesions.

Key words: Histoplasmosis, metastatic lesion, solitary pulmonary nodule

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Introduction

Histoplasmosis is a granulomatous disease, caused by the thermal dimorphic fungus *Histoplasma capsulatum*. It's rare in China, and only some sporadic cases have been reported. Most of the reported cases were from regions through which the Yangtze River flows.[1] Asymptomatic pulmonary histoplasmosis may mimic metastatic lesions due to the similar radiographic appearance. It is important not to confuse histoplasmosis with malignancy in order to prevent inappropriate treatment. We herein report two uncommon cases of asymptomatic solitary pulmonary nodule diagnosed preoperatively as lung metastases, which were confirmed as histoplasmoses by postoperative pathological examinations.

Case Reports

Case 1

A 50-year-old asymptomatic man was referred to our hospital because of a right pulmonary nodule, discovered on a follow-up chest radiogram. He had a history of abdominoperineal resection for rectal carcinoma in our hospital 1-year before, with the pathological examination revealing moderately differentiated tubular adenocarcinoma. He was given four courses of chemotherapy afterwards. He had lived for many years in an endemic region, and had never been outside China. On hospital admission, nothing abnormal was found on physical examination. The contrasted computed tomography (CT) scan showed a 2.0 cm × 1.9 cm irregular nodule in right lower lobe, without obvious enhancement after contrast injection [Figure 1]. No enlarged mediastinal or hilar lymphnode was found. Given the patient's history of tumor resection, the new-undiagnosed lesion in the right lower lobe was mainly suspected of rectal carcinoma metastasis. The patient refused to CT- undergo percutaneous guided lung biopsy. Thus, the thoracoscopic wedge resection of pulmonary nodule was performed. The intraoperative frozen sections showed a granulomatous disease, instead of the tumor. And final pathological testing of the specimen stained by Periodic acid–Schiff (PAS) revealed numerous uniform oval 1- to 5-μm PAS-stained organisms, morphologically consistent with *H. capsulatum* [Figure 2]. Serological tests and culture

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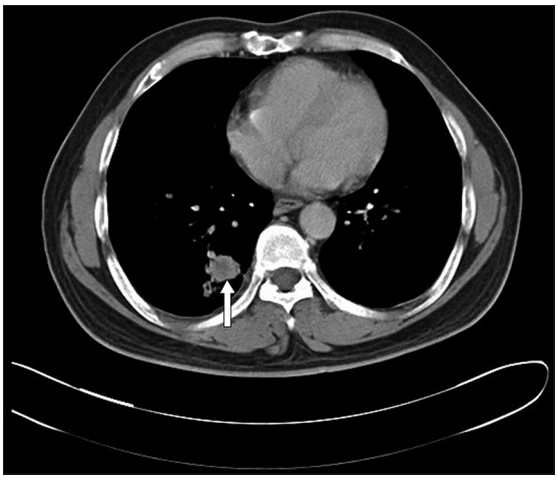

Figure 1: A computed tomography scan of the chest showing the irregular pulmonary nodule located in the right lower lobe (white arrow)

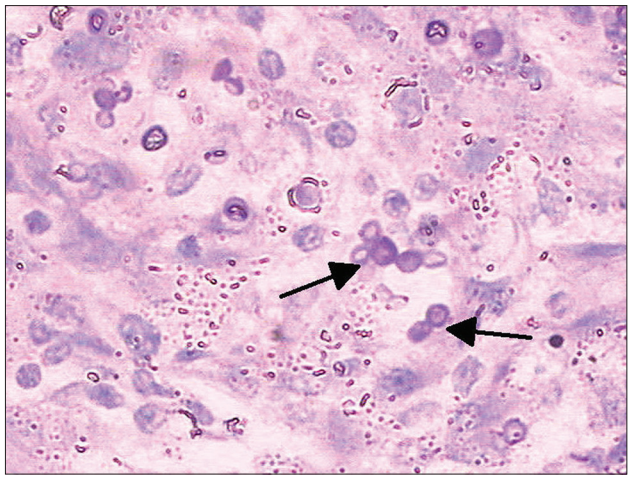

Figure 2: Special stains for fungi (Periodic acid–Schiff [PAS]) revealed numerous uniform oval PAS-stained organisms (black arrow), morphologically consistent with *Histoplasma capsulatum* (PAS, original ×400)

were negative. No specific antifungal therapy was instituted. The postoperative course was uneventful, and the patient was in good clinical condition at 5 years of follow-up.

Case 2

A 53-year-old woman was referred for investigation of asymptomatic left solitary pulmonary nodule, discovered on a periodic chest CT examination. She had a medical history of esophageal carcinoma treated with esophagectomy and adjuvant radiotherapy 2 years before. She came from a nonendemic region, but had traveled to endemic regions 5 years before. The physical examination and routine preoperative laboratory testing were unremarkable. On further investigation, the contrasted CT imaging confirmed a 1.5 cm × 0.8 cm solitary nodule located in left upper lobe, without obvious enhancement. There was no lymphadenopathy. The patient refused the percutaneous CT-guided lung biopsy, and the thoracoscopic wedge resection was performed. The final pathology result demonstrated the diagnosis of histoplasmosis by finding the organism morphologically consistent with *H. capsulatum*. Serological tests and culture were negative. The patient enjoyed a complete uneventful recovery without any treatment of antifungal agent. Three years after discharge, the patient was still well.

Discussion

Our two cases demonstrate a number of difficulties in the diagnosis of histoplasmosis, which include China being a low-prevalence area, the patients having no clear exposure, and the similarity on CT imaging to lung metastases.

Histoplasmosis is endemic in the Americas and parts of Asia and Africa,[2] however, pulmonary histoplasmosis is rare in China and only some sporadic cases have been reported.[3] Pan *et al*. collected epidemiological data of histoplasmosis in China, and found most cases were from regions through which the Yangtze River flows. In our two cases, one came from an endemic region, and the other had been to those areas. The organisms are generally fertilized in soil contaminated by birds and bats feces, and our two patients denied such exposure. Normally, this infection is caused by inhalation of spores. Clinical manifestations can range from asymptomatic infection, with an incidental finding of histoplasmoma on chest CT, to rapidly progressive pulmonary disease and respiratory failure.[4] Progressive disseminated histoplasmosis often occurs in immunocompromised patients, due to human immunodeficiency virus infection, carcinoma, immunosuppressive therapy, etc.[5] The two patients in our report had the medical history consisting of risk factors for immunosuppression such as chemotherapy, radiotherapy and malignancy, which could increase chances of developing histoplasmosis.

The solitary pulmonary nodule or histoplasmoma is a circumscribed lesion around a prior active histoplasmosis and mostly asymptomatic.[6] Sometimes characteristic calcification can be detected in the center of a nodule or in concentric rings and is generally diagnostic.[7] However, calcification wasn't discovered in our two cases, failing to help differentiate from metastatic lesions.

The diagnosis of histoplasmosis is depended on a battery of tests including culture, antigen detection, serological test, histopathology, etc. For asymptomatic histoplasmosis presenting with pulmonary nodules, antigen detections and serological tests are relatively less sensitive,[2] thus transthoracic fine-needle biopsies or surgical removals are often performed to make definitive diagnoses. In our two cases, serological tests and culture were negative. Our two patients both chose surgical resection of pulmonary lesion directly without preoperative lung biopsies. The specimens

are required to be stained with special stains such as Grocott's methenamine silver stains or PAS stains, since routine hematoxylin and eosin stains fail to recognize the organisms microscopically.[5]

Normally, metastatic lesion is first considered about a solitary pulmonary nodule in a patient with a history of cancer surgery. In our cases, thoracic surgical removals and special stains were performed to make the definitive diagnoses. Antifungal treatment is not recommended for histoplasmosis with solitary pulmonary nodule in an asymptomatic patient,[7] and we didn't offer the two patients any antifungal drug. Based on our experience, limited surgical removal is the treatment of choice for these localized lesions. We suggest physicians and thoracic surgeons consider pulmonary histoplamosis in the differential diagnosis of a solitary nodule, and pay attention to some factors including histories of chemotherapy, radiotherapy, or malignancy, which may correlate with immunosuppression and ultimately lead to the occurrence of fungal infections such as histoplasmosis.

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