Case report

Rare case of pulmonary histoplasmosis complicated with bronchocentric granulomatosis in a non endemic area

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A B S T R A C T

Background: Pulmonary histoplasmosis is a fungal infection caused by histoplasma capsulatum, rarely diagnosed in non endemic areas and/or immunocompromised patients. Complication of pulmonary histoplasmosis with bronchocentric granulomatosis is extremely rare.

Case Report: A 48-year-old man with prolonged fever and nausea was admitted to our hospital. Clinical examination revealed pathological auscultatory sounds to the left lung. Computed tomography was performed and revealed a large solid mass of the left upper lobe, limited pleural and pericardial effusion and calcified lymphadenopathy of mediastinum. A computed tomography guided core biopsy of the lung lesion was performed and three samples were obtained. Culture and polymerase chain reaction (PCR) revealed Histoplasma capsulatum. Histological findings were compatible with bronchocentric granulomatosis. Extended laboratory investigation excluded immunosuppression. Our patient although immunocompetent was diagnosed with chronic pulmonary histoplasmosis complicated with bronchocentric granulomatosis and treatment with antifungal medication and methylprednisolone started.

Conclusion: Description of a rare case of chronic pulmonary histoplasmosis in a non endemic area like Greece, with atypical radiological findings, complicated with bronchocentric granulomatosis.

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1. Introduction

Histoplasmosis is caused by a dimorphic fungus which grows in soil fertilized by bird and bat excreta, Histoplasma capsulatum. It can be found in temperate climates worldwide, but it is endemic in the United States, primarily seen in the Ohio and Mississippi River Valleys. While the central United States seemed to have the greatest prevalence of Histoplasmosis capsulatum Brazil, Argentina, India, West Africa and South Africa have all reported small case series. Additionally, sporadic cases have been reported from Central and South America, Oceania, northern sub-Saharan Africa, and Europe (Italy, Po River valley) [1]. To our knowledge, none case has ever been reported in Greece since now. Clinical presentations include asymptomatic pulmonary histoplasmosis, acute diffuse pulmonary histoplasmosis, chronic pulmonary histoplasmosis, disseminated histoplasmosis, endobronchial histoplasmosis, fibrosing mediastinitis, mediastinal granulomas and lung nodules.

Bronchocentric granulomatosis (BG) was first described by Liebow in 1973. This entity represents a common pathological result of a heterogeneous group of diseases and does not represent a single clearly defined clinical syndrome [2,3]. Exclusive peribronchial localization of granulomas can occur in infections and may cause confusion with bronchocentric granulomatosis. Diagnosis is only established with biopsy.

2. Case report

A 48-year-old man was admitted to our hospital due to prolonged fever and nausea. Physical examination indicated the following: Body temperature, 38.5 °C; heart rate, 109 beats/min; blood pressure, 140/80 mmHg and lack of auscultatory sounds in the upper lobe of the left lung. Laboratory examination performed revealed: normal white blood cell count, 8.5 × 10^9/L, an elevated C reactive protein, 7mg/dl (0.01—0.8mg/dl) and negative tuberculosis antibody test. Computed tomography (CT) showed a large solid mass of the left upper lobe, limited pleural and pericardial effusion and calcified lymphadenopathy of mediastinum, Fig. 1. The patient underwent a CT-guided core biopsy of the lung lesion and three
samples were obtained. Specimens were sent for culture, histo-
logical and polymerase chain reaction (PCR) assay. The possibility of
malignancy was excluded, at the same time culture and PCR were
positive for Histoplasma capsulatum and histological findings were
compatible with BG, Fig. 2. Due to the positive culture we inves-
tigated patient’s traveling history and he referred traveling in United
States many years ago just for a few days.

Complete laboratory investigation excluded any kind of immu-
nosuppression in our patient.

The patient was diagnosed as a chronic pulmonary histoplas-
mosis case with bronchogenic granulomatosis. Initially he was
treated with amphotericin B and itraconazole. One month later he
revealed complete clinical recovery, improvement of the inflam-
matory index and decrease of solid mass size, nevertheless, pleural
and pericardial effusions increased. Having in mind the histological
diagnosis of bronchocentric granulomatosis and the aggravation of
effusions, corticosteroids were added to the medication. Our pa-
tient was discharged two weeks later, in a good clinical status with
itraconazole and methylprednisolone.

CT imaging follow up one month later demonstrated a great
decrease of the left lobe mass size. No pleural and pericardial
effusion was reported Fig. 3.

3. Discussion

Histoplasmosis is not an endemic illness in Greece. The most
common cause for histoplasmosis in non-endemic areas is prior
exposure to endemic areas, through travel or residence. Indeed, our
patient had visited America many years ago, but he never referred
any clinical signs or symptoms of histoplasmosis. By 2015, only 76
cases had been reported in the literature. Among these patients, 52
cases were found to present increased risk factors or primary dis-
eases. The majority of healthy persons infected with H. capsulatum
develop subclinical infection or a self-limiting respiratory disease.
Severe or disseminated forms of histoplasmosis usually occur in
immunocompromised individuals, particularly in HIV patients
[4,5]. In our patient immunosuppression was excluded after
extended laboratory investigation however he suffered from severe
chronic pulmonary form of the disease. Imaging manifestations of
pulmonary histoplasmosis vary depending on the disease chro-
nicity. At the acute stage it may be diagnosed as airspace shadowing
with consolidation involving multiple lung segments or lobes
similar to bacterial pneumonia, well-defined nodules with central
calcifications while pleural effusions are possible but uncommon,
[6]. Chronic pulmonary histoplasmosis is characterized in 90% by
cavitations, predominantly in the upper lobes while hilar lymph-
adenopathy is rare. Fibrosing mediastinitis follows acute pulmo-

Fig. 1. a-b. CT image revealing large solid mass of the left upper lobe, limited pleural
and pericardial effusion and calcified lymphadenopathy of mediastinum.

Fig. 2. Lung biopsy histopathological findings compatible with Bronchocentric gran-
ulomatosis. Necrotizing granulomas with bronchocentric localization.
other at 37°C. An "aud's dextrose agar, one incubated at room temperature and the patient culture for fungi was performed on two tubes of Sabourandy when the diagnosis is ambiguous and undetermined [7]. In our attempt to obtain histopathologic evidence and enhance the diagnostic accuracy, the gold standards for diagnosing pulmonary histoplasmosis. CT-guided percutaneous lung biopsy is recommended to diagnose BG. Although culture was positive, diagnosis in our case was confirmed in only 3 days with a positive PCR of the tissue sample.

Tissue biopsy results may reveal the presence of yeast forms in tissue through hematoxylin and eosin staining, Best visualization of H. capsulatum is obtained with methenamine silver or periodic acid-Schiff stains. Using the Grocott-Gomori methenamine-silver procedure, yeast may be detected in areas of caseation necrosis from histoplasmosomas and calcified lymph nodes. Yeast forms in circulating neutrophils and monocytes are rarely detected using Wright-Giemsa staining. Yeasts are typically found within macrophages, most biopsies do not reveal organisms. In our patient hematoxylin staining was performed and none yeast form was observed.

Bronchocentric granulomatosis represents a common pathological result of a heterogeneous group of diseases. It is characterized by necrotizing granulomatous inflammation of bronchial and bronchiolar epithelium with chronic inflammatory changes in the surrounding lung parenchyma. Patients with BG are divided in two groups, the first including the majority of patients, are individuals with asthma and allergic bronchopulmonary aspergillosis and the second the non-asthmatic patients which are usually older and tissue eosinophilia is not a predominant finding. It is though that these cases are idiopathic, although associations with mycobacterial and fungal infection, rheumatologic disease, angiitis, chronic granulomatosis disease and other conditions have been reported [3]. Such a case is the patient we describe as the histological findings were compatible with BG and no medical history of asthma was reported [8]. BG in our case was considered to be an immunologic reaction against endobronchial fungal antigens. According to the literature he was treated with short-term corticosteroids and had a favourable overall prognosis.

We described a rare case of histoplasmosis as it is reported in a non endemic area, with a severe clinical presentation of chronic pulmonary histoplasmosis although our patient had no immunosuppression. Furthermore imaging manifestations were atypical for the diagnosis and histopathological findings revealed complication with bronchocentric granulomatosis, entity rare in non asthmatic patients.

**Conflict-of-interest statement**

All authors declare any conflict interest.

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