Pulmonary Cryptococcoma Masquerading as Lung Cancer

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Abstract

We report a case of pulmonary cryptococcoma, in an adult with recently detected diabetes, mimicking as lung cancer. A 45-year-old gentleman with past history of pulmonary tuberculosis presented with fever, cough with expectoration, pleuritic chest pain and hemoptysis. Chest radiograph and computed tomography revealed right lower lobe mass which significantly enhanced on contrast administration. Ultrasound guided biopsy was done which on histopathological examination showed non-necrotizing granulomas with narrow-based budding yeast cells suggestive of cryptococcosis. Detailed work-up for dissemination of infection was negative. A dramatic response to anti-fungal treatment was observed and the patient is doing fine on follow-up.

Introduction

Cryptococcal infections are usually seen in immunocompromised individuals, especially HIV, and is uncommonly reported in immunocompetent individuals or individuals with mild compromise of the immune system.¹ In the latter group, cryptococcosis involving the respiratory system are relatively uncommon and such patients do not often present with much symptoms. When symptomatic they usually present with fever, cough with expectoration and hemoptysis. Chest imaging commonly shows single or multiple pulmonary parenchymal nodules.

Case and Discussion

A 45-year-old gentleman, recently detected diabetic, presented to us with two weeks history of cough, pleuritic chest pain and high grade fever. He also had history of streaky hemoptysis. The cough was associated with scanty mucoid expectoration, no diurnal or postural variation and without any significant aggravating or relieving factors. He had past history of pulmonary tuberculosis at age of 18 years which was treated adequately and was declared cured following treatment. There was no history suggestive of connective tissue disease, exposure to pets, dust or working in the farm, no history of weight loss, anorexia or night sweats.

At admission, he was febrile with temperature of 100°F. His blood pressure was 110/70 mmHg with pulse rate of 110/min, the respiratory rate was 24/min. There was no pallor, icterus, clubbing, cyanosis, lymphadenopathy, skin rash or pedal edema. The ocular and fundus examination were normal. The examination of upper respiratory tract, oral cavity, tonsils, posterior pharyngeal wall were also unremarkable. The examination of respiratory system revealed reduced breath sounds in right infra-axillary area. The examination of cardiovascular, abdominal and central nervous system revealed no abnormality.

Laboratory investigations revealed haemoglobin – 12.6 g/dl, total leucocyte count – 14.6 x 10⁹/mm³, platelet count – 490 x 10⁹/mm³ and the erythrocyte sedimentation rate – 40 mm at the end of 1st hour. His chest X-ray showed homogenous mass lesion in the right lower lobe (Figure 1) and the CECT chest revealed the lower lobe mass lesion to be enhancing on contrast administration (Figure 2 a, b). The medistinal window showed enlarged lymph nodes.

Fig. 1: X-ray chest showing homogenous mass lesion in the right lower lobe

Fig. 2: CECT chest showing right lower lobe mass lesion enhancing on contrast

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lymph nodes (in the upper paratracheal location) which were non-calcified. As per the imaging findings, malignancy of the lung seemed the most probable diagnosis. Since the patient had an acute history of fever, some other differential diagnoses were also considered - these, along with other causes of ‘mass’ in the pulmonary parenchyma are enumerated in Table 1.

He underwent an ultrasound guided biopsy from corresponding mass lesion for histological examination. Biopsy showed non necrotizing granulomatous inflammation with giant cells and narrow based budding yeast cells suggestive of Cryptococcus (Figures 3 a-d).

His fasting blood sugar was 140 mg/dl (repeated twice) and HbA1C was 6%. Retroviral serology was negative and CD4 count was within normal limits. Detailed evaluation was done to look for evidence of dissemination. Cerebrospinal fluid examination was normal and CSF India ink stain was negative. Serum and CSF cryptococcal antigen were also negative. Brain imaging with MRI was also normal. After ruling-out possibility of dissemination, diagnosis of isolated pulmonary cryptococcoma was made.

He was started on parenteral amphotericin B (conventional amphotericin B in the dose of 0.7 mg/kg/day) for 6 weeks followed by oral fluconazole for 12 months (initially 400 mg daily for 8 weeks followed by 200 mg daily for 10 months). Dietary restrictions (followed later by daily aerobic exercises) along with metformin were suggested to control his hyperglycaemic state.

His had significant symptomatic improvement during first month of treatment and remained asymptomatic afterwards. At the end of 1 year, the chest X-ray showed significant resolution (Figure 4). Repeat glycated haemoglobin (after 6, 12 months) was also within normal limits.

Cryptococcus neoformans is a round to oval yeast surrounded by a polysaccharide capsule. Two pathogenic variants exist: C. neoformans var. neoformans and C. neoformans var. gatti. C. neoformans usually affects immunocompromised individuals while C. gatti primarily affects immunocompetent persons. Individuals with defect in T-cell mediated immunity are especially prone to develop infection with cryptococcus. Port of entry for cryptococcus is respiratory tract. Spores can remain dormant or undergo dissemination depending on individual’s immune status. After respiratory tract central nervous system is second most commonly affected site with meningo-encephalitis being the most common manifestation. HIV seems to be the most common predisposing risk factor for cryptococcosis while the less common causes include chronic steroid use, transplant recipients, malignancy, uncontrolled diabetes.

### Table 1: Causes of mass in the pulmonary parenchyma

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Features</th>
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<tbody>
<tr>
<td>Lung carcinoma</td>
<td>Most common D/D. Can be central/peripheral.</td>
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<tr>
<td>Metastatic carcinoma</td>
<td>Peripheral and basal predominance common</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Usually has air bronchograms</td>
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<tr>
<td>Organising pneumonia</td>
<td>May show ‘reverse halo’ sign</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td>Associated cavitary lesions often seen</td>
</tr>
<tr>
<td>Churg Strauss syndrome</td>
<td>May show cavitary lesions</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Smooth or lobulated mass seen, may have cavitations</td>
</tr>
<tr>
<td>Infections</td>
<td>Atypical manifestations of tuberculosis, fungal infections include lung “mass”</td>
</tr>
<tr>
<td>Pulmonary pseudotumor</td>
<td>Lenticular shaped lesion due to pleural fluid localized in fissures</td>
</tr>
<tr>
<td>Rounded atelectasis</td>
<td>May have tuft of distorted vessels leading to the lesion – the comet tail sign; associated with asbestosis</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Upper lobe and peribronchovascular predominance often seen</td>
</tr>
<tr>
<td>Silicosis/coal worker's pneumonia</td>
<td>Upper lobar predominance seen and is more common in advanced disease</td>
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mellitus, sarcoidosis, liver failure etc. Cryptococcomas refers to mass like lesions usually caused by granulomatous inflammation in cases of cryptococcosis; which may be seen in brain, lungs and rarely in other areas.

Primary pulmonary cryptococcosis is cryptococcal infection limited to lungs. It often is difficult to diagnose as symptoms and radiological findings are usually non-specific. Serological tests are also less sensitive in detecting isolated pulmonary involvement. Presentation of pulmonary cryptococcosis is varied ranging from asymptomatic pulmonary nodule to severe diffuse bilateral disease causing acute respiratory distress syndrome. Immunocompromised individuals have higher chance of presenting with severe and disseminated disease. Immunocompetent individuals are either asymptomatic or present with mild symptoms such as fever, cough, expectoration and pleural symptoms. Physical examination ranges from completely normal to features of consolidation or pleural effusion. There are no specific radiological features of pulmonary cryptococcosis. The most common finding is of nodules in the lung parenchyma. Other findings include ground glassing, consolidation and miliary disease. Cavitation, lymphadenopathy or pleural effusion can also be seen.

Diagnosis of pulmonary cryptococcosis is based on demonstration of cryptococcal yeast by smear or culture in sputum, bronchial lavage or rarely pleural fluid. It is important to note that serum cryptococcal antigen, though highly specific and sensitive to pick up CNS and disseminated cryptococcosis, is often negative in cases of isolated pulmonary involvement. Demonstration of cryptococcal yeast in biopsy specimens is another way of confirming diagnosis. In tissue, it can be easily identified by presence of clear zone indicating capsulated nature. Staining with specific fungal stain, like mucicarmine, is indicated for confirmation.

In immunocompetent individuals with pulmonary cryptococcosis lumbar puncture is indicated to rule out CNS involvement especially in cases with severe manifestations. In cases with asymptomatic pulmonary nodule and negative or low serum cryptococcal antigen (<1:512) lumbar puncture can be avoided. However in immunocompromised individuals, CSF examination is imperative to rule out spread of the disease.

Goal of treatment in pulmonary cryptococcosis is cure of infection and prevention of dissemination. In a patient with no immunologic defects, pulmonary cryptococcosis may resolve spontaneously without antifungal therapy. But in minority of cases there are chances of rapid progression and systemic dissemination. In isolated pulmonary disease, single small cryptococcomas can be treated with fluconazole alone. For large/multiple/severe pulmonary cryptococcomas the treatment is similar to that instituted in CNS infections - Amphotericin B with flucytosine for 4-6 weeks followed by fluconazole 400 mg orally daily for 8 weeks and then 200 mg daily for 6-12 months. Severe pulmonary cryptococcosis include presence of diffuse bilateral lung infiltrates, serum cryptococcal antigen levels >1:512 or involvement of two or more non-contagious sites. Other azoles like itraconazole, voriconazole or posaconazole are also effective but sufficient data is not yet available regarding these drugs. There is no role of monitoring serum cryptococcal antigen to determine treatment response.

References