Photo Quiz

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A 15-Year-Old Healthy Girl with Streaky Hemoptysis and Cavitary Lung Lesion

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WHAT IS YOUR DIAGNOSIS?

A 15-year-old girl, otherwise healthy, presented with low-grade fever, cough, sputum with two episodes of streaky hemoptysis, and left side chest wall pain for a couple of months. Vital signs on admission included a respiratory rate of 18 breaths per minute, a temperature of 37°C, a heart rate of 110 beats per minute, and a blood pressure of 95/65 mmHg. Her physical exam was unremarkable. A chest X-ray showed suspected cavitary lesions in the left lung. A chest computed tomography (CT) scan showed bilateral nodular infiltrations (Figure 1A & 1B) along with cavitary lesions, especially in the left upper and left lower lobes (Figure 1C & 1D).

In primary laboratory studies, the hemoglobin was 14 g/dL, the white blood cell count was 7200/µL, the platelet count was 165000/µL, and the erythrocyte sedimentation rate was 13 mm/hr. Liver and renal function tests and other biochemistry were normal. No microorganism was identified by blood and urine culture. The Inflammatory markers, such as Antinuclear Antibody (ANA), Cytoplasmic and Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (C-ANCA & P-ANCA), Anti-Cyclic Citrullinated Peptide (Anti-CCP), and Rheumatoid Factor (RF), were all negative.

Study of sputum and bronchoalveolar lavage for acid-fast bacilli (AFB), bacteria, and fungi was negative. Thus, CT-guided biopsy from the cavitary lesion was performed (Figure 2).

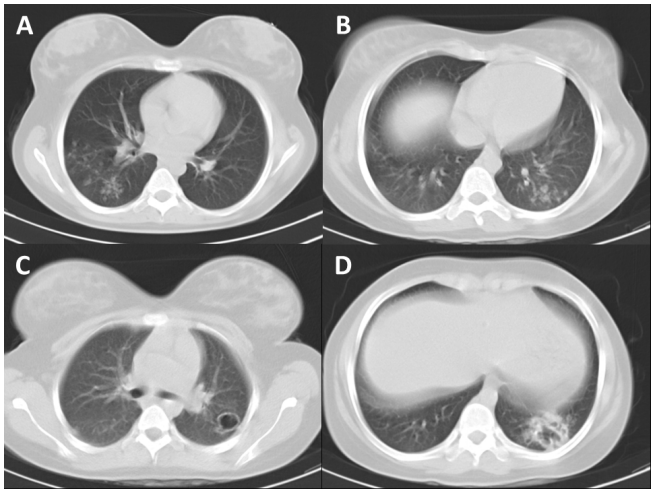

Figure 1. Patient's lung CT-scan

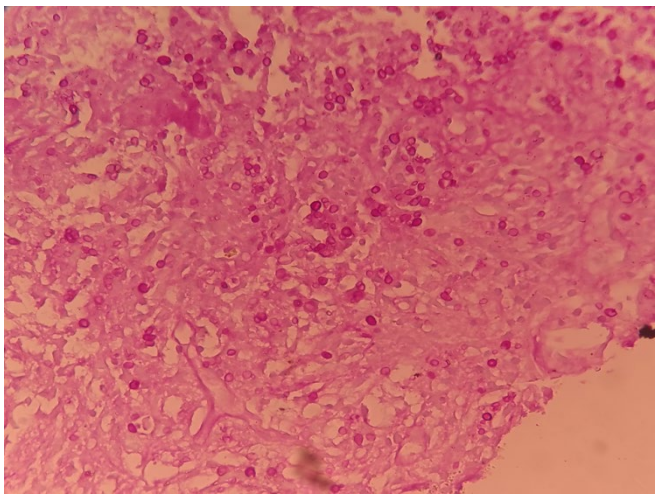

Figure 2. Pathological study of lung tissue

Answer

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Pulmonary Cryptococcosis

Biopsy specimen revealed necrotizing granulomatous inflammation; Ziehl Neelsen staining was negative for AFB, but Grocott methenamine silver (GMS) and Periodic Acid-Schiff (PAS) staining discovered numerous free or intracellular spores, morphologically compatible with Cryptococcus species (Figures 2 &3). Also, cryptococcal antigen (CrAg) was detected in serum. Diagnosis of pulmonary cryptococcosis was made. To rule out concurrent central nervous system (CNS) infection, with a normal brain CT scan, a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis showed white blood cell counts of 10/mm^3 (mononuclear), protein: 9 mg/dl, glucose: 53 mg/dl (43% compared to plasma level), and CrAg was found, but the Indian ink mount was negative. Cultures of lu.ng tissue and CSF were negative for Cryptococcus.

To rule out underlying disease, an immunologic workup was conducted. An enzyme-linked immunosorbent assay (ELISA) test was negative for human immunodeficiency virus. The immunoglobulin profile was as follow: IgG: 12.5 g/L (normal range: 6.58–18.37 g/L), IgA: 1.7 g/L (normal range: 0.71–3.6 g/L), IgM: 1.8 g/L (normal range: 0.4–2.63 g/L), IgE: 45.7 IU/mL (normal range: <13 IU/mL) which has indicated an elevation in IgE level. The Nitro Blue Tetrazolium (NBT) test and flow cytometric immunophenotyping of peripheral blood lymphocyte subsets were normal.

Cryptococcosis is an opportunistic infection that commonly occurs among immunocompromised patients. This organism can be found in soil and bird droppings, particularly those of pigeons (1) and is typically transmitted through the respiratory tract by inhaling the basidiospores (2). Regarding our case, after thorough history taking, we discovered that the patient's father hunts birds as a hobby, and she assisted him in plucking their feathers. Therefore, she probably contracted cryptococcus through contact with hunted birds.

The main risk factors are people with acquired immunodeficiency syndrome (AIDS) and patients who are under treatment with immunosuppressive medications (3). On the other hand, up to 35% of pulmonary cases of cryptococcosis occur in immunocompetent patients (4), among them, the most common radiographic findings are single or multiple nodules (5), in comparison to immunocompromised cases with cavitary lesions (6). The proportion of patients without underlying disease is higher among cases due to *Cryptococcus gattii* (7).

Fisher and colleagues reviewed available reports about immunocompetent patients with pulmonary cryptococcosis for 55 years (8). Compatible with our patient, they found on the basis of case reports that cultures are often negative in the presence of histopathologic features compatible with pulmonary cryptococcosis. In the majority of patients, symptoms of lung disease resolve without any treatment, but resolution of all radiographic findings takes a long period, which may be accelerated with specific antifungal therapy (8). Immunocompetent patients typically show solitary, well-defined peripheral nodules, often mistaken for malignancy. In contrast, immunocompromised individuals exhibit a wider range of findings, including multiple nodules, cavitation, miliary patterns, and bronchopneumonia, with features like the halo sign and air bronchogram being more common (9).

Pulmonary manifestations can present either as isolated features or concomitantly with central nervous system (CNS) involvement, most notably meningoencephalitis and disseminated systemic infection (2). Serum cryptococcal antigen (CrAg) screening is a well-established measure, enabling early identification of cryptococcal antigenemia (10). Even in asymptomatic patients, high serum CrAg titers are an independent predictor of CNS involvement (11). Given the risk of CNS involvement,

particularly in cases of disseminated disease, lumbar puncture (LP) must be routinely performed in all patients diagnosed with pulmonary cryptococcosis, regardless of the presence or absence of neurological symptoms (2).

For cryptococcal meningitis, the standard treatment is combination of liposomal amphotericin B 3-4 mg/daily and flucytosine 25 mg/kg four times a day for two weeks (induction phase); it is continued by fluconazole 400-800 mg/day for 8 weeks (consolidation phase) and 200 mg/day to complete 12 months of treatment (maintenance phase). If flucytosine is not available, it can be replaced with fluconazole 800 to 1200 mg/day during the induction phase (12). The patient was treated with a combination of Liposomal Amphotericin B (3 mg /kg/day) and fluconazole 800 mg/d for two weeks, followed by oral fluconazole 400 mg/d for 8 weeks and then 200 mg/d to complete 12 months of treatment. Upon follow-up, there was clinical improvement, with nearly complete regression of the pulmonary imaging (Figure 4).

Pulmonary cryptococcosis should be considered in a patient with pulmonary nodules and/or cavitary lesions, even in the setting of normal immune status.

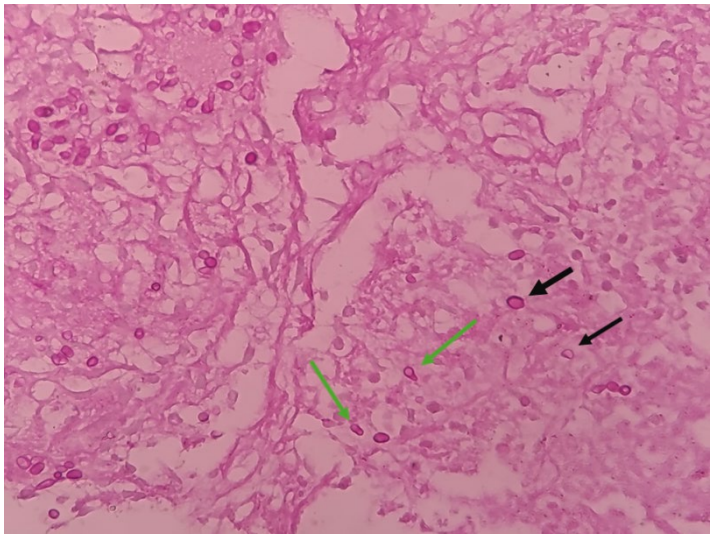

Figure 3. Lung tissue, Periodic Acid-Schiff (PAS) staining; Variably sized round to oval encapsulated yeasts with thin cell walls (black arrows), somewhat narrow-based budding (green arrows)

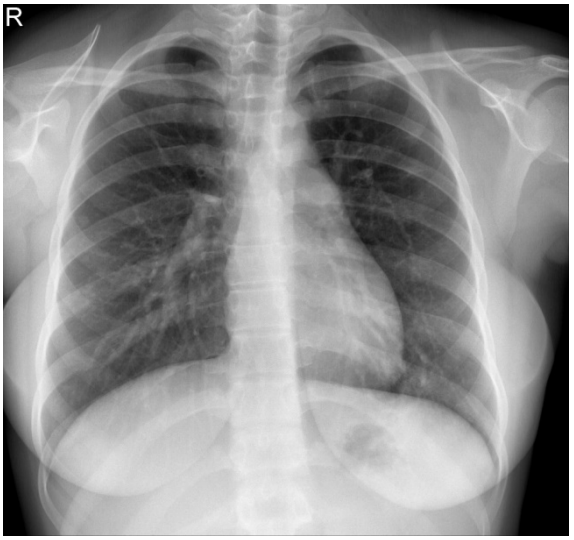

Figure 4. Follow-up chest X-ray after one year of treatment

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