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Massive mediastinal cryptococcosis in a young immunocompetent patient

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Abstract

Pulmonary cryptococcosis with lymph node involvement is relatively rare in immunocompetent patients. We report a case of pulmonary cryptococcosis with massive mediastinal lymphadenopathy in an immunocompetent young patient. In this report, a 17-year-old boy presented with high-grade fever and persistent cough. Chest X-ray and computed tomography showed massive mediastinal lymphadenopathy. Endobronchial ultrasound-guided transbronchial needle aspiration revealed histological evidence of cryptococcal lymphadenitis. He was treated with liposomal amphotericin B plus flucytosine followed by fluconazole and recovered.

Introduction

Pulmonary cryptococcosis is generally more severe in those who are immunocompromised and is often accompanied by disseminated infection, including central nervous system (CNS) disease [1]. Although the disease occurs in both immunocompetent and immunocompromised hosts, the occurrence of massive cryptococcal lymphadenopathy is rare [2]. We report a case of massive cryptococcal lymphadenopathy in a young immunocompetent patient.

Case Report

A 17-year-old otherwise healthy boy was admitted to a local hospital with cough for 1 month and high-grade fever for 1 week. He was subsequently referred to our institution on the suspicion of mediastinal tumor.

The patient had not been exposed to pigeons. He had no habit of smoking or consuming alcohol. His body temperature was 39.4°C. He looked ill and his right supraclavicular lymph node was slightly palpable.

Blood examination findings revealed a white blood cell count of 12,900 cells/mm^3 and a C-reactive protein level of 20.32 mg/dL (Table 1). Blood culture showed no organism growth.

Chest X-ray and computed tomography (CT) (Fig. 1A–C) showed swollen mediastinal lymph nodes compressing the trachea and an area of consolidation with cavitation in the right upper lobe.

Differential diagnosis included mediastinal tumor (e.g. lymphoma), tuberculosis, and fungal infection at that point. Conventional bronchoscopy and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) were performed for diagnosis. Paratracheal and subcarinal lymph nodes were punctured and bronchoscopic findings revealed

Table 1. Results of blood tests

Complete blood count		Immunological and serological test	
WBC	12,900/mm^3	CRP	20.32 mg/dL
Seg.	78%	IgG	1651 mg/dL
Eos.	4%	IgA	476 mg/dL
Mono.	7%	IgM	107 mg/dL
Lym.	7%	sIL-2R	1410 U/mL
CD4	31%	HIV antibody	Negative
RBC	433 × 10^4/mm^3	HTLV-1 antibody	Negative
Hb	12.9 g/dL	Cryptococcal antigen	Negative
Plt	52 × 10^4/mm^3	Anti-IFN γ antibodies	Negative
Blood chemistry		Anti-GM-CSF autoantibodies	Negative
TP	6.8 g/dL	Endocrinological test	
Alb	2.4 g/dL	βHCG	<1.2 IU/L
GOT	41 IU/	Tumor marker	
GPT	77 IU/L	CEA	1.7 ng/mL
LDH	253 IU/L	SCC	0.7 ng/mL
ALP	590 IU/L	ProGRP	16.4 pg/mL
T.bil	0.4 mg/dL	AFP	<1 ng/mL
Na	139 mEq/L		
K	4.8 mEq/L		
Cl	102 mEq/L		
Ca	9 mg/dL		
BUN	5 mg/dL		
Cre	0.59 mg/dL		
ACE	8.8 IU/L		
Glu	97 mg/dL		

ACE, angiotensin-converting enzyme; AFP, alpha fetoprotein; Alb, albumin; ALP, alkaline phosphatase; βHCG, beta-human chorionic gonadotropin; BUN, blood urea nitrogen; Ca, calcium; CEA, carcinoembryonic antigen; Cl, chlorine; Cre, creatinine; CRP, C-reactive protein; GM-CSF, granulocyte-macrophage colony stimulating factor; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvic transaminase; Glu, glucose; Hb, hemoglobin; HIV, human immunodeficiency virus; HTLV-1, human T-cell leukemia virus type 1; IFN γ, interferon gamma; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; K, potassium; LDH, lactate dehydrogenase; Na; sodium; Plt, platelet; ProGRP, pro-gastrin-releasing peptide; RBC, red blood cell count; SCC, squamous cell carcinoma antigen; sIL-2R, soluble interleukin-2 receptor; T.bil, total bilirubin; TP, total protein; WBC, white blood cell count.

constriction of the tracheal lumen on its right-anterior aspect. The histological findings showed inflammation with granulomas and many yeast-like organisms. These organisms were positive for the Grocott stains (Fig. 1D) and were also observed in the fluid obtained through transtracheal aspiration. These were identified as *Cryptococcus neoformans* var. *grubii* by culture and gene analysis.

The result of serum cryptococcal antigen test was negative. A lumbar puncture was performed, and a cryptococcal antigen test and culture of cerebrospinal fluid (CSF) were also negative. The patient tested negative for HIV. Total immunoglobulin levels and cluster of differentiation 4 (CD4) cell counts were also normal.

The patient received 4 weeks of antifungal therapy with intravenous liposomal amphotericin B and 2 weeks of oral flucytosine followed by oral fluconazole. His symptoms such as fever and cough improved. The follow-up chest CT 3 months later showed a significant reduction in consolidation in the right upper lobe and mediastinal lymphadenopathy (Fig. 1E and F).

Discussion

Cryptococcal infection induced by *C. neoformans* usually results from inhalation of fungal spores predominantly found in soil contaminated with pigeon excreta and may be confined to the lungs or disseminated systemically. *C. neoformans* var. *grubii* has worldwide distribution, whereas *C. neoformans* var. *neoformans* commonly causes cryptococcosis in certain European countries. *Cryptococcus gattii*, which is a recognized cause of cryptococcosis in tropical and subtropical regions, has more recently emerged in Vancouver Island, Canada [2].

Radiologically, solitary, or multiple pulmonary nodules are common in immunocompetent patients, but lymph node involvement is rare in pulmonary cryptococcal infection. Lymphadenopathy and pulmonary parenchymal infiltrates are the dominant radiographic manifestations in immunocompromised hosts. Massive mediastinal lymphadenopathy, as we reported, is very rare in immunocompetent hosts, although some cases have been reported [2].

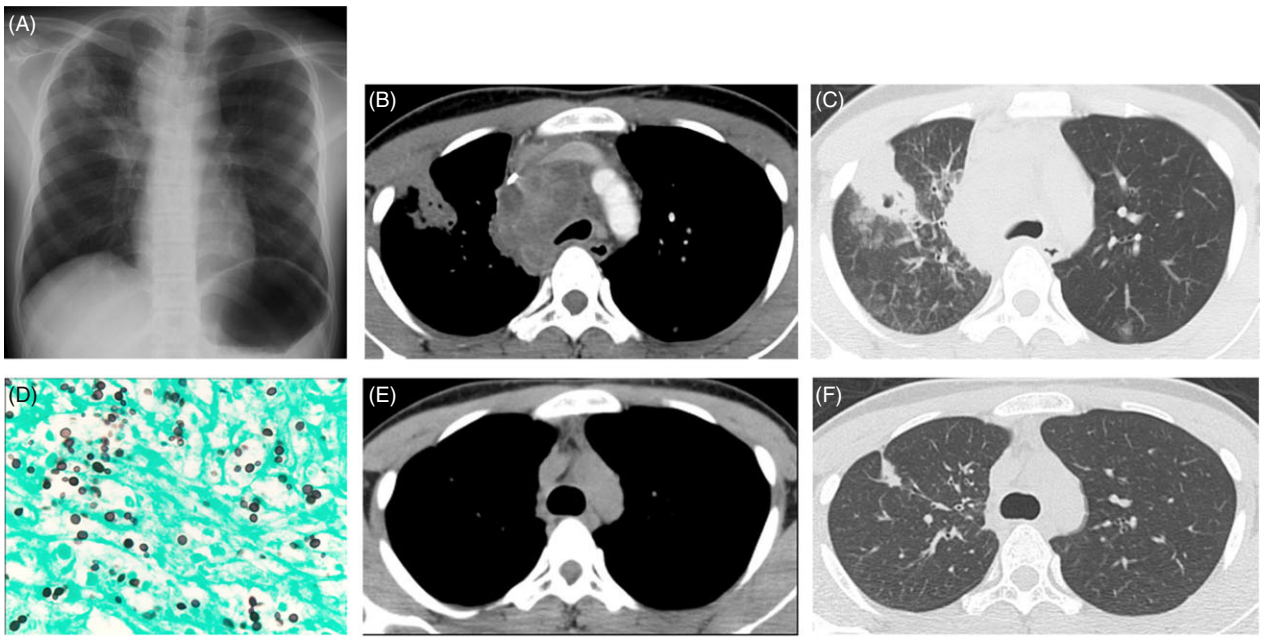

Figure 1. A chest X-ray and computed tomography (CT) scan revealed swollen mediastinal lymph nodes compressing the trachea and an area of consolidation with a cavitation in the right upper lobe (A–C). Pathological findings. A specimen showed many yeast-like cells. These cells were positive for the Grocott stains (×400) (D). The follow-up chest CT three months later showed a significant reduction in consolidation in the right upper lobe and mediastinal lymphadenopathy (E, F).

Serum cryptococcal antigen was negative in the present case. In a previous report, among 166 patients with pulmonary cryptococcosis, serum cryptococcal antigen was positive for 71% of patients with disseminated disease and 22% of those with pulmonary disease alone [3].

EBUS-TBNA is a well-established procedure for the diagnosis of mediastinal diseases such as metastasis from lung cancer, lymphoma, or sarcoidosis. Although the usefulness of EBUS-TBNA in the diagnosis of cryptococcal lymphadenitis is unclear, some cases of mediastinal lymphatic cryptococcosis diagnosed using EBUS-TBNA have been reported [4]. Although conventional TBNA might be also diagnostic, we routinely perform EBUS-TBNA for diagnosis of mediastinal and hilar lymphadenopathy because the usefulness and safety of EBUS-TBNA have been established [5].

We have not performed bronchial washing or bronchoalveolar lavage (BAL) from consolidation in the right upper lobe and this is a weak point of this case report. We suspected that this patient had mediastinal tumor and secondary obstructive pneumonia at first. Therefore, we prioritized biopsy of mediastinal lymph nodes and have not performed transbronchial wash or BAL. A microbiological testing of bronchial washing or BAL from consolidation might be diagnostic.

There are recent reports of autoantibodies associated with disseminated cryptococcal infection. Browne et al. reported that autoantibodies against interferon-γ were associated with severe disseminated opportunistic infection including cryptococcosis in Thailand and Taiwan [6]. An association between anti-granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibodies and some cases of cryptococcal meningitis in otherwise immunocompetent patients has also been reported [7]. In the present case, both interferon-γ and GM-CSF autoantibodies were evaluated, and the results were negative.

The Infectious Diseases Society of America (IDSA) recommends amphotericin B plus flucytosine followed by fluconazole for a CNS infection and severe pulmonary cryptococcosis [8]. In our case, the patient was sick due to high-grade fever and persistent cough. Furthermore, his trachea was compressed by the swollen lymph nodes. Therefore, we treated him with liposomal amphotericin B plus flucytosine as in severe cryptococcosis. Although he showed symptoms of side effects such as hypokalemia, renal dysfunction, and nausea, all of them were corrected. He improved gradually and started to receive oral fluconazole after finishing treatment of amphotericin B plus flucytosine. As images of follow-up showed a significant reduction of the lesions, we finished the treatment for almost 5 months.

In conclusion, we report a case of massive cryptococcal lymphadenopathy in a young immunocompetent patient diagnosed using EBUS-TBNA.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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