Massive Mediastinal Lymph Node Involvement of Cryptococcosis in Immunocompetent Host

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Cryptococcosis is a systemic opportunistic infection mostly occurred in immunosuppressed patients. Pulmonary cryptococcosis in immunocompetent host is usually localized and self-limiting disease. Pulmonary nodule or mass is the most common radiologic finding, however involvement of mediastinal lymph nodes is rare. Here we report a case of pulmonary cryptococcosis with massive mediastinal lymph nodes involvement in immunocompetent host.

Keywords: Cryptococcosis; Lymph nodes; Immunocompetent; Pneumonia

INTRODUCTION

Cryptococcosis is a systemic opportunistic mycosis mostly occurred in immunosuppressed patients such as acquired immunodeficiency syndrome (AIDS) or organ transplanted patients. However, it can also affect immunocompetent persons. The respiratory tract is the principal route of entry for the fungal spores. Organisms are then reactivated from dormant infections in the lung, just as in tuberculosis. The natural history of pulmonary cryptococcal infection in immunosuppressed patients is dissemination in the majority of cases, whereas immunocompetent patients may present with more localized, self-limiting disease [1]. Pulmonary nodule or mass is the most common radiologic finding, however involvement of multiple mediastinal lymph nodes is also reported, especially in patients with defective immunity. It has been scarcely reported in immunocompetent host [2-4]. We reported a case of pulmonary cryptococcosis with massive mediastinal lymph nodes involvement in immunocompetent host.

CASE REPORT

A 39-year-old woman visited the out-patient clinic because of productive cough for a month. She also complained right-sided chest pain and experienced weight loss of 3 kg in one month with decreased appetite. There was no other systemic symptom such as fever or chill. She had no history of tuberculosis, but had history of petit mal seizure 20 years ago that had been controlled with antiepileptic drug such as topiramate, carbamazepine. She was never smoker and denied alcohol intake. She had no specific family history. On admission, she presented with heart rate of 95 per minute, a respiratory rate of 16 per minute, a body temperature of 36.1°C and a 98% of oxygen saturation on room air. Chest physical examination revealed clear breathing sound without crackle. She had no meningeal irritation sign. Her chest X-ray showed an increased opacity in the right lower lung field. It was a 3-cm-sized patchy consolidation with surrounding ground glass opacity (GGO) in the right lower lobe on computed axial tomography (CT) scan. Multiple lymph nodes enlargements in both supraclavicular and mediastinal lymph nodes were also observed. The mediastinal lymph node enlargements were massive involving both upper paratracheal, pre-vascular, lower paratracheal, subcarinal and right hilar lymph node (Fig. 1). Complete blood count profile was normal and the serum antibody test for human immunodeficiency virus (HIV) was negative. Because she had unintentional weight loss of 3 kg for a month and no infectious sign such as fever and chill, lymphoma or primary lung cancer with mediastinal lymph...
node metastasis were suspected. In gram stain of adequately obtained sputum, there was no observed bacteria of fungus. On suspicion of malignancy she underwent whole body positron emission tomography scan, in which hypermetabolic consolidative lesion (standardized uptake value [SUV] 9.9) in right lower lobe, multiple hypermetabolic conglomerated mediastinal, neck lymph nodes (SUV up to 24) was observed. Multiple enlarged, hypoechoic lymph nodes in the bilateral supraclavicular area was found on ultrasonography. Gun biopsy specimen from the right supraclavicular lymph node showed chronic granulomatous inflammation with multinucleated giant cells and many yeasts. Gomori methenamine silver and Periodic acid–Schiff staining revealed a few fungal organism morphologically consistent with Cryptococcus. Acid-fast bacilli staining revealed no acid-fast bacilli and Mycobacterium tuberculosis nested polymerase chain reaction was also negative. Since the result of a serum cryptococcal antigen test was negative and cryptococcal pneumonia with massive lymph node involvement in immunocompetent host was considered to be rare, we got pathologic specimens from mediastinal lymph node to determine whether it shows the same pathologic findings as supraclavicular lymph node. Fiberoptic bronchoscopy and endobronchial ultrasound were performed. There was no endobronchial lesion. Bronchial washing fluid revealed neither bacteria nor fungal organism. In cytology analysis, malignant cell was not observed. Transbronchial needle aspiration (TBNA) from right lower paratracheal and subcarinal lymph nodes was done. Although tissue obtained by TBNA was insufficient for diagnosis, aspiration cytology and cell block from subcarinal lymph node revealed many granulomas and yeast-form organisms which was suspected of cryptococcosis. Mucicarmine staining was equivocal (Fig. 2). Two weeks later, fungus culture of initial sputum specimen yield Cryptococcus neoformans. The final diagnosis was pulmonary cryptococcosis with massive lymph node involvement. Antifungal sensitivity test shows sensitive to amphotericin, fluconazole, and flucytosine. Consequently she was treated with fluconazole for 6 months according to the guideline [5]. At the end of treatment, her respiratory symptom was improved. Right lower lobe consolidation disappeared and mediastinal lymph nodes decreased in size on follow-up chest CT scan after 6 months of treatment.

DISCUSSION

The thin-walled, budding encapsulated yeast, Cryptococcus is human pathogen, which can be found widely in the environment. Cryptococcus neoformans and Cryptococcus gattii (formerly C. neoformans var. neoformans and C. neoformans var. gattii) have now been divided into separate species [6]. Although C. gattii had been responsible for outbreak of immunocompetent host in Canada early 2000s [7], C. neoformans usually affect immunosuppressed host like HIV infected patients. The fungal spore enters the body by direct inhalation. Clinical illness caused by C. neoformans varies according to the host’s immune status, especially T-cell mediated immunity [8]. In AIDS patients, hematogenous spread to central nervous system (CNS), bones, skin was well not-
ed. In immunocompetent host, spores may remain dormant in the lung or reactivated as pulmonary nodule or mass. However, dissemination to extrapulmonary organ is occasionally reported in immunocompetent host. Kerkering et al. [9] reported 17% of healthy hosts with untreated pulmonary cryptococcosis developed CNS dissemination in retrospective review.

Because pulmonary cryptococcosis in immunocompetent host is usually silent, chest CT findings in immunocompetent host has been described in only a few cases [1,10,11]. In recent 2 retrospective studies including 24 immunocompetent host, the most common findings are single or multiple noncalcified nodules, which were small, well defined with smooth margin [3,4]. Lymphadenopathy is usually accompanied with parenchymal lesion mainly in immunosuppressed host [12]. In a retrospective study, lymphadenopathy was reported in only 4 of 24 immunocompetent hosts. Enlarged lymph node was single and located in hilar (3) or paraesophageal (1) area. Thus, massive lymph node involvement and parenchymal consolidation with surrounding GGO in pulmonary cryptococcosis, which were observed in this case, is rare manifestation in immunocompetent host. We made a presumptive diagnosis of lymphoma or lung cancer. This is consistent with the previous report that 85% of patients were initially misdiagnosed with pneumonia (37%), lung cancer (32%), and tuberculosis (17%) because of great variation of manifestation in retrospective review [13]. This was the reason why we got pathologic specimen directly from mediastinal lymph node despite the presence of fungus in a biopsy specimen from supraclavicular lymph node.

The definite diagnosis of pulmonary cryptococcosis is estab-

Fig. 2. (A) EBUS-TBNA of subcarinal lymph node. Aspiration cell block obtained by EBUS-TBNA revealed cryptococcosis in (B) H&E, (C) Gomori methenamine silver, and (D) Mucicarmine stain (×400). EBUS-TBNA, endobronchial ultrasound-transbronchial needle aspiration.
lished by culturing the organism from respiratory specimen as in this case report. Visualization of encapsulated yeast form in smear is suggestive of cryptococcal pulmonary infection but in this case no yeast form was observed in smear of sputum or bronchial washing. Yeast form was observed in tissue specimens obtained by gun biopsy from suprACLavicular lymph node and TBNA from subcarinal lymph node.

Serum cryptococcal antigen obtained by latex particle agglutination is an excellent screening test in immunosuppressed host [14]. But it is not a sensitive test for diagnosis of isolated pulmonary infection in immunocompetent host. Higher titer of serum cryptococcal antigen imply a potential for dissemination and deep tissue invasion [15], but not disease activity. Some investigator have reported that direct detection of cryptococcal antigen in pleural effusion [16], bronchoalveolar lavage [17], and percutaneous transthoracic needle aspiration [18] is helpful in diagnosis pulmonary cryptococcosis. In this case, cryptococcal antigen test was performed only in serum sample and it was negative. In immunocompetent host with pulmonary cryptococcosis, lumbar puncture would be considered to rule out CNS involvement, however for patients without CNS symptoms with negative or very low serum cryptococcal antigen, a lumbar puncture can be avoided [5].

The goal of treatment is to control signs and symptoms of cryptococcal pneumonia and minimize risk of dissemination to the CNS. For pulmonary cryptococcosis in immunocompetent host with mild to moderate symptoms, oral fluconazole is recommended for first line therapy for 6 to 12 months according to the guideline [5]. As our patient had moderate symptoms and intact immunity, we prescribe oral fluconazole for 6 months. After treatment, her respiratory symptom was improved and right lower lobe consolidation disappeared and mediastinal lymph nodes decreased in size on follow-up chest CT scan. We reported a rare case of pulmonary cryptococcosis which was associated with massive mediastinal lymph node involvement in immunocompetent host.

REFERENCES