Tuberculosis of Lymph Node Combined with Pulmonary Mucormycosis

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Mucormycosis is a life-threatening fungal infection which often occurs in patients with underlying disease, and often resulting in a fatal outcome due to the difficulty of early diagnosis and its resistance to antimycotics.[1] Tuberculosis (TB) of lymph node combined with pulmonary mucormycosis is rare. In this article, we reported a case of TB of mediastinal lymph node combined with pulmonary mucormycosis that was presented as obstructive pneumonia combined with lymphoma.

A 22-year-old male presented to No. 309 Hospital of PLA, with a chief complaint of fever and cough for 2 months, which began with afternoon low-grade fever. He had received anti-TB and anti-infective therapy for past 2 months, including paisoniazid, para-aminosalicylate, pasiniazid, rifampin, ethambutol, pyrazinamide, capreomycin, cefaclor, cefminox sodium, sulbenicillin sodium, cefepime, and aztreonam. But his white blood cells were gradually increased, and his temperature became higher (Tmax: 39.6°C). The patient had a hot and dry cough during fever. Physical examination showed that malnutrition, anemia, old surgical scar were visible on the suprasternal fossa, and breath sounds decreased in right upper lobe. No enlarged superficial lymph nodes were touched. Laboratory data showed a white blood cell count of 16.93 × 10^9/L with 79.3% neutrophils, hemoglobin of 93 g/L, platelets of 718 × 10^9/L, procalcitonin of 0.15 ng/ml, and erythrocyte sedimentation rate of 140 mm/h. The results of other tests were negative limulus test (endotoxin) and fungal D-glucandetection, negative interferon determination of peripheral lymphocyte culture, and positive TB antibody (38 kD). Blood culture showed no pathogenic bacteria growth. Chest positron emission tomography/computed tomography (CT) showed enlargement of the right hilar and mediastinal lymph node, uneven enhancement when scanning reinforcement, considering TB; multiple patch and consolidation in the right upper and middle lobe, and considering obstructive atelectasis; small amount of the right pleural effusion and pericardial effusion. He received bronchoscopy examination twice in past 2 months, which showed the right upper lobe bronchial stenosis by external pressure, with mucosal congestion and edema, mucosal of right middle bronchus of the bronchial was rough, and right middle bronchial stenosis, and mucosal showed granulomatous changes and bleeding obvious when biopsy. Fast Bacilli staining were negative in bronchoscope brush slice, and lavage fluid, only inflammatory cell reaction changes in epithelial cells, and pointless nuclear heterogeneous cells were detected, no cancer cells and precancerous cells were found. Right middle lobectomy pathological results showed squamous metaplasia of the bronchial ucosa, moderate chronic and acute inflammation change, and blood clot, acid-fast Bacilli staining negative. These results suggested the possibility of pulmonary TB. Bone marrow biopsy was performed and showed myeloid cell hyperplasia active, increased eosinophils, and thrombocytosis. He had received anti-TB therapy (including isoniazid, rifampin, ethambutol, pyrazinamide, and tobramycin) for 6 months in 2007 since he was diagnosed with lymphoid TB by mediastinoscopy and lymph node biopsy.[2]

The patient received a combination of anti-infective therapy (cefotaxime sodium, sulbactam sodium, meropenem,

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and teicoplanin), and antituberculous treatment, but the therapies were ineffective. Body temperature decreased after application of corticosteroid but re-raise quickly with reduction of corticosteroid. Nine days after admission, CT examination showed pulmonary lesions enlarged significantly [Figures 1 and 2]. The third bronchoscopy confirmed no endobronchial lesion. Bronchoscopy lavage specimen was negative for the acid-fast Bacilli smear and culture test, and also negative for the microbial and fungal culture test. So the patient was advised to transfer to cancer hospital for continue treatment. A CT-guided percutaneous lung biopsy of left upper lobe showed thick fungal hype with right-angle branching, highly suggesting for mucormycosis. The aid endoscopic tracheal biopsy of lymph node showed TB. When the diagnosis of TB with mucormycosis was confirmed by pathologic examination, the patient began therapy with liposomal amphotericin B (LAmB). In the first 2 days, his temperature dropped below 38°C, but died of respiratory failure after 2 more days treatment.

Pulmonary mucormycosis is one of fatal opportunistic fungal infection often happened in the immunocompromised host, such as patients with diabetes mellitus, hematological malignancy, or cancer undergoing induction chemotherapy. The infection was accompanied by a high mortality rate (50–70%). Fever, cough, and hemoptysis are main, but nonspecial symptoms of pulmonary mucormycosis. Radiological manifestations include infiltrates, consolidation, cavitation, focal masses, or nodules. Reverse halo sign is a diagnostic radiological clue for the diagnosis of mucormycosi.[2] It is usually found in invasive mucormycosis in immunocompromised individuals either in the early state or during immune recovery phase. The air-crescent sign in chest radiography is the sign of massive fatal hemoptysis which is the cause of death, careful assessments are needed. Although chest radiography has no specific sign for mucormycosis, a sputum culture is impossible for a patient without a productive cough. Tissue-based diagnosis remains the gold standard.[3] Definitive diagnosis requires demonstration of tissue invasion by the characteristic nonseptate hyphae. A resected specimen is often not suitable for diagnosis, because necrosis is the main portion of the lesion. Serological tests are not useful for diagnosis of mucormycosis, and its identification by polymerase chain reaction is not standardized. Above factors are the obstacles for diagnosis of the mucormycosis infection.

The main principles of the therapy for mucormycosis are the management of the patient's underlying disease and a combined medical-surgical approach. Surgical resection of invaded lobe and antifungal agent are required for the pulmonary mucormycosis accompanied with massive hemoptysis.[4] Treatment strategy involves timely diagnosis, aggressive surgical debridement combined with antifungal agents, and reversal of underlying predisposing factors whenever possible. Treatment initiation should not wait for fixed histopathological staining results and should, therefore, be based on biopsy of frozen tissue samples.[1] Demonstration of hyphae in clinical samples by direct microscopy is important because it is rapid and highly suggestive of the disease. Some studies have shown a 2-fold increase in mortality with delayed initiation of therapy (starting more than 6 days after diagnosis). Control of underlying conditions is critical in mucormycosis. Rapid correction of metabolic abnormalities is mandatory, corticosteroids should be discontinued, if feasible, and other immunosuppressive drugs should be tapered as much as possible. Among the more recent therapeutic developments in mucormycosis treatment including LAmB (now the drugs of first choice), the new triazole posaconazole with promising efficacy as salvage treatment, polyene should be used as backbone therapy either in monotherapy or in combination therapy. Although AmB deoxycholate was the cornerstone of mucormycosis therapy for decades, LAmB is less nephrotoxic and can be safely administered for higher doses for a longer period of time.[5]

The white blood cell of the patient in this case significantly increased, not leukopenia as the past reported. Because no relevant pathogens were found in blood and lavage, we

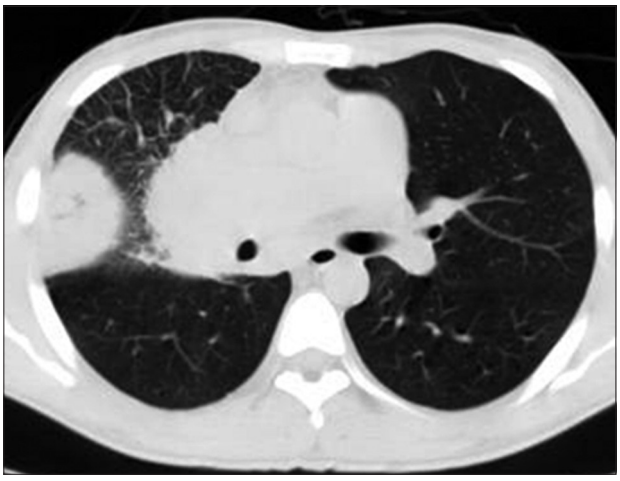

Figure 1: Computed tomography showed right hilar and mediastinal lymph node enlargement, and consolidation in the right middle lobe.

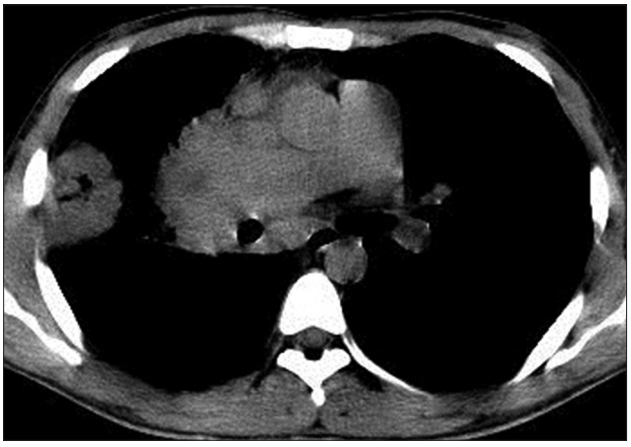

Figure 2: Computed tomography showed partial liquefaction of mediastinal lymph nodes in the mediastinal window.

suspected the patient with obstructive pneumonia combined with lymphoma. Definitive diagnosis of the patient was confirmed by tissue pathology with several times biopsy. But the diagnosis and treatment were delayed. The main predisposing factors in this study were prolonged antibiotic therapy, steroid therapy, and TB. The patient has received anti-infection therapy for more than 2 months, and also received hormone intermittently. The recurrence of lymph node TB after short-term of anti-TB may be the cause of mucormycosis. In this case, the patient had pulmonary mucormycosis and lymph node TB, surgical resection was impossible, and he died of respiratory failure despite the use of LAmB. Following this case, we need to concern if a patient has a history of TB and has no response to anti-TB therapy, we could not deny the diagnosis, but should consider the other combined disease. And all negative serological examination cannot deny the TB and mucormycosis, tissue-based diagnosis remains the gold standard, and biopsy must be performed when there is doubt about the diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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