□ CASE REPORT □

Acute Respiratory Distress Syndrome Due to Chronic Necrotizing Pulmonary Aspergillosis

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Abstract

This is the first case report of acute respiratory distress syndrome (ARDS) due to chronic necrotizing pulmonary aspergillosis (CNPA). This patient had pulmonary fibrosis of unknown etiology with a right upper bulla. The wall of the bulla became thicker with the surrounding lung infiltration and the patient suddenly developed severe respiratory failure. It is necessary to confirm the possibility that ARDS may occur in CNPA and that peripheral eosinophilia might forebode worsening of CNPA.

Key words: pulmonary fibrosis, pulmonary aspergillosis

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Introduction

In invasive pulmonary aspergillosis, the cause of death is generally severe inflammation or chronic respiratory failure. Chronic necrotizing pulmonary aspergillosis (CNPA) is a rare slowly progressive form of invasive aspergillosis. We encountered a patient with acute respiratory distress syndrome (ARDS) who died due to CNPA; this is apparently the first such case report. It is important to be aware that ARDS may occur in CNPA.

Case Report

A 64-year-old woman with persistent high grade fever for two days presented at our hospital in early September 2005. She was followed-up at our outpatient clinic under suspicion of interstitial pneumonia on chest radiograph. She had been well until two months earlier, when she began to complain of a dry cough and low grade fever. She had undergone right breast resection due to breast cancer and radiotherapy 25 years earlier. On the present admission, the white-cell count was 7,900 per cubic millimeter, with 69 percent neutrophils, 20 percent lymphocytes, 9 percent monocytes, 1 percent eosinophils and 1 percent basophils. Serum C-reactive protein (CRP) showed an elevation to 7.50 mg/dl. The values of AST (aspartate aminotransferase) and ALT (alanine aminotransferase) were elevated to 349 IU/l and

580 IU/l, respectively. Renal function was normal and the serum fasting glucose level was normal. Plain chest radiograph demonstrated bilateral lung infiltration, especially in the right upper lobe (Fig. 1a). Chest computed tomography showed large bulla surrounded by a thick wall in the right upper lobe. The bilateral lower lobes tended to contract and showed traction bronchiectasis. The right upper lobe also showed marked volume loss with mediastinal deviation to the right (Fig. 1b). Sputum smear demonstrated *Aspergillus fumigatus*. Abdominal ultrasonography did not show any abnormal findings. The temperature was 38.5°C. The lungs, heart, abdomen, arms and legs were normal. Sultamicillin tosilate (6 g/day) was initiated on September 9 and after 6 days of therapy, the CRP value decreased to 1.37 mg/dl. However, as high fever persisted, the antibiotics were changed to ceftazidime (2 g/day). Although her temperature decreased to below 37°C after 8 days of ceftazidime therapy, the CRP value increased to 20.59 mg/dl. On September 20, her temperature rose to 38°C again. The AST and ALT values were slightly improved to 45 and 209 IU/l, respectively and CRP was slightly decreased to 6.95 mg/dl. We suspected an acute chronic disease state due to infection (e.g., aspergillus, nontuberculous mycobacterium), collagen vascular disease or an allergic disease (e.g., allergic bronchopulmonary aspergillosis, hypersensitivity pneumonia). Despite the inability to obtain a precise diagnosis, prednisolone was initiated at 10 mg/day on September 21. As the temperature of 38°C persisted, we increased prednisolone to 20 mg/day

Figure 1 . (a). Chest radiograph on admission. (b). Chest computed tomography on admission. (c). Chest radiograph on October 24.

with biapenem of 0.6 g/day on September 30. On October 1, her temperature became normalized and remained normal for 23 days. Gallium scintigraphy showed abnormal uptake in the right upper lobe, which corresponded with the right upper cavity-like lesion. Culture of bronchial lavage fluid by fiberoptic bronchoscopy showed *Aspergillus fumigatus*, but the serum β -D glucan and aspergillus antigen were within

normal ranges. The serum aspergillus antibody increased to $\times 64$. We diagnosed chronic necrotizing pulmonary aspergillosis (CNPA). As her temperature had normalized and her condition was improving, we did not change the therapy. On October 24, the chest radiograph showed a worsening of right lung infiltration with right pleural effusion (Fig. 1c). The white-cell count increased 10,400 per cubic millimeter, with 13 percent eosinophils. In the morning of October 25, she suddenly lost consciousness and the value on pulse oximetry decreased to 77%. She returned to consciousness 30 minutes later but left hemiplegia and motor speech disturbance appeared. Cranial magnetic resonance (MR) imaging showed a slightly high signal in the upper frontal lobe in fluid-attenuated inversion-recovery (FLAIR) image. A cerebrospinal fluid examination did not show any abnormal findings. On October 27, her consciousness level and speech disturbance improved. On October 31, she had a convulsion with severe hypoxemia of 60% on pulse oximetry. Though oxygen was administered by nasal prongs at a rate of 5 liters per minute, analysis of arterial blood showed that the partial pressure of oxygen was 63 mmHg, the partial pressure of carbon dioxide was 33 mmHg, and the pH was 7.475. Echocardiography did not show left ventricular dysfunction or pulmonary hypertension. Twelve hours after the first severe anoxic spell, respiratory failure worsened again and her consciousness did not return. She died after 3 hours despite mechanical ventilation.

At autopsy, fibrous adhesive pleura were observed in the bilateral upper lobes and there was a cavity-like lesion in the right apex. The wall was formed from necrotizing granule due to aspergillus infection (Fig. 2a). This cavity-like lesion was compatible with aspergilloma. The alveolar space surrounding the cavity-like lesion was accompanied by hyaline membrane formation and scattered inflammatory cells (Fig. 2b). We diagnosed the findings as diffuse alveolar damage. We were not permitted to perform necropsy of the brain.

Discussion

To our knowledge, this is the first reported case of ARDS due to CNPA. An indolent form of invasive aspergillosis, termed CNPA (1), or “semi-invasive” pulmonary aspergillosis (2), has been described. This infection occurs in mildly immunocompromised host (e.g., diabetes mellitus, low-dosage glucocorticoids) and often progresses slowly, usually over a period of several months (3, 4). This patient had pulmonary fibrosis of unknown etiology with a right upper bulla. As the wall of the right upper bulla became thicker with surrounding lung infiltration, we thought mycetoma in the bulla invaded the tissue adjacent to the bulla. After aspergillus invaded these tissues, the patient developed ARDS due to CNPA. When the fatal respiratory failure occurred, the patient was afebrile and serum CRP was not elevated. Therefore, we did not add antifungal drugs and the low dosage prednisolone was continued.

Figure 2. (a). Necrotizing granuloma in the wall of the cavity-like lesion with hyphal fungal elements. (b). High power view showing hyaline membranes admixed with scattered inflammatory cells.

Six days before fatal respiratory failure, this patient had a cerebral accident. Initially, we thought the episode had resulted from cerebral infarction due to a vascular event rather than septic emboli, as the patient had not demonstrated fever or clear inflammatory findings. Therefore, we began treatment for cerebral infarction without antifungal drugs.

Though we could not perform a brain necropsy, considering the clinical course, we thought that the cerebral accident was due to septic emboli for CNPA. Depending on the size of the emboli (5), the MR findings may vary from major arterial branch infarction to multiple small abscesses located at the gray-white matter junction, secondary to occlusion of small arteries and arterioles. The small abscesses are accom-

panied by surrounding edema and mass effect, which is well demonstrated on MR (6). If the septic emboli are small, they are difficult to detect as in the present case. One day before the first cerebral accident, the percentage of serum eosinophils increased to 13%. After the first cerebral attack, the elevated percentage of eosinophils persisted around 13-22%. We thought this peripheral eosinophilia might have reflected activation of the lung aspergillus lesion. We might have administered antifungal drugs along with a higher dose of steroid.

We should confirm the possibility that ARDS may occur in CNPA and that peripheral eosinophilia might forebode worsening of CNPA.

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