Idiopathic pulmonary fibrosis with chronic necrotizing pulmonary aspergillosis: a case report

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Abstract: Objective: IPF with CNPA is rare, and its clinical manifestations and radiologic features lack specificity compared with other types of pulmonary aspergillosis. This study aims to assess the clinical features of idiopathic pulmonary fibrosis (IPF) with chronic necrotizing pulmonary aspergillosis (CNPA). Methods: One case of IPF with CNPA is reported and literature review is performed. Results: The patient had a history of intermittent hemoptysis without history of smoking and alcohol. CT scan of the chest showed bilateral ILD and nodules in the upper lobes of bilateral lungs and middle lobe of the right lung of the patient. CT-guided pulmonary puncture biopsy using microscopy revealed mold hyphae. Based on combined medical history and radiologic findings, the patient was diagnosed with CNPA. Conclusion: A discriminating pathological feature favors the discovery of aspergillus hyphae in pulmonary tissues, which provides assistance for the early anti-fungal therapy.

Keywords: Idiopathic pulmonary fibrosis, chronic necrotizing pulmonary aspergillosis

Introduction

Idiopathic pulmonary fibrosis (IPF) represents a chronic, progressive fibrotic interstitial lung disease that is usually confined to the lung with unclear etiology. Its histologic and/or high-resolution computed tomography (HRCT) feature of the chest facilitates the diagnosis of usual interstitial pneumonia (UIP) [1, 2]. The incidence of IPF has been rising in recent years and the annual morbidity and incidence of IPF are 14-28 per 100 thousand people and 6.8-8.8 per 100 thousand people, respectively in the US [3]. IPF is usually implicates a poor prognosis with an average survival of only 2-5 years [3]. Several case reports on ILD with aspergillosis have been published recently [4, 5], but IPF complicated with chronic necrotizing pulmonary aspergillosis (CNPA) is relatively rare. In this study, we reported a case of IPF with CNPA who was treated in our hospital and literature review was also performed.

Clinical information

The patient was a male, and aged 64, who was hospitalized due to relapse and aggravation of symptoms for 2 months on June 25th, 2017 after 17 years of recurrent cough and expectoration. The patient was diagnosed as pulmonary fibrosis 17 years ago based on the CT scan of chest due to dry cough and only received anti-infection treatment when the symptoms were aggravated (medication unknown) rather than standard treatment. He received CT scan of the chest in our hospital in August 2015, which revealed bilateral ILD (Figure 1). The diagnosis of IPF was confirmed afterwards at Nanjing Drum Tower Hospital (Figure 4). However, the patient was not treated with standard therapy. CT scan of the chest on June 2017 due to aggravated dry cough revealed: 1. Multiple nodules in bilateral lungs, which further grew compared with the results in August 2015; 2. Bilateral UIP; 3. Bilateral pleural thickening and adhesion (Figure 2). The patient had history of intermittent hemoptysis without history of smoking and alcohol. Physical examination: T, 36.8°C; P, 96 beats/min; R, 19 breaths/min; BP, 130/66 mmHg. Velcro crackles were heard in bilateral lungs. No other abnormalities were found in the heart and abdomen. The preliminary diagnoses of IPF and multiple pulmonary nodules of unknown origin were then
made. The patient received further examinations after admission. The results of routine blood test, C-reactive protein, procalcitonin, blood coagulation, troponin, CK-MB, complete set of immune tests and immunoglobulin test were basically normal. Erythrocyte sedimentation rate (ESR) was 38 mm/h, and 1-3-β-D-glucan was 113.6 pg/ml. Acid-fast bacilli smear was normal, and sputum culture and sputum fungal culture were negative. The patient received CT-guided pulmonary puncture biopsy on June 28th, 2017. Pathological examination using microscopy revealed mold hyphae (Figure 3). Combining the medical history and radiological findings, the patient was diagnosed with CNPA. The patient received intravenous administration of 0.2 g voriconazole twice daily for one week starting from July 1st, 2017. He was prescribed with itraconazole tablet (0.2 g) after discharge. However, the patient showed poor compliance and withdrew medication. Unfortunately, this patient is currently lost to follow-up.

Discussion

Pulmonary aspergillosis is a common opportunistic infection. Depending on the types of lung changes, it can be divided into aspergilloma, allergic bronchopulmonary aspergillosis (ABPA), CNPA, and invasive pulmonary aspergillosis (IPA) [6, 7]. Pulmonary aspergillosis mainly affects patients with malignancies, receiving organ and bone marrow transplantation, glucocorticoid therapy, immunosuppressive therapy, wide-spectrum antibiotics therapy, or having chronic respiratory diseases [8]. CNPA is a rare type among these. Binder et al [7] first proposed the concept of CNPA in 1982. CNPA is mainly observed in patients with structural lesions of lungs, such as COPD, bronchiectasis, and pulmonary cystic fibrosis. However, the clinical manifestations of CNPA, such as cough, expectoration, and hemoptysis, lack specificity,
and the course of disease can last for several weeks, months or even years. In our case, the patient had dry cough with occasional hemoptysis. Chest CT scan is indispensable for the diagnosis of CNPA, and the common findings include unilateral or bilateral shadows of substantial lesions or nodules, with or without cavities. The reported case indicated shadows of substantial lesions upon radiologic examination along with an air crescent sign. However, this patient did not receive standard treatment and the disease progressed slowly over time. Since the symptoms of CNPA are not specific, it is necessary to distinguish it from other types of infections, such as lung cancer and tuberculosis [9]. In clinical practice, respiratory tract samples, such as sputum and bronchoalveolar lavage fluid are directly used for microscopy or culture to detect potential aspergillus infection [10]. However, it is still difficult to exclude colonization or pollution. Serum precipitin test for detection of aspergillus antibody (IgG) is the most effective method to differentiate between infection and colonization in the diagnosis of CPA [11]. Serum galactomannan (GM) test is also used for the detection of aspergillosis, though there is a lack of specificity it has limited indicative values [12]. At present, a confirmed diagnosis of CNPA still relies on pathology. Unfortunately, a non-invasive test was not performed for CNPA in our hospital, and the samples were collected by pulmonary puncture biopsy. The pathologic examination revealed a large amount of mold hyphae, which prompted the diagnosis. CNPA patients usually require long-term anti-fungal treatment, such as voriconazole, Amphotericin B, and itraconazole, and a few patients have the chance for surgical resection [13]. Given its chronic nature, the 2006 European Guidelines recommend that the treatment for CNPA patients should last for at least 4-6 months [14] and they should be further evaluated in terms of drug tolerance and economic capacity. In this report, the patient had poor compliance and economic support, and did not receive standard therapy after discharge, which may be a major reason for radiologic progression.

Glucocorticoids and immunosuppressants are the main medications for ILD [15], though they may increase the risk of aspergillosis. In our case, the patient had no history of long-term use of glucocorticoids or immunosuppressants. There was no history of smoking and environmental exposure, and his immune system functioned normally. All these findings are extremely rare in reported IPF with aspergillosis. This patient presented UIP upon chest CT scan. After literature review, it was considered that the extensive honeycomb-like changes in the lungs caused structural damage to the lungs. Thus this UIP patient lacked the essential resistance to aspergillus, and aspergillus was much likely to colonize the lungs. The colonizing bacteria may serve as pathogenic bacteria when the host immunity is impaired. According to the published reports, UIP that is diagnosed upon radiologic examination accounts for 80.4% of all patients with ILD plus IPA [4]. Moreover, a Japanese study has shown that UIP patients are inclined to have aspergillosis [5], indicating, from another perspective, the potential role of structural lesions of the lungs in the development or pathogenesis of aspergillosis.
Taken together, the clinical manifestations and radiologic findings of CNPA are unable to ensure diagnostic specificity, which is a major reason for the misdiagnosis of CNPA. The diagnosis of CNPA is usually confirmed based on pathology, and the patients usually require long-term antifungal treatment after diagnosis. The low incidences of IPF and CNPA, along with the difficulty of diagnosis of CNPA, suggest physicians be aware of this rare disease.

Disclosure of conflict of interest

None.

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