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Primary ciliary dyskinesia presenting with spontaneous pneumothorax: Case report and review of the literature

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ABSTRACT

Background: Primary ciliary dyskinesia (PCD) is an autosomal recessive heterogeneous group of conditions with variable clinical findings.
Case presentation: A 36-year-old nonsmoking Chinese man present to the emergency department of our hospital with acute-onset breathlessness and sudden-onset left-sided chest pain. The patient had 6 years primary infertility and suffered from recurrent episodes of respiratory tract infections since childhood. Chest X-ray was performed, which showed a left-sided pneumothorax with lung collapse. His conditions improved in clinical symptoms after 3 days of closed thoracic drainage. Radiographic findings after lung recruitment revealed bronchiectasis and bronchiolitis but no situs inversus. Paranasal sinus computed tomography (CT) showed maxillary sinusitis and ethmoid sinusitis. Pulmonary function tests demonstrated severe obstructive ventilation functional impairment. Bronchial mucosal cilia showed the absence of both outer and inner dynein arms of the microtubules (ODA and IDA). A culture of bronchoalveolar lavage fluid was positive for *Pseudomonas aeruginosa*. His clinical symptoms and CT images showed improvement after 1 month of treatment. A literature review revealed that few patients are diagnosed with PCD complicated with spontaneous pneumothorax. Within one year of follow-up, the patient showed good responses to local ICS+ LA beta$_2$ agonist combined with oral carbocistein.
Conclusions: Pneumothorax might be one of the complications of the PCD. Combination therapy including ICS+ LA beta$_2$ agonist and carbocistein could be a potential therapy to reduce the frequency of acute exacerbations and delay progression of PCD.

1. Introduction

Most cases of primary ciliary dyskinesia (PCD) is an autosomal recessive disease with extensive clinical and genetic heterogeneity characterized by defects of mucociliary clearance, chronic bacterial infection, and neutrophilic inflammation [1–5]. Cilia abnormalities are the underlying cause of this syndrome. Recent studies in which diagnosis was based on ultrastructural study of the cilia have shown that the prevalence of PCD is ~1/10 000 live births [6].

The symptoms of the syndrome are a consequence of the defective motility of the cilia found in the respiratory tract, paranasal sinuses and reproductive tract. Ciliary dysfunction, affecting mucociliary clearance, leads to recurrent airway infections, characteristic of chronic sinusitis and bronchiectasis, sometimes associated with male infertility and situs inversus (Kartagener syndrome; KS) [2]. Although airway symptoms usually begin in early childhood, the diagnosis is sometimes delayed for several years [7,8]. Therefore, it is of importance to recognize this disease early in order to start appropriate therapy of respiratory tract infections and minimize lung damage. We herein report the case of a PCD patient with spontaneous pneumothorax and obstructive emphysema. Of note, the patient has good response to budesonide/formoterol and carbocistein during 1year of outpatient follow-up.

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2. Case report

A 36-year-old nonsmoking Chinese man presented to us with acute-onset breathlessness and sudden-onset left-sided chest pain. He had experienced repeated productive cough and purulent sputum since childhood. He had been experiencing a productive cough and dyspnea [British Medical Research Council (MRC) Dyspnea Scale Grade 3] for 1 month prior to admission to our hospital. Clinically, he had tachypnea, tachycardia and hyper-resonant percussion note with decreased breath sounds on the left side of the chest. He also had a barrel-shaped chest wall. There was no evidence of digital clubbing, lymphadenopathy, oral ulcers or skin lesions. Cardiovascular examination was unremarkable and no organomegaly, masses or ascites were detectable in the abdomen. Chest X-ray was performed, which showed a left-sided pneumothorax with lung collapse (Fig. 1). After 72 h of intercostal drain insertion, his lung showed complete expansion with no air leak and he was symptomatically improved. High-resolution computed tomography (HRCT) of the chest was performed, which showed fully expanded lungs with left lower lobe bronchiectasis, bronchial wall thickening, patchy bilateral ground-glass opacities, and bilateral panacinar emphysema. (Fig. 2A–C). Spirometry showed FVC of 2.61L (54% of predicted), FEV_1 of 1.52L (37% of predicted), and FEV_1/FVC of 0.58. The patient had no history of allergic symptoms, negative skin-prick tests, and normal amounts of serum IgE. A physical examination upon admission showed blood pressure of 130/80 mmHg and a regular pulse of 110 beats/min. Lung auscultation revealed bilateral moist and expiratory wheezes in the left lung.

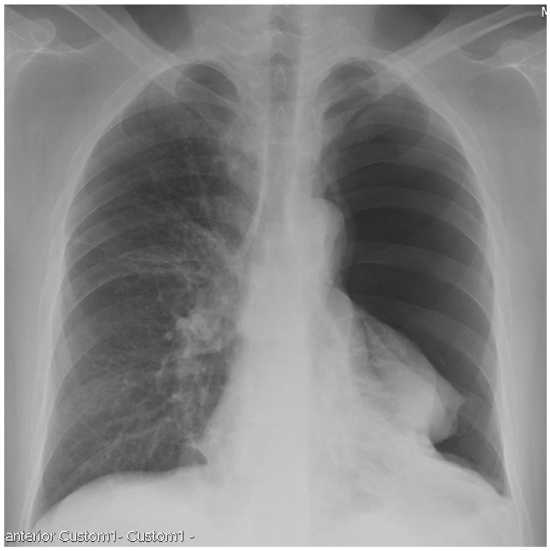

Fig. 1. Anterior posterior view of the chest taken in the emergency department, demonstrating left-sided pneumothorax with lung collapse.

Laboratory test and arterial blood gas analysis on admission demonstrated neutrophilia and mild hypoxemia. Flexible bronchoscopy at 16 days after admission revealed a massive amount of yellowish bronchial secretions from the right middle lobe bronchus (Fig. 3D). *P. aeruginosa* was detected continuously in cultured sputum. Electron microscopic examination of biopsy specimens obtained from the bronchial mucosa revealed a combined defect of both IDA and ODA in the cilia and disorganization of doublet distribution (Fig. 3B). The patient divorced after 6 years of marriage without conception. We next performed a ciliary motility study by looking at sperm motility. All the spermatozoa were found to be non-motile. Based on these findings, the patient was diagnosed with PCD.

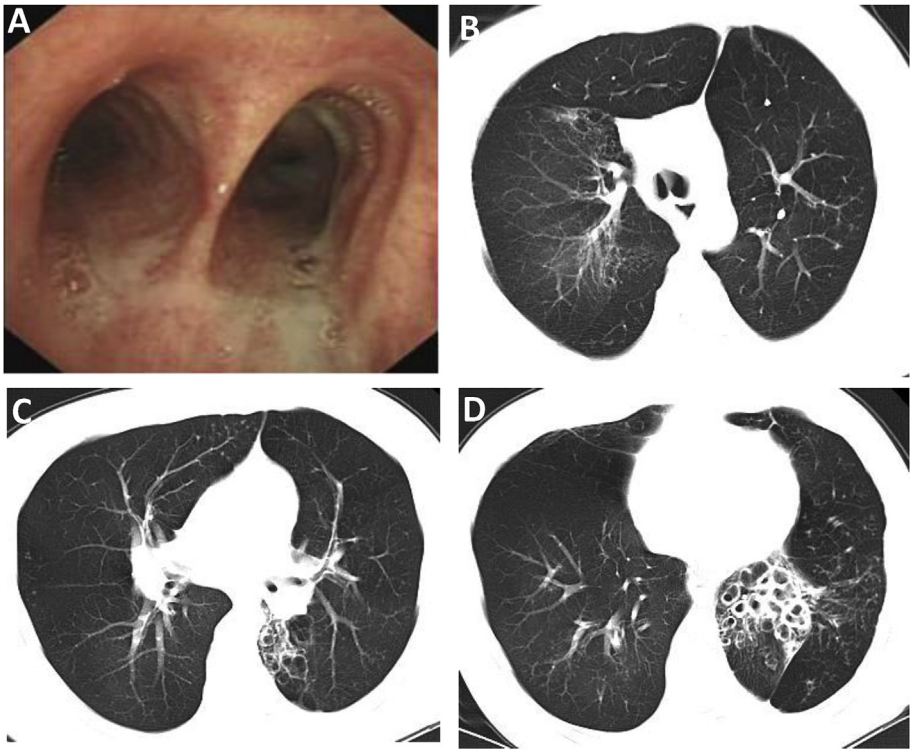

Fig. 2. CT images of the chest and flexible bronchoscopy findings. A–C: HRCT shows bronchiectasis in the left lower lobe, opacities in both lower lungs, and bilateral panacinar emphysema. D: Flexible bronchoscopic findings 1 week after complete lung expansion, revealing a large amount of yellowish bronchial secretions from bilateral bronchi. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

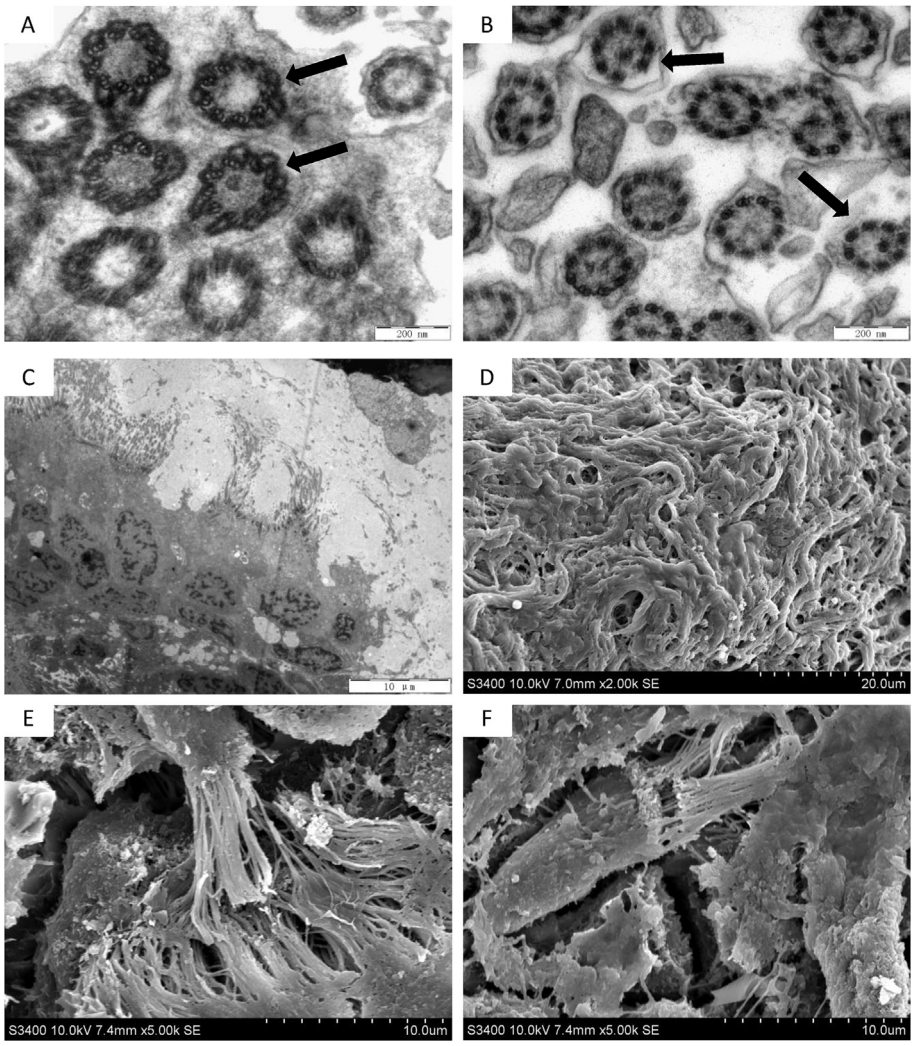

Fig. 3. Electron microscopy of cilia from bronchial mucosa. A, B: Transmission electron micrograph of cross-section of cilia shows absence of both inner and outer dynein arms, and transposition defect: some cilia demonstrate absence of a central microtubule pair '9 + 0'(black arrows); in other cilia a peripheral microtubule doublet has crossed to take the central position providing an apparent '8 + 2' structure (black arrows) and microtubular disorganization. C: Cilia of bronchial epithelia were sparse and presented with local defects. D–F: Scanning electron microscopy showed loss of surface cilia, and a large number of red blood cells and mucinous structures adhered to the surface of the mucous membranes.

Treatment of the persistent exacerbations of bronchiectasis consisted of 16 days broad-spectrum antibiotics and mucolytics (oral carbocistein tablets, at a dose of 500 mg, three times daily, were effective). Daily physiotherapy and physical exercise were applied. Theophylline and short-acting inhaled β_2 agonists were administered to relieve dyspnea. All these methods reduced the patient's symptoms and improved his quality of life.

Upon discharge from inpatient care, our patient remained on inhaled long-acting bronchodilators in combination with corticosteroids (budesonide/formoterol at a dose of 160 μg/4.5 μg twice daily) and carbocistein (500 mg three times daily). Daily physiotherapy was administered as well. The frequency of acute exacerbations of lower respiratory tract infections decreased (mean annual rate: 3.5 vs 1.0) and lung function did not deteriorate during 1 year follow-up.

3. Discussion

PCD is a rare heterogeneous group of conditions with variable clinical findings, the majority of cases is autosomal recessive. The disease phenotype is caused by defects of respiratory cilia, sperm tails, and cilia of embryonic nodes. The most common symptoms include bronchiectasis, male infertility due to impaired sperm motility, and female ectopic pregnancy or infertility because of ciliary dysfunction in the fallopian tubes. KS, which is characterized by the triad of situs inversus, bronchiectasis and chronic sinusitis, was the first reported type of PCD in 1933 [9]. In PCD, the clinical phenotype is intensive and it overlaps with other chronic diseases of the respiratory tract [10].

Diagnosis of PCD is often delayed or missed completely. One study reported that 70% of patients had seen a physician >50 times before the diagnosis was made [11]. This emphasizes the importance of including PCD as a differential diagnosis in patients with recurring symptoms in the upper and lower respiratory tract [12]. If the diagnosis is made early, individuals may benefit from a good quality of life, while preventive medicine is initiated, based on physiotherapy, physical exercise, and treatment of incipient infections.

The patient in this report had suffered from recurrent episodes of respiratory tract infections since his childhood. His clinical manifestations included chronic sinusitis, primary infertility, and bronchiectasis but no situs inversus in HRCT images. Of note, our patient's pulmonary function tests demonstrated severe obstructive ventilation functional impairment, and HRCT revealed the

presence of bronchiectasis and emphysema. Although PCD with obstructive airflow limitation has been extensively described, to the best of our knowledge, this is very rare that the coexistence of obstructive emphysema with spontaneous pneumothorax and PCD. Air flow limitation and emphysema formation could be the result of chronic respiratory inflammation secondary to many years of respiratory infection.

There have been no long-term randomized trials of therapy in PCD, and there is a lack of evidence-based medicine in the management of this condition. As a result, many aspects of patient care are empirically based on other chronic suppurative or inflammatory lung disease. The current patient received an ample spectrum of curative methods: short cycles of antibiotics, mucolytics, bronchodilators, and daily physical therapy during hospital stay. Of note, he received inhalation of budesonide/formoterol in combination with oral carbocistein for 1 year with intent to alleviate the pulmonary inflammation and respiratory symptoms. The frequency of acute exacerbations of lower respiratory tract infections decreased significantly and lung function kept stable during 1 year of outpatient follow-up, suggesting that our patient benefited from the ICS+long-acting (LA) beta$_2$ agonist combined with carbocistein. However, he also had a continuous productive cough after initiation of treatment.

In conclusion, this report describes a case of PCD with secondary spontaneous pneumothorax, and the patient has good responses to local ICS+ LA beta2 agonist combined with carbocistein. Although there is a lack of significant scientific evidence to support, our report suggests that above combined treatment might be one of the potential therapies to reduce the frequency of acute exacerbations and delay progression of PCD via modification of the activities of the immune system. Further accumulation of evidence regarding the response to combined therapy is expected to confirm our speculation.

Conflict of interest

The authors declared no conflict of interest related to this study.

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