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Case report

Asthma-like tracheobronchial amyloidosis: a case report and review of the literature

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Abstract

Tracheobronchial amyloidosis(TBA) is a rare disorder which refers to localized aberrant protein deposits within the airways. Because of the lack of characteristic presentation, long lasting and insidious course, patients with TBA are often misdiagnosed as other pulmonary diseases. At present bronchoscopic biopsy was the gold standard for the diagnosis of TBA. We present a case of TBA which was misdiagnosed as asthma due to asthma-like wheezing and the effectiveness of anti-asthmatic treatment. The definite diagnosis was confirmed by CT scan, bronchoscopic findings and Congo red staining of biopsy specimen. The literature involving the recent progression of diagnosis and treatment of TBA that is reviewed.

Key words: amyloidosis; diagnosis; treatment

INTRODUCTION

Amyloidosis is a disorder in which aberrant protein is formed by amyloid fibrils accumulation in the extracellular tissue or organ[1]. This kind of disorder exhibits different subunits, including primary systemic amyloidosis, secondary systemic amyloidosis related to chronic inflammatory states, and localized forms of abnormal amyloid deposition[2]. The precise mechanism that causes amyloidosis is unknown. Generally, primary amyloidosis appears to be related to abnormal production of amino globulins by plasma cells whereas secondary amyloidosis is associated with the presence of chronic infectious diseases.

Tracheobronchial amyloidosis(TBA) is a rare disease which refers to aberrantly localized protein deposits within the airways[3]. A patient with TBA may present many different symptoms, such as coughing, expectoration, dyspnea, hemoptysis and hoarseness, and part of patients with TBA presented recurrent gasping[1,2]. We provide a case of a patient with TBA who presented with asthma-like dysnea masquerading as asthma over one year. The last diagnosis was made by broncoscopy and biopsy.

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CASE REPORT

In October, 2004, a 62-year-old male patient was admitted to our hospital because of recurrent coughing, wheezing and dyspnea over the past one year. One year ago, the patient was diagnosed as "bronchial asthma" and treated by short acting beta agonist and inhaled corticosteroid(ICS). Although the above symptoms were relieved by anti-asthmatic treatment, the symptoms were recurrent. One week prior to admission, the patient began to complain of a fever(around 39.5℃) and increasing coughing with yellow purulent sputum and shortness of breath, especially after exertion. His past medical history and family history were noncontributory. He was a lifetime nonsmoker. On physical examination a barrel chest was found, and a diffuse wheezing rale and a coarse crackle were observed in both lungs. Mild depressed edema was found on the both lower limbs. All other findings, particularly the size of the heart, liver and spleen, were within normal limits.

Laboratory data on admission showed that the

biochemistry, serology and urinalysis for Bence-Jones proteins were normal. The blood routine indicated that white blood cells number increased to 15.85×10^9/L due to pulmonary inflammation. Arterial blood gas analysis on room air revealed a PO_2 of 10.14 Kpa, PCO_2 of 3.91 Kpa and pH = 7.56. An echocardiographic examination showed normal left ventricular function with normal appearance and thickness of the myocardium. There was no evidence of organ disorders including liver, spleen, kidney and urinary bladder through abdominal B-mode ultrasonography. Initially, a posteroanterior and lateral chest radiograph revealed that the lung markings increased in both lower lung field, especially in the right lower lung field. A chest CT scan demonstrated that thickening and narrow of the trachea were noticed, which extended into the bilateral mainstem bronchi(***Fig. 1***). The results of the CT scan was confirmed by bronchoscopic appearance. Flexible bronchoscopy showed markedly thickened and tuberculiform mucosa along the tracheal wall began 3 cm proximal to the hypolarynx and extended distally with circumferential involvement of the carina and bilateral mainstem bronchi. The tracheal and bronchial lumina were irregular and narrowed. The narrow of the left main bronchus was so significant that the bronchoscopy could not be passed(***Fig. 2***). Endobronchial biopsy specimens showed that amyloid deposits were detected in the specimens of these bronchi after Congo red staining(***Fig. 3***). Thus, our patient was definitely diagnosed as primary TBA, because there was no clinical and laboratory evidence of systemic disease.

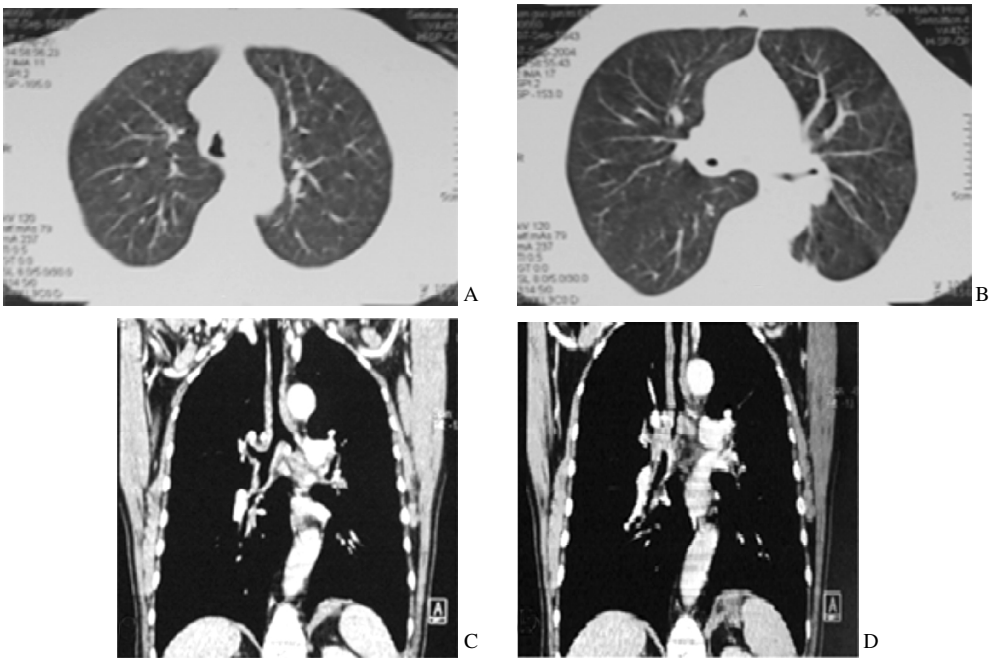

Fig. 1 Chest CT scan(2004, 9) revealed deformation and narrow of the trachea(A); which extended into the bilateral main bronchi(B); and accompanied with significant circumferential thickening of the trachea and bilateral main bronchi(C, D)

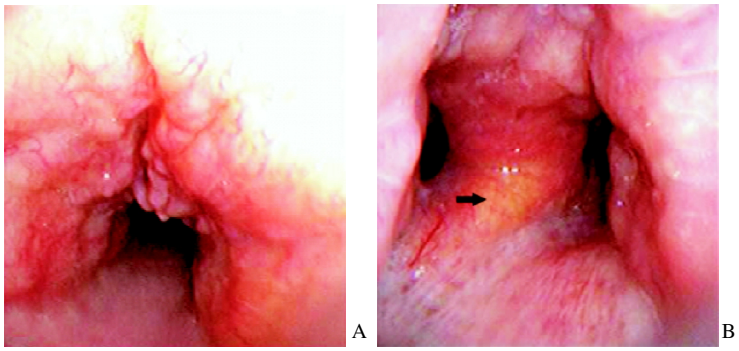

Fig. 2 Bronchoscopy(2004, 9) displayed that thickened and tuberculiform mucosa along the tracheal wall were observed(A), which extended distally into the bilateral main bronchi(B) accompanied with submucosal yellowish plaque in the carina(B:arrow); the tracheal and bronchial lumen was irregular and narrowed

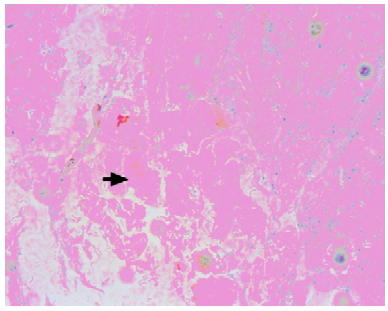

Fig. 3 Bronchial biopsy demonstrated that submucosal deposition of amyloid fibrils were seen(arrows)(Congo red, × 100)

The patient was not given special treatment, such as laser resection or stent placement, as the amyloid deposits distributed throughout the trachea and bronchial lumina. The patient had a relatively good response to ICS. The patient was seen in follow-up again in March 2006 when he still had the symptoms of cough, wheezing and dyspnea, and the lesions of bronchoscopic appearance was similar to that in October 2004.

DISCUSSION

Pulmonary amyloidosis can occur in three forms: diffuse interstitial deposits, single or multiple pulmonary nodules, and submucosal tracheobronchial deposits. TBA is the most common form of localized bronchopulmonary amyloidosis, although its diagnosis is rarely made in daily clinical practice. The symptoms depend mainly on the degree, location and area of involvement of the tracheobronchial tree, but two thirds of patients may be asymptomatic[4]. For lacking of characteristic presentation and insidious course, initially, patients with TBA are often misdiagnosed as other pulmonary diseases[5]. The patient presented here had an illness masquerading as asthma because of the asthma-like presentations and the relatively anti-asthmatic effectiveness. In order to decrease masquerading rate when we meet similar patients again, we should strengthen the recognition of this disease and arrange for further examination as early as possible. TBA is more prevalent in males than in female, with a median onset age of 50~60 years old[6]. The chest CT scan may serve as an important tool in both the evaluation of the extent of disease as well as guidance and follow-up after therapy. The typical features of CT appearance of TBA are circumferential soft tissue density wall thickening of the trachea and/or bronchi leading to diffuse or nodular stenosis. Nodules or confluent intramural plaques are situated in the subepithelial interstitial tissue[7, 8], while biopsy by bronchoscopy is the only diagnostic method. Positive specimen with Congo red staining is a strong proof for amyloidosis. F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) is widely accepted as an important diagnostic tool in evaluating patients with possible cancers. Recently, Japanese scholars reported that a 60-year-old woman with bilateral multiple lung nodular lesions revealed by the chest CT scan was diagnosed as localized nodular pulmonary amyloidosis by histological examination. FDG-PET demonstrated the lung lesions with intense FDG activity, while the accumulation of FDG returned to normal after her disease was relieved by treatment. The result suggested that FDG-PET apparently reflected the disease activity of pulmonary amyloidosis[9].

Multiple or diffuse TBA often results in progressive airway obstruction. Thus, a rapid, effective and safe treatment is necessary. Medicines including colchicine, prednisone and melphalan were proved to have limited effect[10]. Varied local treatments through bronchoscopic methods such as endobronchial Nd-YAG laser resections, tracheobronchial stents, balloon dilation and bronchoscopic ablation of intraluminal amyloid deposits have been reported. Local excisions often prove temporarily effective, but none of them have proved to be completely successful[11,12]. While, these bronchoscopic interventions are indeed associated with a variable risk of bleeding, due to structural weakness of increased friability of arterial walls from amyloidosis involvement, that has been reported[13]. To our knowledge, there have been no proposals for treating TBA that have proved to be safe and effective. Researchers are still continuously trying new methods for treating TBA. Our patient did not receive special treatment because of fairly limited management options and financial constraints, while the wheezing symptom of the patient can be relieved by ICS. Recently, Neben-Wittich and his collaborators reported that seven patients with TBA treated by external beam radiation therapy(EBRT) had a favorable response to treatment including symptom relief, decrease in the frequency of pulmonary infections, and obvious improvement in pulmonary function. They believed that EBRT is safe and may provide a symptomatic and objective improvement[14]. The mechanism and long-term effect of this kind of treatment can not be ascertained at present, as the patients with TBA are few.

TBA is a benign disease; however, the course and prognosis does not appear benign. There are no certain data about the natural history of this disorder. At present, there are no effective schemes for treating the disease. Some medicines, such as colchicines, can be used for treatment of TBA. However, the therapeutic effect is uncertain. We found that individual patient had a relatively good response to ICS, which indicated that ICS may be favorable to the symptomatic improvement of patients with TBA. Local treatment through bronchoscopic often proves to be temporarily effective, while treatments(such as EBRT) still need to be further evaluated for their efficiency, side-effects and long-term effects.

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