Delayed diagnosis for primary tracheobronchial amyloidosis

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ABSTRACT

Objective: To determine clinical features and diagnostic methods for primary tracheobronchial amyloidosis (TBA).

Methods: The clinical manifestations and diagnosis of a male patient who had been misdiagnosed for many years were described and analyzed.

Results: The patient was a 68-year-old male who complained of recurrent cough, expectoration, and progressive dyspnea for more than 30 years. He had been diagnosed with chronic bronchitis, bronchiecstasis, and endobronchial tuberculosis in other hospitals and treated with antibiotics frequently and anti-tubercular agents for 3 months. Despite the treatments, the patient’s symptoms were progressively worse. Finally, he came to Xiangya Hospital, Central South University, and was clearly diagnosed with primary TBA based on histopathological evidence after bronchoscopy.

Conclusion: TBA, a rare disease resulting from abnormal submucosal amyloid deposition in the trachea and bronchi, may display with many different symptoms. TBA is often misdiagnosed with other pulmonary diseases. The use of bronchoscopic techniques is essential for the diagnosis of TBA. Histopathology remains the gold standard for diagnosis of primary TBA. So, for patients with chronic cough of unknown etiology, bronchoscopy should be performed to obtain biopsy samples for the definitive diagnosis.

KEY WORDS

primary tracheobronchial amyloidosis; misdiagnose; bronchoscopy
Tracheobronchial amyloidosis (TBA) is a rare disease that is characterized by amyloid deposits restricted to the trachea, main bronchi, and segmental bronchi [1]. TBA is a slowly progressive disease that requires histopathology to confirm the diagnosis. The most common presenting symptoms of TBA include cough, dyspnea, wheezing, hemoptysis, and recurrent pneumonia [2-4]. Lacking a characteristic presentation in the early stage, patients with TBA are often misdiagnosed with other pulmonary diseases. Herein we present a case of TBA which was misdiagnosed for more than 30 years.

1 Case presentation

The patient is a 68-year-old male who complained of recurrent cough, expectoration, and progressive dyspnea for more than 30 years. He was admitted to our hospital (Xiangya Hospital) after being diagnosed with chronic bronchitis, bronchiectasis, and endobronchial tuberculosis in other hospitals and treated with antibiotics frequently. Despite the treatments, his symptoms were progressively worse. In 1988, the patient was managed with a combination of isoniazid, streptomycin, and rifampicin for a diagnosis of endobronchial tuberculosis after bronchoscopy in another hospital. Three months later, with no improvement on these anti-tubercular agents and seeking a second opinion and treatment, the patient came to our hospital.

The patient presented with diminished breath sounds and slight wheezing rales as well as bibasilar crackles. Routine blood tests were normal. The tuberculin test was negative. Sputum samples were negative for bacteria, acid-fast bacilli, and fungi. A recent computed tomography scan of the chest demonstrated extensive thickening on the walls of the trachea and bronchi at different levels with luminal narrowing (Figure 1). Electronic bronchoscopy revealed significant swelling and hypertrophy of the tracheal and bronchial mucosa (Figure 2). Pathologic examination (Figure 3) of the endobronchial biopsy specimen revealed positive staining with Congo red, negative staining with periodic acid-Schiff (PAS) and digestive PAS in the mucosa with amyloid deposition. There was no evidence of extrapulmonary organ involvement in amyloidosis. Based on the above comprehensive evaluation, the diagnosis of primary TBA was established. In the absence of an effective drug therapy, local management of this disease with endoscopic techniques for bronchial repermeabilization was able to alleviate the symptoms and improve the prognosis of the disease. Also, external beam radiation therapy (EBRT) would achieve significant clinical improvement, although it requires individualization of treatment, given the possible complications due to the radiation. Since this patient had a wide range of bronchial lesions, we could not treat him with bronchoscopy. He also refused EBRT and was discharged from our hospital.

Figure 1 CT images revealing extensive thickening on the walls of the trachea and bronchi at different levels with luminal narrowing
A: Left and right main bronchus; B: Left main, left upper lobe bronchus, and right middle bronchus; C: Left upper lobe and lower lobe bronchus and right middle bronchus; D: Left and right lower lobe bronchus
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Figure 2  Electronic bronchoscopy revealing significant swelling and hypertrophy of the tracheal and bronchial mucosa

Figure 3  Positive staining with Congo red in the mucosa with amyloid deposition (×400)

2 Discussion

This patient presented with symptoms of cough, expectoration, and progressive dyspnea. A lung CT scan revealed diffuse thickening of the tracheobronchial airway wall. Bronchoscopy showed an edematous tracheobronchial airway with thickened mucosa, nodular protuberances, and a rough surface. Segments of the bronchial lumina were narrowed. Pathologic examination of biopsy samples revealed chronic inflammation of the mucosa, with amyloid deposition and Congo red stain (+). All of these findings confirmed a diagnosis of primary TBA.

TBA was a slowly progressive disease. It is reported\(^5\) that it would take 1 to 20 years to make a definite diagnosis of TBA from spotting non-specific respiratory symptoms. Its prognosis varies according to the degree of impairment and individuals\(^5\). There were no definite and sufficient data about the natural history of this disorder. In some cases, the disease remains stable for a long period of time. Conversely, some cases can evolve to deterioration of pulmonary function and clinical complications which lead to death. In diffuse tracheobronchial amyloidosis, the estimated five-year survival rate was 30%–50%\(^6\). Patients with severe proximal airway stenosis always indicate poor prognosis. The patient in our study showed a long life expectancy because of slow progression in disease and less severe proximal airway stenosis.

The patient had a long disease course, which had been misdiagnosed for many years. Indeed, the misdiagnosis induced by several reasons. First, the patient was not diagnosed in a timely fashion because of limited health care resources. The onset of his disease was in 1976, when lung CT scan and bronchoscopy were not available, so the patient had been misdiagnosed as chronic bronchitis or bronchiectasis on a number of occasions. Second, the clinicians at that time were not acquainted with or unknowledgeable about TBA and the symptoms of the disease were atypical. Therefore, it was difficult based on symptoms to differentiate the condition from common diseases of the respiratory system. Third, the medical
staff accepted the diagnosis of other hospitals instead of performing further examinations. The clinicians caring for the patient had accepted the diagnosis of chronic bronchitis or bronchiectasis, resulting in a delay in performing a bronchoscopy, and hence a failure to establish the correct diagnosis for the patient.

Bronchoscopy is the cornerstone in the diagnosis of TBA that allows better visualization of the lesions and has the advantage of allowing excision of amyloid deposits for histopathological analysis. Histopathology remains the gold standard for diagnosis of primary TBA. So, for patients with refractory asthma or chronic cough of unknown etiology, bronchoscopy should be performed to obtain biopsy samples for definitive diagnosis of rare diseases including primary TBA.

References


(Cited by CHEN Liwen)