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Case report

Laryngotracheobronchial amyloidosis: A case report

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ABSTRACT

Primary laryngotracheobronchial amyloidosis is a rare pulmonary disease that can cause endobronchial stenosis. This disease has never previously been reported in Vietnam. We aimed to report a laryngotracheobronchial amyloidosis case in a 43-year-old female, which may be the first reported case in Vietnam. The patient had a 4-year history of progressive hoarseness, dyspnea, and hemoptysis. Multiple bronchial biopsies combined with detailed clinical information suggested an amyloidosis disease. Red congo staining was positive in bronchial samples, and a further workup found positive red congo staining in subcutaneous fatty tissue biopsy samples. Tracheostomy was performed due to severe dyspnea related to laryngeal stenosis. A multidisciplinary consultation was held, and chemotherapy with melphalan and dexamethasone were prescribed due to the systemic effects of the disease. After 2 cycles of chemotherapy, the patient showed improvement in dyspnea and cough. Due to the inexperience of both the clinicians and pathologists, this case was diagnosed quite late. In the future, if this diagnosis is considered in the differential diagnosis, an earlier diagnosis and better treatment outcome can be reached.

1. Introduction

Amyloidosis is a benign disease characterized by the extracellular deposition of amyloid [1], which often involves multiple organs, including the heart, liver, kidney, spleen, and gastrointestinal tract. Respiratory tract involvement in amyloidosis is extremely rare [2]. The etiology of amyloidosis can vary, with some cases caused by genetic mutations [3]. Amyloidosis can be subdivided into the following subtypes: primary light chain (AL) amyloidosis, secondary amyloid A (AA) amyloidosis, familial amyloidosis, and β2-microglobulin-related amyloidosis [3]. The symptoms of amyloidosis related to respiratory tract are typically nonspecific, and patients often present with coughing, dyspnea, wheezing, hemoptysis, and dysphonia [4]. Histopathology is the gold standard for diagnosis. To date, no curative treatment exists to treat this disease [1].

2. Case report

A 43-year-old female patient with a 4-year history of hoarseness was diagnosed with chronic laryngitis but failed to respond to corticosteroids. In the past 6 months, the patient developed additional dyspnea with exertion, stridor, wheezing, and hemoptysis. The clinical examination revealed a temperature of 37 °C, a pulse of 95 beats/min, blood pressure of 120/80 mmHg, respiratory rate of 18 breaths/min, and oxygen saturation of 96% on room air. Respiratory examination revealed coarse crackles in both lungs. Blood tests showed elevated leukocytes at 11,000/mm^3 with normal hemoglobin and platelet levels. Liver and kidney functions were normal. A mycobacteria growth indicator tube (MGIT) culture of bronchoalveolar lavage was negative. A thoracic computed tomography (CT) scan revealed thickened bronchial branches and normal lung parenchyma (Fig. 1). Abdominal ultrasound and echocardiography did not detect any abnormalities. Laryngoscopy revealed the swelling and ulceration of the vocal cords. Bronchoscopy

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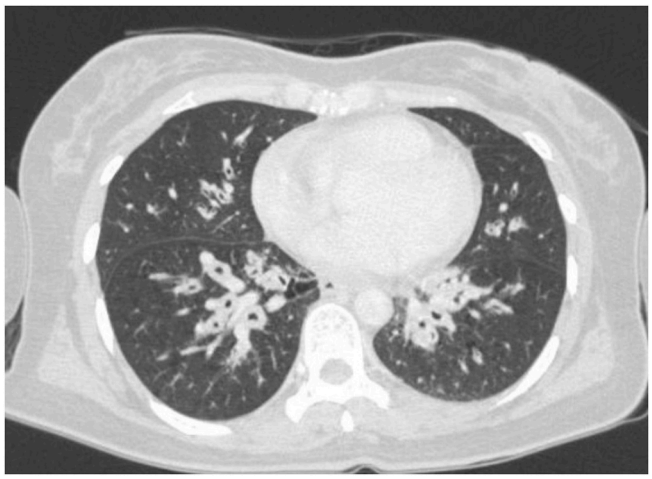

Fig. 1. Chest computed tomography (CT) images showed thickened bronchial branches and normal lung parenchyma.

showed that the bronchial airway was edematous, resulting in bronchial airway narrowing. The biopsy results revealed bronchial airway inflammation. The patient experienced progressive dyspnea, and the second bronchoscopy showed multiple masses resembling submucosal tumors of the trachea, causing tracheal narrowing (Fig. 2). The patient underwent an emergency tracheotomy due to severe dyspnea. The results of the mass biopsy revealed subepithelial, dense, amyloid deposits that were Congo red-positive (Fig. 3). A subcutaneous fatty tissue biopsy was also performed, which was Congo red-positive, and immunofluorescence (IF) analysis found evidence of light chain deposition (Fig. 3). The final diagnosis was systemic amyloidosis with predominant tracheobronchial involvement, suspected to be AL amyloidosis. This patient was treated with oral melphalan 0.22 mg/kg/day and dexamethasone 40 mg/day every 28 days. To date, the patient has received 2 cycles of chemotherapy, and the symptoms have improved slightly.

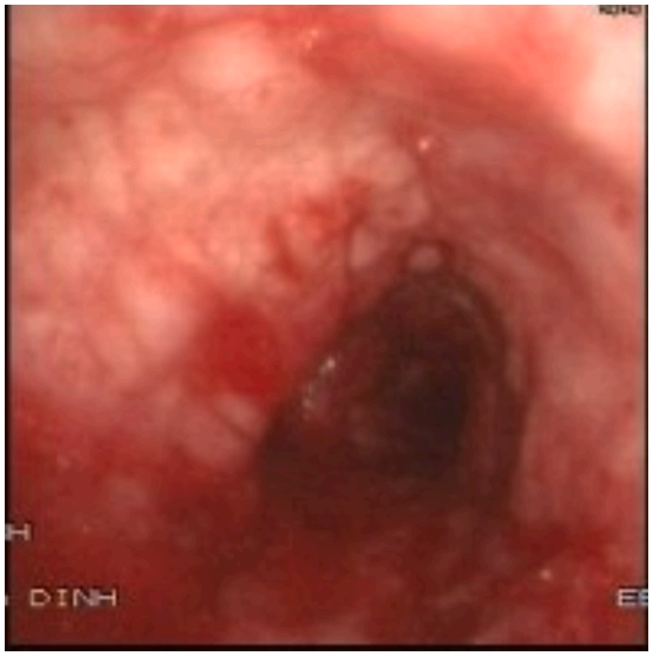

Fig. 2. The second bronchoscopy showed many submucosal masses of the trachea and tracheal narrowing. The mucosa was hyperemic and edematous.

3. Discussion

Amyloidosis is a heterogeneous disease in which extracellular protein deposition causes the subsequent dysfunction of the affected organs [5]. Amyloidosis can be localized or systemic, hereditary or acquired [6]. The incidence of AL amyloidosis has been reported to be nine cases per million person-years [3]. However, respiratory tract involvement is rare [7]. More than 30 proteins have been identified, associated with varying amyloidosis subtypes [8]. AL amyloidosis is caused by the deposition of free monoclonal antibody light chains and represents the most frequently occurring amyloidosis subtype [9]. Allelic variants located in codons 52 and 57 of the gene encoding amyloid A have been associated with AA amyloidosis, resulting in the deposition of amyloid A [3]. Mutations in the transthyretin gene may cause familial amyloidosis [8].

The clinical presentation of amyloidosis can vary widely depending on the organs involved [8]. Patients with tracheobronchial tree or laryngotracheal involvement often present with hoarseness, stridor, choking, or dyspnea on exertion [10].

On endoscopy, tracheobronchial amyloidosis may present as submucosal nodules, luminal stenosis or occlusion, bronchial wall thickening, mucosa that is brittle and bleeds easily, mucosal roughness or unevenness, mucosal hyperemia and edema, pale mucosa, and wall rigidity [11].

Respiratory amyloidosis can appear in three forms: nodular pulmonary amyloidosis, diffuse alveolar-septal amyloidosis, and tracheobronchial amyloidosis [12]. CT imaging is the primary technique used to delineate respiratory lesions. Nodular pulmonary amyloidosis presents as one or more nodular amyloid deposits involving the lungs [12]. The CT scan features of diffuse alveolar septal amyloidosis include interlobular septal thickening, micronodules, ground-glass opacification, traction bronchiectasis, and honeycombing [12]. Tracheal and bronchial wall thickening or hyperattenuating soft tissue nodules, which occasionally contain calcifications, can be observed on CT scans of tracheobronchial amyloidosis patients [12,13].

The gold standard for amyloidosis diagnosis is the presence of homogeneous extracellular amyloid deposits and green birefringence under polarization microscopy with Congo Red staining [2]. Currently, no specific treatment exists for this disease [2]. The treatment of symptomatic laryngeal and tracheobronchial amyloidosis includes resolving narrowed airway segments by stenting, the piecemeal resection of tumor masses, open thoracotomy, or laser ablation therapy [10]. Other therapy options include chemotherapy and oral dexamethasone [13].

This was the first case of amyloidosis with respiratory tract involvement ever reported in Vietnam, and the radiologists and clinicians treating this patient had no prior experience with some of the potential treatment options; therefore, they suggested chemotherapy and tracheostomy. After a multispecialty consultation, we opted to perform a tracheostomy to resolve the dyspnea, followed by chemotherapy, which is likely a more suitable treatment course for patients with multiple organ involvement. After 2 months of treatment, the patient experienced mild improvements in dyspnea and cough.

4. Conclusion

Laryngotracheobronchial amyloidosis is a rare disease. This case was diagnosed late due to the inexperience of both the clinicians and pathologists. In the future, an earlier diagnosis and treatment outcome may be achieved if this diagnosis is considered in the differential diagnosis. In cases of slowly progressive tracheobronchial stenosis with thickening of the airway, amyloidosis should be suspected. Multiple tracheobronchial biopsies should be performed, and Congo red staining should be performed to determine an amyloidosis diagnosis.

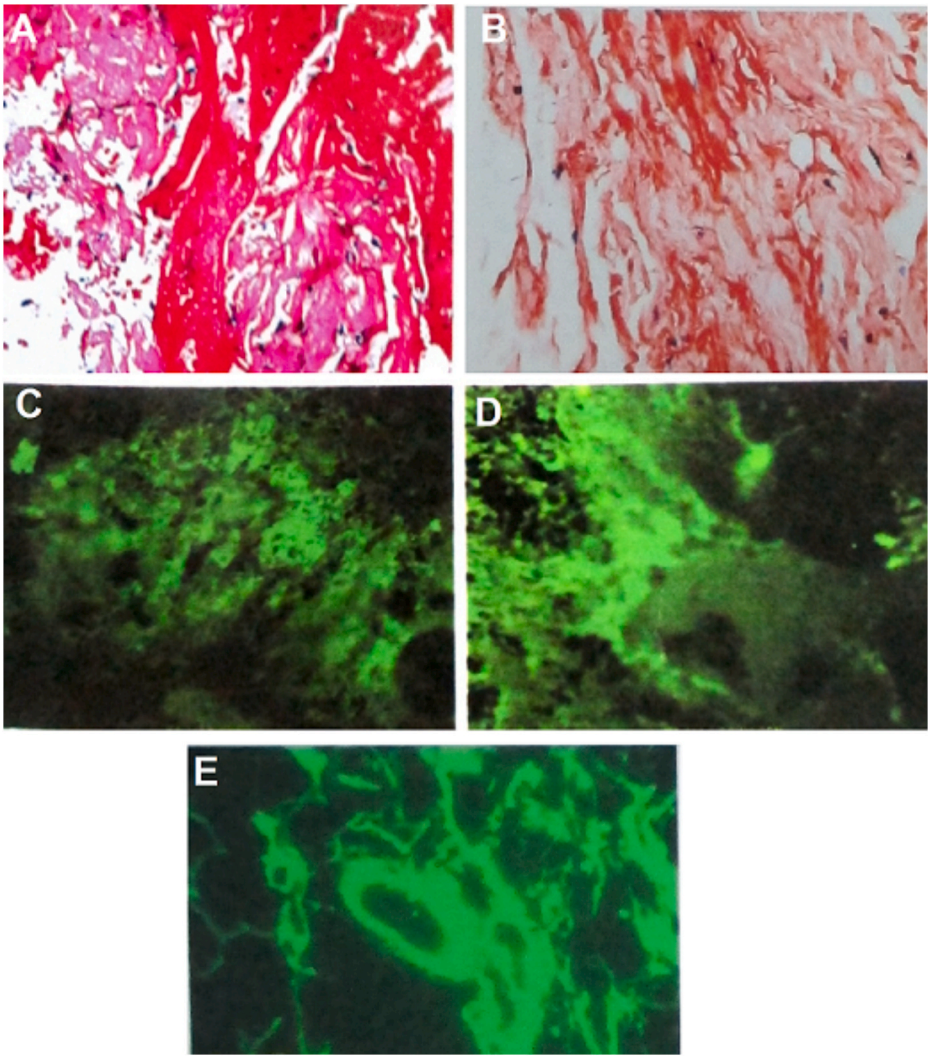

Fig. 3. The histopathology results of submucosal masses. (A) Biopsy showed dense, subepithelial amyloid deposits that were Congo red-positive and displayed apple-green birefringence under polarized light (C). Similar results were observed in the subcutaneous fatty tissue (B and D). Immunofluorescence staining showed strong positivity for the light chain in the subcutaneous fatty tissue (E). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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Author contribution

Le TV and Nguyen MD contributed to this article as co-first authors. All authors have read the manuscript and agree to the content.

Declaration of competing interest

Authors do not have any conflict of interests.

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