Primary Laryngo-tracheobronchial Amyloidosis: An Unusual Cause of Hoarseness and Dyspnea

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To the Editor: Amyloidosis refers to the extracellular deposition of amyloid, a fibrillar proteinaceous insoluble material that has characteristically light, ultrastructural, and histochemical features. It consists of a well-circumscribed dense amorphous eosinophilic amyloid protein, surrounded by an inflammatory cellular infiltrate of plasma cells and lymphocytes with an occasional granulomatous reaction. The two major types are primary and secondary amyloidosis. Primary amyloidosis is the type that most commonly affects the respiratory system.[1]

A 67-year-old male was referred to pulmonology clinic for progressive hoarseness and dyspnea on exertion for 15 years, presenting as severe dyspnea and orthopnea with acceleration in the past two months. He had no history of cough, fever, or weight loss. He had a 50-pack-year smoking history but had quit smoking about 15 years ago. Computed tomography (CT) scan showed irregular airway wall thickening with calcifications and luminal narrowing [Figure 1a and 1b, arrows]. Pulmonary function tests at the time of presentation showed forced expiratory volume 1 s/forced vital capacity ratio of 62% prediction. Meanwhile, total lung and carbon monoxide diffusing capacity were normal. Serum protein electrophoresis, cardiac biomarkers, echocardiogram, and bone marrow biopsy showed normal. Bronchoscopy revealed diffuse nodular deposits that involve the larynx and trachea [Figure 1c and 1d], and the biopsies revealed abundant amorphous eosinophilic material on staining with Congo-red [Figure 1e and 1f, arrowheads]. The diagnosis of this patient is primary amyloidosis localized to larynx and tracheobronchial region without any systemic involvement. Because the patient had specific dyspnea syndrome, the Nd:YAG laser was used to resect obstructive lesions by bronchoscope and was prescribed with oral low-dose prednisone.

Amyloidosis may involve the respiratory system in larynx, trachea, bronchus, lung, and mediastinal lymph nodes. Respiratory tract amyloidosis may happen in systemic amyloidosis but more often happens in isolation.[2] Pulmonary amyloidosis is usually due to primary amyloidosis with deposition of immunoglobulin light-chain fragments. It has three patterns: proximal, mid, and distal. Proximal symptoms appear in upper airway with symptoms of hoarseness, dyspnea, wheezing, and cough. Mid or distal symptoms appear in lower airway include hemoptysis, postobstructive atelectasis, and recurrent pneumonia.

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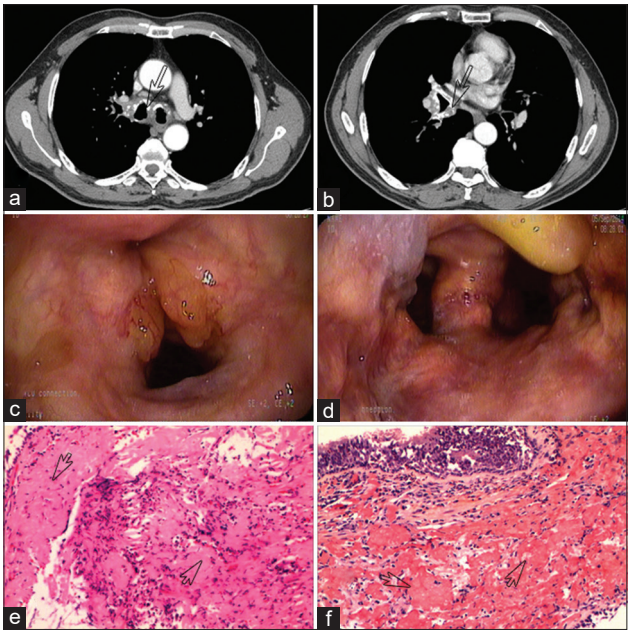

Figure 1: (a and b) Computed tomography scan showed circumferential wall thickening with calcifications as well as luminal narrowing at various levels of the trachea-bronchial tree (arrows). (c and d) Bronchoscopy findings include multifocal flat plaques of gray-white amyloid material distributed throughout the larynx, the trachea, and bronchial lumina. (e) H & E section showed abundant amorphous eosinophilic material in keeping with amyloid. (f) Amyloid with Congo-red positivity (arrowheads) (original magnification, ×200).

CT scan is more sensitive than chest radiograph in detecting the respiratory tract deposits, revealing their calcific nature, and

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demonstrating calcification of chest wall blood vessels. Patients with unexplained dyspnea, chronic renal failure, hypercalcemia in the presence of a normal chest radiograph should be suggested for a CT scan. Findings involve diffuse, pleural plaques, luminal narrowing, and irregular airway wall thickening with calcifications. The mechanism of calcification is unknown. The two common factors involved are high levels of parathyroid hormone and a remarkable increase in the calcium-phosphate solubility product; however, calcification can also be seen without any of these two factors. The role of ^{18}F-fludeoxyglucose positron emission tomography (^{18}F-FDG PET) scanning in diagnosis of pulmonary amyloidosis has been unknown. Positive ^{18}F-FDG PET results, especially with a maximum standardized uptake value of more than 3, in patients with pulmonary amyloidosis should raise suspicion about associated lymphoma or plasmacytoma.

The diagnosis of amyloidosis usually needs confirmation with histopathology examination. To obtain a precise diagnosis, biopsy tissue specimens are needed for an accurate histological characterization. In our case, the presence of amyloid deposits in the resected nodule by bronchoscope was revealed by the appearance of positive Congo-red staining followed by immunohistochemical analysis. Meanwhile, primary amyloidosis must be accurately checked to exclude a systemic involvement. In this patient, the immunofixation electrophoresis of serum did not show any monoclonal gammopathy. The bone marrow plasma cells were 5% without amyloid deposits. Cardiac biomarkers and echocardiogram were normal. There was no other organ involvement.

Laryngo-tracheobronchial amyloidosis has a poor prognosis.[3] Therapies are limited, including laser surgery, surgical treatments, implantation of endobronchial silicone stent, radiation, chemotherapy, and oral dexamethasone.[3] However, the effect of above-mentioned therapies is unsatisfactory in some patients because tracheobronchial relapse is reported after several years of treatment.[4] For this patient, we gave laser treatment and oral prednisone. After 2 years, the patient died of recurrent episodes of pneumonia.

Laryngo-tracheobronchial amyloidosis should be considered when a patient is presented with hoarseness and dyspnea. A detailed history, physical exam, and CT scan are necessary; however, the gold standard of diagnosis is histopathological examination. Treatment should be initiated after final diagnosis and should be aimed to improve the prognosis.

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Conflicts of interest

There are no conflicts of interest.

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