

Primary tracheobronchial amyloidosis associated with tracheobronchomegaly evaluated by novel four-dimensional functional CT

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Abstract

Amyloid is a heterogeneous family of extracellular proteinaceous deposits characterized by apple-green birefringence on polarized light microscopy. There are rare case reports of these extracellular deposits accumulating in the upper and central airways. Progressive infiltration may impair glottic and airway function with some cases requiring intervention to improve flow. Bronchoscopy and lung function testing provide dynamic information to monitor for disease progression; however, the recent development of 320 multislice computed tomography (320 CT) enables dynamic, four-dimensional (4-D) evaluation of laryngeal and tracheal structure and function and presents as a noninvasive, low-radiation dose surveillance tool. We reviewed a 43-year-old man with primary amyloidosis of the larynx and central airways who presented with an 18-year history of progressive dysphonia without breathlessness and preserved lung function. 4-D CT demonstrated marked thickening of supraglottic folds and trachea with marked tracheal dilatation. Despite gross structural abnormalities, dynamic function assessed throughout inspiration and expiration was normal, demonstrating neither rigidity nor dynamic collapse. This combination of structural and functional assessment of the proximal airway by 4-D CT is a novel application to surveillance for laryngeal and tracheal amyloid.

Introduction

Amyloid is a heterogeneous family of extracellular proteinaceous deposits with characteristic microscopic, histochemical, and ultrastructural features. Amyloidosis can affect virtually any organ or tissue in the body. Amyloid infiltrates of the larynx are normally at the subepithelial extracellular locations and are characterized by deposits of a cellular, eosinophilic material displaying apple-green birefringence with polarized light when stained with Congo red or being meta-chromatic with crystal violet or methyl violet. Primary laryngotracheal amyloidosis is a rare localized condition not associated with systemic involvement. Nodules or polypoid lesions infiltrate anywhere in the larynx or trachea. Eventually, thick airway may narrow

airway lumen requiring intervention. The effect of these infiltrates on dynamic function of the larynx and trachea is not well characterized. Visualization of the affected area that bronchoscopically provides important information, however, offers poor quantitative evaluations for surveillance. Similarly, lung function testing that provides a global assessment of dynamic airway function, however, provides poor regional assessment particularly the extrathoracic upper airways that rely on poorly reproducible inspiratory flow volume loops. Three hundred twenty multislice computed tomography (320 CT) enable dynamic, four-dimensional (4-D) assessment of central airways that provides important structural as well as dynamic evaluations and ongoing surveillance for patients with infiltrative conditions such as primary central airway amyloid.

Case Report

Our patient was a 42-year-old man and nonsmoker who presented with an 18-year history of nonprogressive dysphonia characterized by hoarse voice. He did not describe any dyspnea or cough. He was previously well and exercised frequently without symptoms. Initial bronchoscopic assessment in 2001 confirmed multiple large nodular lesions along the laryngeal and upper tracheal wall without major airway narrowing. Biopsy of the laryngeal nodules showed subepithelial deposits of amorphous eosinophilic materials consistent with amyloid. These materials revealed apple-green birefringence on Congo red stain that confirmed the diagnosis.

Repeat bronchoscopic evaluation in 2013 demonstrated progressive infiltration of amyloid to the lower trachea (Fig. 1). The laryngeal features remained unchanged. However, there had been no symptom progression. The spirometry was within normal limits. Evaluation of heart, liver, and kidneys did not detect systemic involvement.

Investigations

Myeloma, vasculitic, and connective tissue screens were negative. Tuberculosis, sarcoidosis, and other granulomatous disease were excluded. A diagnosis of primary (AL) amyloidosis was made.

Noncontrast dynamic volume 4-D CT (Aquilion One, Toshiba Medical Systems, Tokyo, Japan) of this patient's larynx and trachea over a distance of 16 cm was performed to investigate the cause of dysphonia. Scanning parameters were 80 kVp, 300–350 mA, gantry rotation of 0.35 s, and radiation dose of 1.2 mSv. Multiplanar and three-dimensional (3-D) images over the duration of breathing cycle were generated at 0.35-s interval. The 3-D images could be viewed on workstation in cine 4-D mode.

The CT scan confirmed diffuse circumferential nodular wall thickening in keeping with amyloid deposits along the larynx, trachea, and main bronchi giving rise to a very

irregular luminal contour of the entire major airway that was more pronounced in the subglottic and upper trachea around the thoracic inlet (Fig. 2). There was no definite vocal cord involvement. The tracheal wall was markedly infiltrated and measuring 5 mm in thickness. Tracheobronchomegaly was also recognized on the CT with tracheal dimensions of 40 mm in coronal and 32 mm in sagittal diameters (the upper limits of normal for coronal and sagittal tracheal diameters in men aged 20–79: 25 and 27 mm, respectively) [1]. Tracheal luminal diameter excluding wall measured 33 mm in coronal and 20 mm in sagittal diameters. The 4-D CT showed no paradoxical vocal cord movement during breathing and phonation.

Despite dilatation, there was no apparent loss of structural integrity of his major airway on the 4-D CT. In particular, there was no excessive dynamic airway collapse or excessive rigidity. Normal movement of trachea during breathing was evident on 4-D CT (Fig. 3).

Discussion

Primary tracheobronchial amyloidosis is a very uncommon disease entity. A literature review in 1983 identified only 67 cases worldwide. Fifty-seven of which were diffusely infiltrative and the remainders were nodular or “tumor like.” The disorder has been associated with tracheobronchopathia osteoplastica, which is characterized by calcified or cartilaginous submucosal nodules within the airways. Tracheobronchial amyloidosis typically presents after the fifth decade with dyspnea, cough, and, occasionally, hemoptysis. Narrowing of the airways may occur and can cause distal atelectasis or recurrent pneumonia and solitary nodules may be mistaken for endobronchial neoplasia [2]. Recent advent of 320 slice multidetector CT has enabled 4-D study of laryngeal and tracheal functional disorders, including laryngeal dysfunction, excessive dynamic airway collapse, and tracheobronchomalacia [3]. The patient was referred for the 4-D CT since his dysphonia raised concern about amyloid infiltration of the larynx that might impair



Figure 1. Bronchoscopy surveillance – amyloid involving trachea.

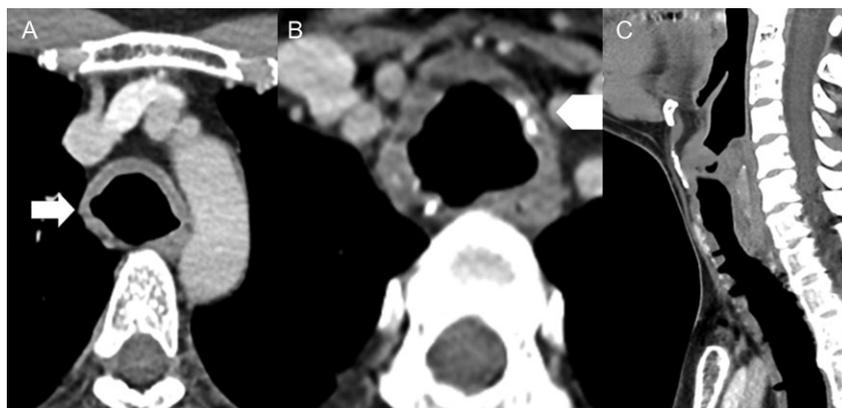


Figure 2. (A–C) Axial images at different levels (A and B) and sagittal image in midline from the noncontrast four-dimensional computed tomography showed diffusely and irregularly thickened laryngeal and tracheal wall that contained foci of calcifications, and tracheomegaly.

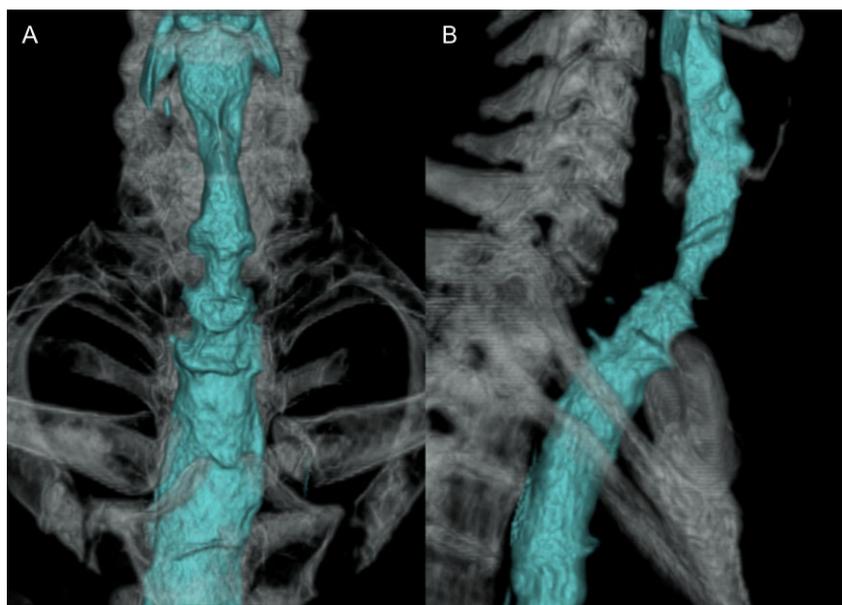


Figure 3. (A, B) Representative images of the four-dimensional computed tomography in coronal (A) and sagittal (B) reformats of the laryngeal and tracheal airway confirmed the very irregular airway contour and tracheomegaly secondary to amyloidosis. There was no wall movement disorder, such as airway collapse or rigidity on cine images.

proper vocal cord function. Despite the clinical symptoms of hoarseness in this patient, there was no abnormal or paradoxical vocal cord movement during phonation and respiration. The hoarseness appeared to be related to thickened supraglottic tissue encroaching on the laryngeal aperture. The laryngeal and tracheal wall was heavily infiltrated with amyloidosis that resulted in an irregularly tortuous and dilated major airway contour. Tracheal dilatation would be best explained by the loss of integrity of the tracheal wall secondary to amyloid infiltration. Surprisingly, there was no tracheal wall movement abnormality, either excessive dynamic airway collapse or rigidity.

Tracheobronchomegaly itself is a rare disorder of the major airways characterized by marked dilatation of the trachea and central bronchi. It is associated with impaired dynamic function, in particular dynamic collapse. Tracheomegaly was first described by Czyhlarz in a series of autopsy studies [4]. Mounier-Kuhn later correlated the endoscopic and radiographic appearances in 1932 [5]. The most common causes include congenital and connective tissue disorders (Ehlers–Danlos, cutis laxa, Marfan syndrome, Kenny–Caffey syndrome). Rarely, sarcoidosis, usual interstitial pneumonia, and cystic fibrosis may cause sufficient fibrotic traction of the central airways to produce

tracheal enlargement. Amyloidosis also appears to cause tracheobronchomegaly as shown in our patient.

To our knowledge, this is the first report in the literature that demonstrates these combined characteristics in this rare airway infiltrative disorder. The CT scan findings might help to explain the lack of dyspnea and preservation of lung function in this patient despite extensive infiltration being present. The findings might also help to conclude a more favorable intermediate prognosis in this patient.

Treatment

In the absence of symptoms and systemic involvement, monitoring clinically without specific treatment was undertaken.

Learning Points/Take Home Messages

To our knowledge, this is the first report of tracheobronchomegaly in primary amyloidosis and the use of 4-D CT in dynamic airway assessment for this condition. Despite tracheobronchomegaly and very irregular and diffuse amyloid wall infiltration, there has been no functional disorder on the CT or abnormal spirometry result. These indicate a favorable prognostic outcome as shown in our patient who has had this condition for 18 years.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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