Case Report

Radiological appearance of primary laryngotracheal amyloidosis

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ABSTRACT

Primary laryngotracheal amyloidosis is a rare entity and can present with a very nonspecific symptom such as hoarseness of voice. We present one such case highlighting the radiological appearance with follow-up imaging so that one can identify computed tomography features of this rare entity if other clinical and histological conditions are met.

KEY WORDS: Amyloidosis, hoarseness, larynx, trachea

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INTRODUCTION

Hoarseness is a common symptom of altered voice quality, experienced by many, at least at some point in life. Generally, it is managed clinically with no major role of imaging. According to the American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guidelines, cross-sectional imaging is not advised for patients with a primary complaint related to voice, before visualization of the larynx.[1] Of the focal lesions causing hoarseness, primary laryngotracheal amyloidosis is an extremely rare diagnosis. Primary (light chain, amyloid light chain [AL] type) amyloidosis can have a prevalence up to 10 cases per million patient years, 15% of which may have only a localized involvement.[2] Isolated primary laryngeal amyloidosis conforms to just about 1% of all the primary disease spectrum.[3] We report this case of primary laryngotracheal amyloidosis, with an intention to highlight the imaging appearances and its unexpected euphemistic clinical presentation.

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CASE REPORT

A 47-year-old male, nonsmoker, presented with the painless change in voice, with hoarseness of about 2-year duration. There were no associated features suggestive of dyspnea, dysphagia, respiratory wheeze, or neck masses. A detailed clinical examination and relevant biochemical and hematological investigations did not reveal any abnormality. Posteroanterior view radiograph of a chest and abdominal ultrasound scan findings at that time were unremarkable as well.

Initial indirect laryngoscopy revealed a congested polypoidal glottic lesion involving the anterior third of right true vocal cord with contiguous extension to the anterior commissure. Partial encasement of left true and false vocal cords was also present. Another friable, ill-defined subglottic lesion was seen with focal ulcerations and diffuse mucosal congestion in the vicinity. Significant airway compromise was noticed due to anteroposteriorly

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collapsed wall, and a tracheostomy was performed. The biopsy was taken from the vocal cord, subglottic lesion, and proximal trachea.

To see the entire extent of the lesions and for further characterization, a contrast-enhanced computed tomography (CT) scan was performed from the base of the skull to carinal level [Figure 1]. Homogenously and mildly enhancing soft-tissue thickening was present involving true as well as false vocal cords (right > left) and anterior commissure with loss of discrete contours of bilateral paraglottic fat. No extralaryngeal or laryngeal cartilaginous infiltration was present. Neither transmural infiltration of airway nor significant cervical and mediastinal lymphadenopathy was appreciated. Significant subglottic airway luminal compromise was evident with anteroposteriorly compressed, posteriorly concave crescent-shaped lumen (minimum AP distance of ~3.1 mm) with adhesions therein. Contiguous, mildly enhancing, circumferential diffuse wall-thickening was observed caudally, beyond the tracheostomy tube involving the proximal trachea. On lung window images, there were no discernible air bronchograms, cavitation, parenchymal nodules, or ground glass opacities.

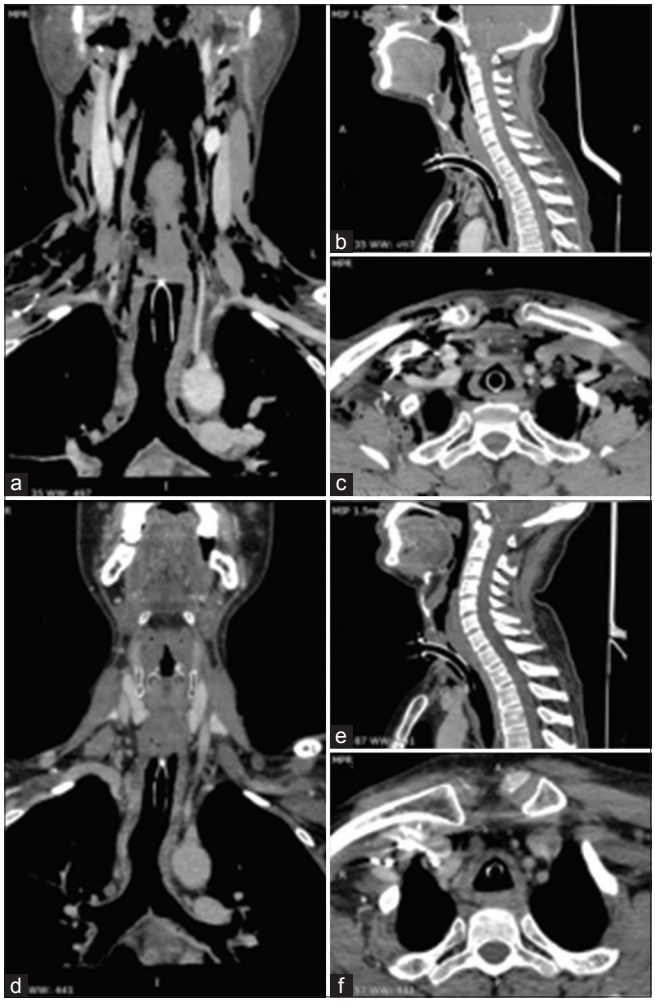

Figure 1: Multiplanar reformats of contrast-enhanced computed tomography neck (a-c) initial study of February 2017; (d-f) follow-up study of February 2018. (a) Oblique coronal – diffuse, uniformly enhancing tracheal wall thickening up to carina. (b) Sagittal – tracheostomy tube *in situ* and with diffuse laryngotracheal wall thickening. (c) Axial – circumferential involvement without sparing the posterior tracheal wall; (d-f) reformats at same levels showing the persistence of circumferential wall thickening and extent of disease. Tracheostomy related subcutaneous emphysema seen on the initial study is resolved on follow-up images

While on follow-up, fiber-optic bronchoscopy revealed diffuse mucosal congestion in trachea and carina with no focal mass lesions. No contiguous involvement of the main bronchi or distal airway was observed. Biopsies were obtained from the larynx and tracheal walls. Histopathologic examination revealed abundant subepithelial pale eosinophilic material which showed characteristic apple-green birefringence under a polarizing light, characteristic of amyloidosis [Figure 2].

Follow-up assessment after 1 year by direct laryngoscopy under general anesthesia was performed with a plan of extubating the tracheostomy tube. Vocal cord lesions were persistent, with mild improvement in the prolapse of subglottis with ~75% stenosis. There was no significant change in the extent of the disease. Contrast-enhanced CT scan at this time also exhibited the persistence of the diffuse wall thickening confined to the laryngotracheal airway. The patient was extubated with advice for follow-up with counseling about the significance of his airway-related symptoms and plan for interval laser therapy.

DISCUSSION

The term "amyloid," popularized by Virchow, means "starch-like," indicating the contents and staining

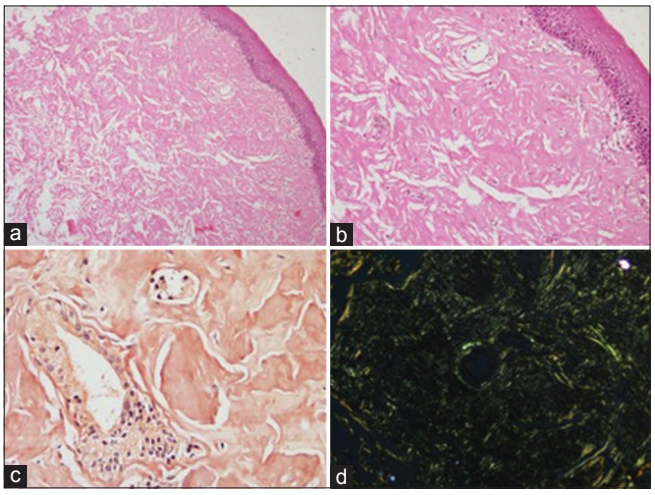

Figure 2: (a) Low magnification showing abundant pale eosinophilic material present in the subepithelium (H and E, ×100); (b) no dysplasia is noted in the overlying epithelium. Pale eosinophilic material is also seen around the subepithelial capillaries (H and E, ×200); (c) pale eosinophilic material demonstrates positivity with Congo-red stain (Congo-red, ×400); (d) characteristic apple-green birefringence for amyloid noted with polarizing light (Congo-red, ×200)

patterns, initially observed in the organ deposits.[4] For the first time in 1877, Lesser described the amyloid deposits limited to the inferior respiratory tract, incidentally found on autopsy.[5] Amyloidosis is now found to be due to abnormal folding of the protein which forms insoluble aggregates in the extracellular compartment. Anomalously folded glycosaminoglycan, fibril proteins, and amyloid *P* into a β-pleated sheet are a sine qua non for its formation. Both amyloid fibril nomenclature and the clinical classification are aptly done by chemical identity of the amyloid fibril-forming protein.[6] Characteristically, there is retention of Congo red dye and a red-green birefringence under the polarized light when viewed with a microscope.

As described by Stark and New (1949), the three forms of primary laryngeal amyloidosis are diffuse subepithelial infiltration, tumor-forming, and amyloid degeneration in a preexisting tumor.[7] While the larynx is otherwise shown to be the most common site in head-and-neck region for secondary, nodular, or mass-like amyloid deposition, tracheobronchial distribution is more often found in the primary diffuse form of the disease. Both the upper and lower airway primary amyloidoses do not usually coexist in similar forms. Clinical presentation in primary airway forms can vary from a dry cough, dysphagia, hoarseness of voice, and even chest pain to a life-threatening airway obstruction. Hence, the disease entity may be misdiagnosed as recalcitrant asthma, chronic obstructive pulmonary disease, or recurrent pneumonia.[8] Dabholkar *et al*. described a mass-like glottic lesion requiring tracheostomy and surgical excision.[9] Lanks *et al*. reported a primary (AL) form of localized laryngotracheal amyloidosis with anatomical extent, similar to our case, but with the presence of preexisting bronchiectasis (AA form) in both lungs.[2] Our patient had a combination of a friable focal subglottic growth as well as a diffuse subepithelial involvement of larynx and trachea.

For primary laryngotracheal amyloidosis, an absence of abnormal chest radiograph findings and of significant cervical lymphadenopathy of the neck-ultrasound in the presence of positive laryngoscopy findings is the initial cue on imaging. On CT scan images, laryngeal lesions can be varied; frank mass lesions, mimicking primary or secondary malignancies to minimal mucosal thickening contiguous with the tracheal airway. Diffuse tracheal wall thickening with uniform hyperdensity and homogenous mild contrast enhancement is the most common feature; however, irregular nodularity may also be associated at places. In our patient, the presence of tracheostomy and procedure-related subcutaneous emphysema were added confounding factors on the initial CT scan for interpreting the diffuse wall thickening. Infective laryngotracheitis, radiation injury, and submucosal tumor spread were possible differentials for the same. The abrupt change of wall morphology to normal at the carinal level, lack of characteristic mucosal stratification, and absence of transmural infiltration in the same scan images and temporal persistence of the extent and morphology after about 1 year on follow-up CT scan were the imaging pointers to the diagnosis. Characteristically, there is no sparing of the posterior wall, thus differentiating the localized amyloidosis from tracheal cartilage inflicting disorders such as tracheobronchopathia osteochondroplastica or relapsing polychondritis. No focal nodularity, polypoidal growths, or infiltrative transmural lesions are usually discernible, unlike the tumors affecting the respiratory epithelium.

Diagnostic approach of primary airway amyloidosis follows that of a local malignant lesion until a suspicious finding and histopathology surprise the clinician. Its final diagnosis is established by a combination of indirect laryngoscopy; contrast-enhanced CT scan of neck and chest, fiber-optic bronchoscopy, and histopathologic confirmation of biopsied tissue from multiple apt sites. An extensive investigation for an inciting systemic cause as well as follow-up for the same should remain the management strategy.

CONCLUSIONS

Primary amyloidosis of larynx and trachea is a rare diagnosis with varied clinical presentations. It may have a benign natural course, with trivial symptoms and signs. It remains amenable to elective management strategies; before a potentially catastrophic airway obstruction ensues. A high index of suspicion with inputs from involved specialties and apt staining at histopathology are needed to diagnose it definitively. An extensive search for a systemic inciting cause needs to be performed when the histopathologic diagnosis is established.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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