Isolated laryngeal amyloidosis: a case report

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Received 8 February 2018
Accepted 21 May 2018

The Egyptian Journal of Otolaryngology
2018, 34:359–362

Background
Amyloidosis is extracellular deposition of an amorphous amyloid substance in various tissues. It can occur in any bodily organ. Clinically, it is divided into systemic and solitary amyloidosis. Isolated laryngeal amyloidosis is very rare in prevalence. We report a case of isolated laryngeal amyloidosis in a healthy 54-year-old lady who presented chronic dysphonia for 2 years with no history of smoking or alcohol intake. The histological, immunohistochemical study and further examinations confirmed the diagnosis of isolated laryngeal amyloidosis without systemic involvement. The larynx is a rare site for isolated laryngeal amyloidosis. Hoarseness or dysphonia is the main presentation of this disease, followed by difficulty in breathing, stridor, and chronic cough. Laryngoscopy may falsely suggest a neoplastic disease. Histopathology is the gold standard diagnostic tool to diagnose this disease. Amyloid can be identified histologically as subepithelial extracellular deposits of acellular, homogeneous, and amorphous eosinophilic material displaying apple–green birefringence with polarized light when stained with Congo red. Surgery is the mainstay of treatment of symptomatic laryngeal amyloidosis. The survival of patients with laryngeal amyloidosis often exceeds 10 years and the prognosis is better than systemic amyloidosis.

Keywords:
amyloidosis, Congo red, hoarseness, laryngeal neoplasms

Egypt J Otolaryngol 34:359–362

1012-5574

Introduction

Amyloidosis comprises a heterogeneous group of disorders characterized by the deposition of amyloid protein in various target organs of the body that can lead to organ malfunction and failure if there is extensive deposition of this amyloid protein [1]. Amyloid deposition can be anywhere in the body and in the head and neck region particularly, larynx is a rare site for localization of amyloidosis, where it represents only about 0.17–1.2% of benign laryngeal tumors [2]. Other sites of amyloid deposition in the head and neck regions include the eye, and the major and minor salivary glands, whereas submucosal deposits have been observed in the nose, paranasal cavities, nasopharynx, oral cavity, tracheobronchial tree, and lungs. Oral and paranasal amyloidosis is usually a manifestation of systematic amyloidosis, mainly plasma cell dyscrasia [3].

Hoarseness is the main presentation in a patient with amyloidosis of the larynx. The deposition of amyloid may occur either diffusely or in a single tumor nodule. Tissue biopsy is the 'gold standard' investigation for the diagnosis of amyloidosis. Amyloid can be identified histologically as subepithelial extracellular deposits of acellular, homogeneous, and amorphous eosinophilic material displaying apple–green birefringence with polarized light when stained with Congo red or it is metachromatic with crystal violet or methyl violet.

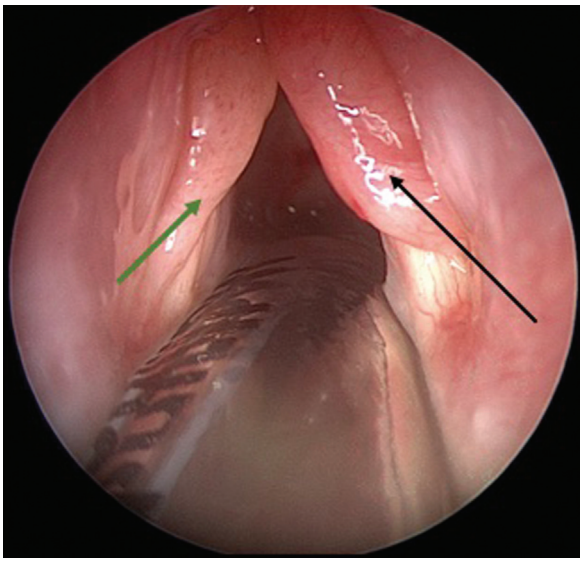
Here, we report a case of isolated laryngeal amyloidosis in a 54-year-old lady who is presented with persistent hoarseness for 2 years.

Case report

A 54-year-old Chinese lady, who is a teacher, complained of persistent hoarseness for 2 years before presentation to our clinic. Perceptual voice assessment using GRBAS revealed overall dysphonia grade 3, main component of strain (roughness=2, breathiness=1, asthenia=2, and strain=3). There was neither history of breathing difficulty or noisy breathing, nor painful deglutition or swallowing. A 70° rigid laryngoscopy revealed a diffuse erythematous mass at the laryngeal surface of the epiglottis and bilateral false cord. Systemic examinations revealed no generalized lymphadenopathy or hepatosplenomegaly. The patient underwent direct laryngoscopy, laser surgery, and debulking twice in 2012 and 2017. Intraoperatively, multiple broad-based polypoidal masses were found arising from the right ventricle, left vocal cord, and laryngeal surface of the epiglottis (Figs 1 and 2). Histological sections revealed a

tissue segment showing nodular fragments of fibrocollagenous tissue lined focally by stratified squamous epithelium that contain a cluster of amorphous eosinophilic material which are positive for the Congo red stain and show apple–green birefringence with polarized light (Figs 3 and 4). Further examinations were performed to rule out systemic amyloidosis and multiple myeloma. Complete blood counts, erythrocyte sedimentation rate, liver and renal function test, serum calcium, and serum and urine electrophoresis were within normal limits. Office follow-up at 2 months following the second debulking showed improvement in the GRBAS score, with overall dysphonia grade 2, main component of the strain (roughness=1, breathiness=1, asthenia=1, and strain=2).In addition, at 5-year follow-up from the initial diagnosis, no progression to systemic amyloidosis was observed.

Figure 1

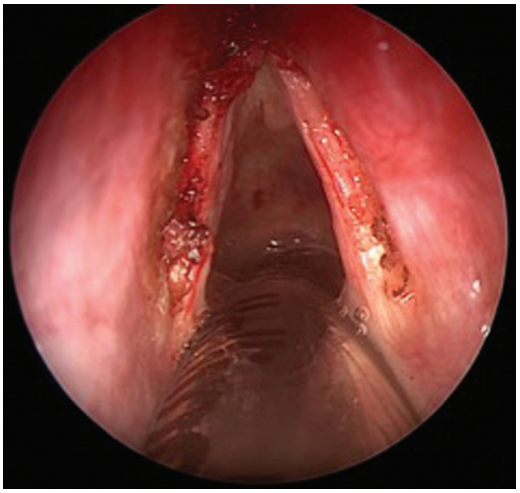


Laryngeal amyloidosis; right pedunculated mass arises from the right ventricle (black arrow) and broad base mass arises from the left true cord (green arrow).

Discussion

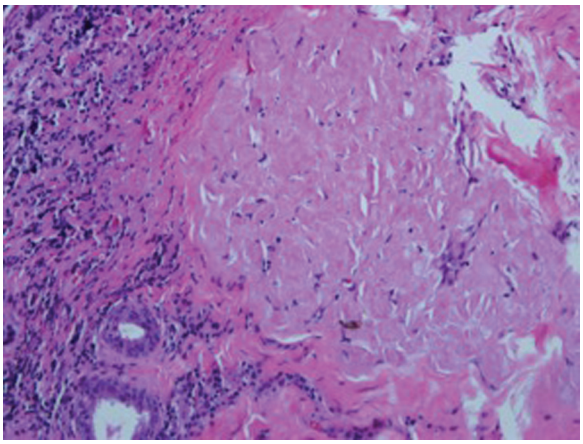
Amyloidosis occurs due to the deposition of insoluble proteinaceous material that has typical staining properties and electron microscopic appearance. When observed under the microscope, it will show a diffuse submucosal globular deposition of a largely acellular eosinophilic material that exhibits apple–green birefringence under polarized light when stained with Congo red. Under the electron microscope, amyloid appears as a mass of rigid, nonbranching fibrils. Meanwhile, radiographic crystallography reveals that these fibrils have a regular, antiparallel, β-pleated sheet configuration.

Figure 2



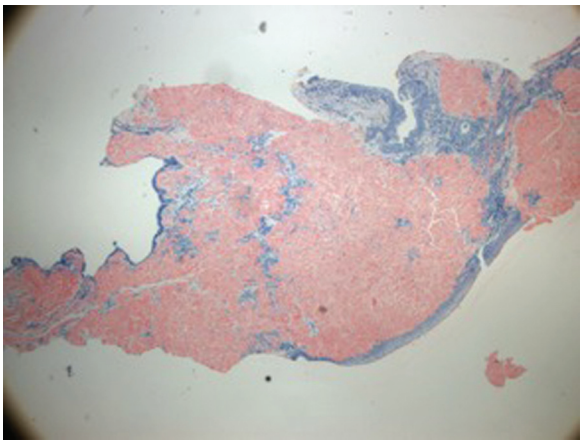
Laryngeal amyloidosis postablation using CO_2 laser.

Figure 3



Histologic examination showing homogenous eosinophilic deposits in the stroma.

Figure 4



Apple–green birefringence with Congo red stain confirmed the diagnosis of amyloidosis.

There are few types of recognized amyloidosis. They are (i) AL (amyloid light chain) primary amyloidosis is derived from plasma cells and contains kappa or lambda immunoglobulin light chains. It may be localized or systemically associated with myeloma. (ii) Amyloid-associated amyloidosis is a nonimmunoglobulin protein synthesized by the liver. It is a reactive systemic amyloidosis associated with acquired or hereditary chronic inflammatory diseases. (iii) AB amyloidosis is the cerebrovascular and intracerebral plaque amyloid in Alzheimer's disease and occasional familial disease. Clinical forms can be divided into systemic and localized amyloidosis, with systemic form being more common than the isolated form [4]. The isolated forms affect mainly the abdominal organs and structures of the head and neck, especially the larynx, which is the most common site of isolated amyloidosis in the head and neck region [4].

Clinical presentation depends on the anatomical site and extension of the disease. Clinically, patient will be presented with hoarseness or dysphonia. Besides that, patients also can present shortness of breath, stridor, persistent dry cough, obstructive sleep apnea symptoms, hemoptysis, or dysphagia [5,6].

Two theories have been postulated to explain the occurrence of localized or isolated laryngeal amyloidosis. The first suggests a plasma cell reaction to inflammatory antigens giving rise to amyloid deposits. This theory was supported by pathologic studies showing the presence of mixed polyclonal plasma cells interspersed with the amyloid tissue. Second theory points to the inability of the body to clear the light chains produced by plasma cells located in the mucosal-associated lymphoid tissue [7].

Systemic disease should be ruled out in the case of laryngeal amyloidosis. Therefore, full and proper investigation and workup should be done, as well as an accurate assessment of the laryngeal involvement should be carried out. There are few systemic causes such as multiple myeloma, rheumatic diseases, and tuberculosis that should be considered. The workup should include a chest radiograph, tuberculin skin test, full blood cell count, renal profiles, liver enzyme, erythrocyte sedimentation rate, serum rheumatoid factor, urinalysis, and antinuclear antibody.

Treatment modalities of laryngeal amyloidosis vary from continuous observation of the lesion to partial laryngectomy, according to the extension of the disease into the larynx. Endoscopic CO_2 laser excision of the mass is the main surgery of choice for this disease. CO_2 laser and cold instruments can be used to remove the localized lesions at the larynx [8]. The use of CO_2 laser tends to be effective because of its ability to vaporize high fluid content within the deposits. Even with surgical resection either through cold instruments or CO_2 laser method, recurrence still can occur. Recurrences usually occur within 5 years after the treatment, but sometimes more than that or very late [4]. In view of that, regular follow-up is indicated for early diagnosis of recurrence, and multiple surgical procedures may be needed [1]. In our case, the patient needs the second surgery after 5 years, in view of progressive hoarseness and voice fatigue.

Medical treatment also had been used to treat this disease and the treatment options that have been described include corticosteroids, radiotherapy, and agents like colchicine and melphalan. However, these modalities have showed inconsistent and variable results [9,10]. The survival of patients with laryngeal amyloidosis often exceeds 10 years and it is better than in patients with systemic amyloidosis.

Conclusion

Laryngeal amyloidosis is an uncommon disorder that usually represents an isolated form of amyloidosis. Recurrence of laryngeal amyloidosis is common. Conservative surgical intervention to maintain laryngeal function for as long as possible is indicated. The prognosis of isolated laryngeal amyloidosis is much better than systemic forms.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflict of interest.

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