Extensive laryngeal amyloidosis presenting with stridor: Review of literature and case presentation

Hani M. Almuslim a,*, Nada A. Alshaikh b

a Department of Otolaryngology Head and Neck Surgery, University of Dammam, Saudi Arabia
b Department of Otolaryngology Head and Neck Surgery, Dammam Medical Complex, Saudi Arabia

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Abstract  Background: Laryngeal amyloidosis is a rare disease with poorly understood etiology. It accounts for 0.2–1.2% of benign laryngeal tumors and usually appears as an isolated localized laryngeal amyloidosis, but can also be part of systemic amyloidosis.

Method: Case report of extensive localized laryngeal amyloidosis with discussion and literature review.

Results: 35-year-old woman presented to our ENT clinic with history of progressive hoarseness over 2-years duration associated with shortness of breath during the last month before presentation. Clinic based endoscopy showed bilateral mobile vocal cords with subglottic mass. Computed tomography scan showed a subglottic non-invasive polypoidal mass with no cartilage invasion or lymphadenopathy. Microlaryngoscopy and biopsy of the mass were performed and histopathology confirmed the diagnosis of amyloidosis with Congo red stain. There was no clinical nor laboratory evidence for systemic involvement. Patient was managed by surgical excision of the mass and long term follow-up.

Conclusion: Localized laryngeal amyloidosis, although rare, must be considered among the differentials of benign laryngeal tumors. Complete clinical examination and laboratory investigations to exclude systemic involvement are of paramount value since treatment and prognosis differs markedly.

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1. Introduction

Amyloidosis is a heterogeneous family group of disorders characterized by extracellular pertinacious deposits in various target organs of the body.\(^1\) This process can be localized to one organ or can be a part of systemic involvement.\(^2\)

Localized laryngeal amyloidosis is rare, accounts for 0.2–1.2% of benign laryngeal tumors.\(^3\) It is a subepithelial extracellular deposits of acellular, homogenous, and amorphous eosinophilic material displaying apple green birefringence under polarized light when stained with Congo red dye.\(^4\)

Symptoms are largely dependent on the location and the size of deposits.\(^1\) Typically, the usual manifested symptom is progressive dysphonia.\(^1\) However, deposition sometimes can be extensive leading to alerting symptoms and signs that requires urgent surgical intervention.

The aim of this article is to report an unusual case of isolated extensive laryngeal amyloidosis and to provide a review of the literature regarding the diagnosis and management of laryngeal amyloidosis.

2. Case presentation

35-year-old seven-month pregnant woman who is a house-wife with 5 children presented to our ENT clinic with history of progressive hoarseness of 2 years duration. She gave history of heart burn and occasional epigastric pain. Initially, endoscopic examination showed severely congested and swollen arytenoids with free mobile vocal cords. Accordingly, she was managed as a case of gastroesophageal reflux disease (GERD) with proton pump inhibitor, life style modifications to reduce GERD, and was advised for voice rest. She was also referred for speech therapy and for further evaluation by gastroenterologist. Three months post-partum, her symptoms did not improve. Hoarseness became worse and was accompanied by progressive shortness of breath with occasional biphasic stridor despite her compliance with treatment. The endoscopic examination showed granulomatous polypidal lesions extending from the undersurface of both vocal folds down to subglottic region causing Cotton grade II subglottic stenosis (Fig. 1).

Computed tomography scan with contrast showed localized subglottic polypoidal non-enhanced soft tissue lesion sparing the posterior wall of the subglottis with no evidence of cartilage invasion or cervical lymphadenopathy (Fig. 2). She was managed surgically with initial tracheostomy followed by microlaryngoscopy and multiple biopsies from the lesion which extensively involved the anterior subglottic region (Fig. 3). The histopathology examination showed evidence of amyloidosis that was confirmed with positive Congo-red stain (Figs. 4 and 5).

Patient underwent thorough clinical examination and extensive laboratory work-up including chest X-ray, echocardiogram, complete blood count, renal function test, liver function test, urine analysis, 24-h urine collection for protein and creatinine, urine protein electrophoresis, plasma protein electrophoresis, urine- and serum-immunofixation tests, but they were all within normal limits. As such, there was no clinical nor laboratory evidence for systemic amyloidosis. A second microlaryngoscopy 3-weeks later showed small remnants of subglottic amyloid deposits anteriorly with new deposits on the right arytenoid. They were removed using cup forceps and were all stained positive with Congo red. Final diagnosis was localized multi-focal laryngeal amyloidosis.

Two weeks later, flexible fiberoptic examination showed normal looking larynx with no evidence of remnant or recurrent amyloidosis. As such, she was decanuulated successfully. Her voice showed marked improvement and she was advised to continue speech therapy and regular follow-up at the clinic for early detection and management of potential recurrence.

3. Discussion

Amyloidosis is a rare benign disease characterized by extracellular deposition of proteinaceous material in the targeted tissue.\(^5\) Amyloidosis is classified clinically into systemic and localized types. Approximately, 10–20% of reported cases are localized.\(^1\) The first reported case of laryngeal amyloidosis was on 1873 by Borow.\(^4\) In Saudi Arabia single case was reported on 1996 by Shamim et al.\(^5\) Systemic amyloidosis is

Figure 1 Granulomatous polypidal lesions extending from the undersurface of both vocal folds down to subglottic region.
Further divided into hereditary, idiopathic (primary), and secondary (reactive) systemic amyloidosis. Etiology remains unknown, but the understanding of biochemical mark-up of amyloidosis improved markedly. Thus, a new classification of amyloidosis includes 15 different biochemical forms. However, the three most common types are light chain amyloidosis (AL) which is derived from plasma cell containing kappa or lambda immunoglobulin light chains and presents as either localized or systemic disease in association with myeloma, amyloid associated amyloidosis (AA) which is a non-immunoglobulin hereditary chronic inflammatory disease, and AB amyloidosis which is characterized by the presence of beta 2-microglobulin in the amyloid fibrils.

Amyloidosis of the head and neck can be either primary isolated disease or secondary to systemic involvement. Sites of localized head and neck involvement by amyloidosis include larynx, nasopharynx, oropharynx, oral cavity, salivary glands, nose, paranasal sinuses, eye, and tracheobronchial tree. Larynx is the most common site of involvement in the head and neck region and is more commonly affected by localized rather than systemic amyloidosis. Localized laryngeal amyloidosis is characterized by monoclonal deposits of the light chain type (AL).

The peak incident of localized laryngeal amyloidosis is between the fifth and the sixth decades of life. Males are predominantly affected with a male to female ratio of 3:1. Clinical presentation is strongly related to site and size of lesion. The most affected site of the larynx is the supraglottis including ventricles and false cords. Accordingly, the commonest presenting symptom is hoarseness. However, it may also present with dyspnea, dysphagia, and stridor. When stridor is the presenting symptom, urgent airway management is indicated. In our reported case, the patient presented with progressive hoarseness and eventually with shortness of breath and stridor that necessitates an urgent tracheostomy to secure the airway.

Definitive diagnosis of amyloidosis requires tissue biopsy and histological examination with Congo red and immunohistochemical staining which look red or pink in color under normal light and characteristic apple green birefringence under polarized light.

The role of radiological studies in the diagnosis of localized laryngeal amyloidosis is supportive and relies on the exclusion...
of other pathologies such as granulomatous diseases and malignancies. Nevertheless, amyloidosis is demonstrated on computed tomography scan as marked thickening of the laryngeal structures with high density as measured with Hounsfield units. MRI, however, is the radiological investigation of choice. Laryngeal amyloidosis appears as an intermediate signal on T1 weighted MRI scan and low signal intensity on T2 weighted MRI scan similar to that of skeletal muscles. This is because protein fibrils of amyloid deposits lie in the form of parallel sheets similar to the organization of the skeletal muscle fibers.

Once the diagnosis of laryngeal amyloidosis has been established, work up should be carried out to exclude systemic involvement. Localized laryngeal amyloidosis has excellent prognosis, in contrast to the poor prognosis associated with systemic disease. Systematic work-up has a wide range of laboratory, imaging, and invasive investigations. Lewis et al. studied 22 patients diagnosed with laryngeal amyloidosis during the period 1950–1988. As a result, they recommended the performance of both urine and serum electrophoresis in order to rule out systemic involvement. Invasive investigations such as bone marrow and bowel biopsies are not necessarily indicated as the vast majority of cases of laryngeal amyloidosis are actually localized in nature.

The treatment of localized laryngeal amyloidosis is a surgical excision. Different approaches have been described in the literature varying from external approach to more conservative endoscopic excision using cold knife or CO2 laser. Endoscopic CO2 laser excision has been shown to result in good control of the disease. However, recurrence may occur after long period of time either locally or in multifocal manner, and rarely as a systemic disease. Due to the recurrent slowly progressive nature of the disease, a long term follow-up with regular clinic based endoscopic examination is strongly recommended.

4. Conclusion
Laryngeal amyloidosis is a slowly progressive disease and must be considered in patients with long standing hoarseness that is not improving with maximum medical treatment. Tissue biopsy is required for definitive diagnosis which is confirmed histologically using Congo red stain. Despite rarity, systemic amyloidosis must be ruled out in all cases of laryngeal involvement. Finally, long-term follow up is an important part of the management of the disease.

References