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Laryngeal Amyloidosis – Challenging Diagnosis and Management

ABSTRACT

Amyloidosis is a benign process with systemic or localized extracellular deposition of fibrillar, proteinaceous material. We report two cases of isolated laryngeal amyloidosis from our case series of 13 over the past decade, one highlighting its challenging diagnosis and the other focusing on the challenging management of this condition.

Key words: Amyloidosis, Larynx, Laser surgery, Phonosurgery

INTRODUCTION

"Amyloidosis" stems from the word 'amylon', introduced by Virchow, referring to the starch-like reaction on treatment with iodine and sulfuric acid.[1] Although it occurs more frequently in men than women,[2] in our center, an incidence of seven females and six males was found over the past decade. The most common sites affected in the larynx are the ventricles (55%), followed by false vocal folds (36%), subglottis (36%), true vocal folds (27%), arytenoids (23%), and anterior commissure (14%).[3] Clinically, two types of laryngeal deposits are described; discrete tumor nodule or diffuse subepithelial disease.[4] Grossly, amyloid-laden tissue appears as non-ulcerated, yellow-orange or gray-hued sub-mucosal lesion. Three distinct forms of amyloidosis are described; AL (amyloid light-chain) derived from plasma cells, amyloid-associated non-immunoglobulin protein synthesized in the liver, and A-beta found in cerebral lesions.

Diagnosis of laryngeal amyloidosis may be challenging not only due to its variable presentation but also as a result of its low incidence in the practice of an otorhinolaryngologist. In our dedicated voice and swallowing center, we have seen only 13 cases of laryngeal amyloidosis in the past decade. Although frozen-section sometimes suggests only granulation tissue or a foreign-body type of reaction,[5] all 13 of our cases were identified accurately and reconfirmed on histopathology and Congo red staining followed by visualization of apple-green birefringence under polarized light. As treatment is primarily surgical excision, a frozen report indicting the diagnosis at the very first surgical sitting can accomplish complete surgery, or staged surgery, in case of extensive disease. The aim of treatment is to obtain a prolonged disease-free interval while preserving voice, breathing, and swallowing.

From our cohort of 13 cases, we present two cases of isolated laryngeal amyloidosis; one representing the challenges posed during diagnosis while the other represents the challenging management of the disease.

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CASE A

A 66-year-old male with a gradual voice change since one year had undergone a laryngeal biopsy at another center, which reported unremarkable salivary gland tissue. A month later, the patient presented to us with worsening hoarseness. Laryngoscopy revealed, non-ulcerated, pale yellow, subepithelial deposits in the infraglottic region in a circumferential pattern [Figure 1]. On stroboscopy, it was noted that the infraglottic amyloidosis interfered with the lower lip formation of the mucosal waves resulting in hoarseness of voice, even though the vocal folds were otherwise mobile with normal adduction and abduction. The yellow-tinged subepithelial appearance and previous biopsy negative for neoplasm led us to consider the possibility of amyloidosis. The patient was advised staged excision of the lesion. Histopathology confirmed the diagnosis.

CASE B

A 22-year-old male presented with a gradual hoarseness over seven years. Laryngoscopy revealed bilateral, yellow-gray subepithelial smooth lesions causing massive enlargement of the false vocal folds hampering visualization of true vocal folds [Figure 2a]. High-resolution computed tomography scan of the neck suggested extensive dystrophic calcifications involving the bulky false vocal folds, aryepiglottic folds,

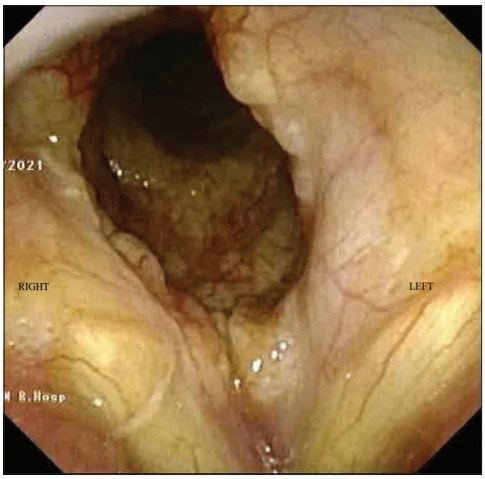

Figure 1: Laryngoscopy picture of patient A, revealing pale-yellow sub-epithelial infraglottic circumferential lesions

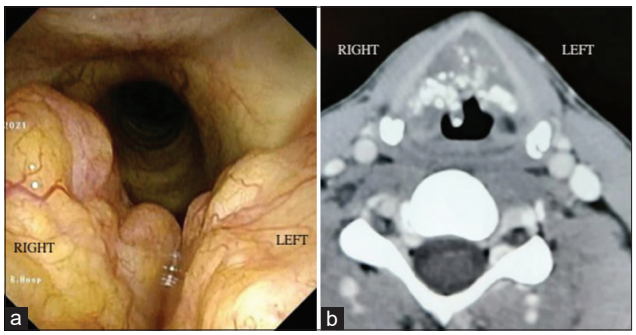

Figure 2: (a) Laryngoscopy picture of patient B, revealing bilateral bulky false vocal folds, hampering visualization of the true vocal folds. (b) HRCT image of patient B, showing extensive dystrophic calcifications within the bulky false vocal folds with no destruction of the thyroid cartilage

right true vocal fold, and right posterolateral wall of subglottis [Figure 2b]. Staged carbon dioxide laser excision was performed following frozen confirmation, wherein first, the right side lesions were removed. After 6 weeks, once good healing was confirmed, laser excision of the opposite side was performed. Follow-up laryngoscopy revealed good healing and a serviceable voice.

DISCUSSION

Diagnosis of laryngeal amyloidosis requires a high index of clinical suspicion. Its possibility must be kept in mind when high-definition laryngoscopy reveals single or multiple sub-epithelial bulges with no other specific clinical diagnosis. A CT two-dimensional reconstruction image offers the best radiological assessment[5] and usually, well-defined soft-tissue density masses with variable enhancement and no associated bone involvement or lymphadenopathy are observed. Sometimes, diffuse intralaryngeal soft tissue infiltration with intralesional calcifications may be reported[5] as was seen in patient B.

Since amyloid deposits in the subepithelial layers, a representative biopsy specimen will only be obtained if it is deep to the epithelium. Laser-assisted excision of tissue using precision of the acublade is preferable as amyloidosis is un-encapsulated and the laser beam aids in developing planes of excision in a relatively hemostatic manner. In patient A, diagnosis was difficult as a previous biopsy from another center was inconclusive, and had possibly altered the anatomy and pathology by inducing postoperative fibrosis. Isolated involvement in the infraglottis further confounded the diagnosis.

In patient B, the challenge was tackling the bilateral, extensive, bulky deposits in the false vocal folds and ventricle extending into the true vocal folds and subglottis on the right, without developing extensive scarring and permanent voice deterioration. A carbon dioxide laser acublade was used for surgical excision in two stages with gradual excision from cranial to caudal end, allowing adequate exposure of the anatomy. While operating on true vocal folds, surgical excision from lateral to medial is advantageous to preserve the superficial lamina propria and restore maximum possible phonation.

The surgical goal in laryngeal amyloidosis may be comparable to recurrent respiratory papillomatosis, where the aim of treatment is not to attain a picture-perfect larynx, but to remove as much disease as possible for long-term disease-free interval and restore serviceable voice with minimal synechiae. Staged surgical excision in bulky bilateral disease is recommended as it allows adequate healing and prevents webbing, which would compromise voice and possibly, respiration.

In laryngeal amyloidosis, workup for generalized amyloidosis is often negative.[5] In our case series of 13, two patients had extralaryngeal involvement, namely in the soft palate and nasopharynx. One patient had plasma cell neoplasm along with laryngeal amyloidosis. Systemic work-up with hematological tests should be performed with the physician. Multiple myeloma, rheumatic diseases, tuberculosis, and familial syndromes are systemic causes that must be considered.[5] Radiolabeled serum amyloid protein scanning available at few international centers helps evaluate and monitor accumulation of amyloid in the body, although deposits in hollow organs may not be detected.[6]

Diagnosis and management of laryngeal amyloidosis require a coordinated teamwork by the otorhinolaryngologist, pathologist, and physician. Hazenburg *et al*. reported that revision for amyloid was necessary in 60 % of patients within 6 years after the last surgery.[7] However, in our case series of 13 patients, three required a revision surgery with a follow-up from 10 years to 1 year. Periodic follow-ups are advised to check for recurrence of disease.

CONCLUSION

The above case reports reiterate the importance of a high index of clinical suspicion and obtaining a representative biopsy for the timely diagnosis of laryngeal amyloidosis. Staged surgical management in bilateral disease to render serviceable voice and a routine follow-up is recommended.

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