CASE REPORT

Isolated Primary Laryngeal Amyloidosis: A Case Series of a Rare Presentation of Change in Voice

Anmol Wadhwa[1], Bhavika Verma[2], Yogesh G Dabholkar[3]

Abstract

Introduction: Amyloidosis is a benign disease which comprises heterogeneous group of disorders that are characterized by accumulation of amyloid proteins in various body organs. Of the various types, laryngeal amyloidosis is a rare disease of unknown etiology.

Case report: We report three cases of isolated primary laryngeal amyloidosis who presented with hoarseness of voice as their chief complaint. A diagnosis was made based on histopathology after a thorough clinical and laboratory workup, and the patients responded well to the surgical excision of the growth and to a combination therapy of oral corticosteroids and bortezomib.

Conclusion: Laryngeal amyloidosis, though a rare disease, is a common site for isolated amyloid deposits to occur in head and neck regions, and its diagnosis requires a high index of suspicion as well as thorough workup to exclude systemic involvement.

Keywords: Amyloidosis, Hoarseness of voice, Laryngeal.

Otorhinolaryngology Clinics: An International Journal (2021): 10.5005/jp-journals-10003-1384

Introduction

Amyloidosis is a slowly progressive heterogeneous group of disorders, benign in nature and characterized by extracellular proteinaceous deposits in various target organs.[1] This leads to organ dysfunction. The Greek words "Amylon" which means starch and "Eidos" which means resemblance together comprise the word amyloidosis. The word amyloid was introduced by Virchow, because the protein showed starch like reaction when he treated iodine with sulfuric acid.[2]

About 50–70 year-old individuals are predominantly affected by amyloidosis with male:female predominance of 3:1.[1] Symptoms depend on site and size of amyloid deposits with laryngeal involvement being witnessed at all levels of larynx. Various other sites that have been reported to be involved include eyes, orbit, salivary glands, nose, paranasal sinuses, nasopharynx, oral cavity, bronchotracheal tree, and lungs.[3]

Laryngeal amyloidosis can present with varied symptoms such as hoarseness of voice, cough, globus hemoptysis, stridor, dyspnea, and rarely dysphagia. Amyloid deposits in the larynx may occur diffusely or in the form of a single tumor nodule. Microscopic examination classically shows acellular, homogeneous, and amorphous eosinophilic substance displaying apple green birefringence under polarized light when stained with Congo red dye (Fig. 1).[4]

Case Report 1

A 30-year-old female patient was brought to our outpatient department with complaints of hoarseness of voice since 1 year and shortness of breath with foreign body sensation in throat since 6 months. These symptoms aggravated in last 1 month, and patient now presented with stridor. The symptoms were associated with 3–4 episodes of hemoptysis in the past 7–8 months. A chest X-ray was performed to rule out any lung pathology, which showed no obvious abnormalities. Bilateral vocal cords were mobile but were found to be diffusely edematous on indirect laryngoscopy.

[1–3]Department of ENT, DY Patil School of Medicine, Navi Mumbai, Maharashtra, India

Corresponding Author: Anmol Wadhwa, Department of ENT, DY Patil School of Medicine, Navi Mumbai, Maharashtra, India, Phone: +91 9620789351, e-mail: anmol.wadhwa94@gmail.com

How to cite this article: Wadhwa A, Verma B, Dabholkar YG. Isolated Primary Laryngeal Amyloidosis: A Case Series of a Rare Presentation of Change in Voice. Int J Otorhinolaryngol Clin 2021;13(2):73–75.

Source of support: Nil

Conflict of interest: None

Enhancing mucosal thickening involving bilateral true and false vocal cords, anterior commissure, and bilateral aryepiglottic folds extending inferiorly to involve the subglottic region of the larynx with mild to moderate narrowing of the airway was noted on CT scan of neck.

Patient underwent elective preoperative tracheostomy in view of stridor and difficult intubation which was followed by microlaryngoscopy, which showed severe narrowing of glottic inlet with diffuse laryngeal swelling involving bilateral vocal cords, aryepiglottic fold extending inferiorly to the subglottic region. A debulking procedure was performed, and the tissue sample was sent for histopathological examination (Fig. 2).

On staining the specimen with Congo red dye, it showed apple green birefringence on polarized microscopy, to give a confirmed diagnosis of laryngeal amyloidosis. A detailed clinical examination and broad laboratory workup ruled out systemic amyloidosis, and involvement of other organs like liver or spleen. Various other blood investigations like serum protein electrophoresis, serum immunofixation electrophoresis, serum immunoglobulin, serum light chains, and serum B-2 microglobulin were tested which were present within normal limits, hence ruling out multiple myeloma. After consulting a hematologist, a combined therapy of oral bortezomib and corticosteroids was started and the patient

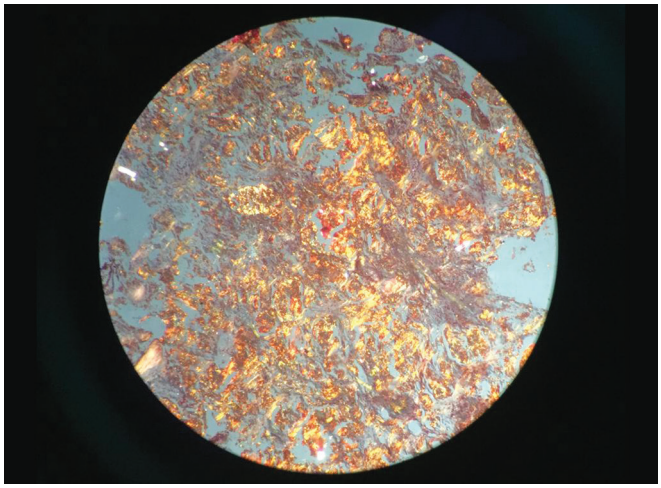

Fig. 1: Apple green birefringence under polarized light when stained with Congo red dye

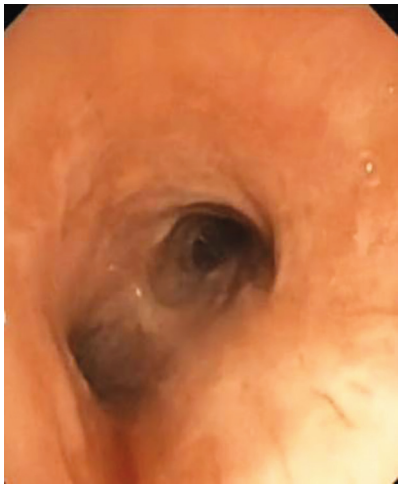

Fig. 3: Bronchoscopy showing normal mucosa of trachea and primary bronchi

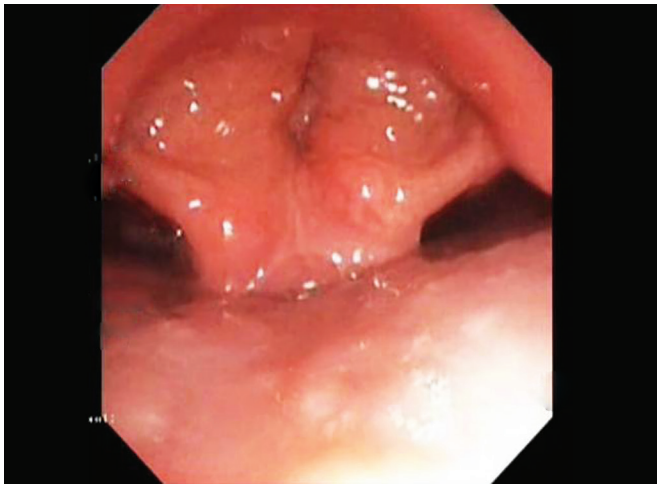

Fig. 2: Mucosal edema involving bilateral true and false vocal cords, anterior commissure, and bilateral aryepiglottic folds

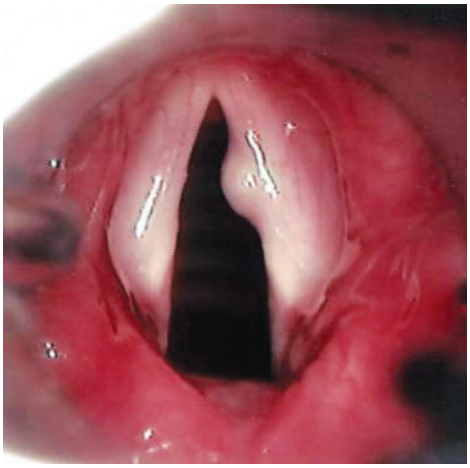

Fig. 4: Laryngoscopy showing right vocal cord nodule

was discharged on a metallic tracheostomy tube. On follow-up, bronchoscopy was performed to evaluate the trachea and the bronchus (Fig. 3).

Case Report 2

A 29-year-old female admitted in our hospital with complaints of hoarseness of voice since 5 months. Nasopharyngolaryngoscopy was performed that revealed about 1 × 1 cm sized nodule over the right vocal cord which hindered glottic closure leading to a phonatory gap. A workup was sent to take the patient under general anesthesia. Microlaryngoscopy with CO_2 laser excision of the vocal cord growth was then done, and the sample was sent for histopathological examination which showed multiple polypoidal tissue bits lined by stratified squamous epithelium and focal respiratory epithelium. Subepithelium and deeper tissue showed pink, amorphous, and rounded tissue suggestive of amyloidosis surrounded by fibrous stroma and chronic inflammatory cell infiltrate. When subjected to Congo red stain, the tissue showed apple green birefringence on polarized light leading to the definite diagnosis of amyloidosis. Other systemic involvement was then ruled out, and patient was advised regular follow-up (Fig. 4).

Case Report 3

A 70-year-old female, a known case of hypertension, came to our outpatient department with complaints of change in voice since 1 year. Indirect laryngoscopy was performed which showed approximately 0.5 × 0.5 cm nodule on the left vocal cord. Histopathological report of the sample sent after microlaryngoscopic excision of left vocal cord growth using CO_2 laser revealed small tissue fragments lined by flattened respiratory and squamous mucosa. Subepithelium showed deposits of eosinophilic homogenous material, which stained positive with Congo red stain. Hence, the patient was diagnosed of isolated primary laryngeal amyloidosis after ruling out other systemic involvement. The patient was subjected to speech therapy after 1 week of the surgery and her symptoms significantly improved. The patient was on regular follow-up for a period of 2 years.

Discussion

Amyloidosis of the larynx is a rare and poorly understood disease of unknown etiology with limited long term studies in the literature. One study done by Thompson LD et al. reported only 11 cases in 37 years.[5] Amyloid fibrils are polymers of identical monomer units of protein. Functional amyloids play a crucial role in physiological processes that involve long-term memory and slow release of stored peptide hormones. Congregation of morbific amyloids in different tissues of the body causes amyloidosis.

Amyloids have fibrillar appearance on electron microscopy, whereas they have amorphous eosinophilic appearance on hematoxylin and eosin staining. Apple birefringence on Congo red-binding material is established in a biopsy specimen to make the diagnosis of amyloidosis. Determining the type of amyloidosis in addition to its diagnosis is essential as different types of treatment are present for different types of amyloidosis. This is achieved by immunostaining the biopsy specimen. Ventricles and the false and true vocal cords of the larynx are most common sites to be affected in laryngeal amyloidosis. Amyloidosis of head and neck can be of two types, a primary isolated disease or secondary to systemic involvement. Larynx is the most common site of involvement in the head and neck regions and is frequently affected by localized rather than systemic amyloidosis. Monoclonal deposits of light chain type (AL) are features of laryngeal amyloidosis.[6] It accounts for 0.2–1.2% of benign tumors of larynx.[5]

There are two theories that have been proposed to explain localized amyloidosis of the larynx. One is due to the presence of plasma cells mixed with the amyloid tissue and the reaction they generate to inflammatory antigens. This is known as secondary amyloid or amyloid of chronic inflammation (AA amyloid). Another, more likely scenario, points to the inability of the body to clear light chains produced by plasma cells located in the mucosal-associated lymphoid tissue known as primary amyloid (AL amyloid).[7]

Once diagnosis of laryngeal amyloidosis is made, a thorough workup should be done including investigations to rule out systemic diseases like multiple myeloma, rheumatic diseases, and tuberculosis that must be contemplated as a differential diagnosis. Amyloidosis related with familial syndromes and endocrinopathies, such as medullary thyroid cancer, also needs to be investigated. In our patients, once laryngeal amyloidosis was confirmed by biopsy, other system involvement was ruled out.

Treatment of laryngeal amyloidosis may vary from simple observation to partial laryngectomy depending upon the level of involvement of larynx. However, in case of localized laryngeal amyloidosis, endoscopic CO_2 laser excision of the lesion is considered to be the first modality of treatment while using microlaryngeal cold steel instruments is another approach of excision.[8]

In case of diffuse vocal cord edema, a combination therapy with oral bortezumib and corticosteroids could be considered.[9] Bortezumib which is a proteosome inhibitor is considered effective in treating AL type of amyloidosis with improvement in overall response rate.[10]

Conclusion

One must always keep in mind the diagnosis of laryngeal amyloidosis while evaluating a patient of long-standing hoarseness of voice, not improving with maximal treatment. Tissue biopsy is always required to confirm the diagnosis of laryngeal amyloidosis including workup to rule out systemic involvement. Also, establishing the type of amyloidosis helps in providing definite treatment and improving the overall response rate.

Orcid

Anmol Wadhwa https://orcid.org/0000-0003-3734-3050

References

1. Saleem T, Fatima S, Ghaffar S, et al. Two cases of primary laryngeal amyloidosis. J Pak Med Assoc 2009 Nov;59(11):789–91. PMID: 20361683.
2. Alaani A, Warfield AT, Pracy JP. Management of laryngeal amyloidosis. J Laryngol Otol 2004;118(4):279–283. DOI: 10.1258/002221504323012021.
3. Lachman HJ, Hawkins PN. Amyloidosis of the lung. Chron Resp Dis 2006;3(4):203–214. DOI: 10.1177/1479972306070066.
4. Sonkhya N, Mittal P, Sonkhya D, et al. Localized laryngeal amyloidosis: a case report and review of literature. Global Adv Res J Med Med Sci 2012;1(3):45–48.
5. Thompson LD, Derringer GA, Wenig BM. Amyloidosis of the larynx: a clinicopathologic study of 11 cases. Mod Pathol 2000;13(5):528–535. DOI: 10.1038/modpathol.3880092.
6. Lewis JE, Olsen KD, Kurtin PJ, et al. Laryngeal amyloidosis: a clinicopathologic and immunohistochemical review. Otolaryngol Head Neck Surg 1992;106(4):372–377. DOI: 10.1177/019459989210600410.
7. Behnoud F, Baghbanian N. Isolated laryngeal amyloidosis. Iran J Otorhinolaryngol. 2013;25(70):49-52. PMID: 24303419; PMCID: PMC3846235.
8. Siddachari RC, Chankar DA, Pramesh CS, et al. Laryngeal amyloidosis. J Otolaryngol 2005;34(1):60–63. DOI: 10.2310/7070.2005.03131.
9. Wadhwa A, Dabholkar YG, Bhatt BV et.al. Primary diffuse laryngeal amyloidosis, a rare cause of hoarseness of voice. Int J Health Sci Res 2019;9(11):111–114.
10. Jiang F, Chen J, Liu H, et al. The effect and safety of bortezomib in the treatment of AL amyloidosis: a systematic review and meta-analysis. Indian J Hematol Blood Transfus 2018;34(2):216–226. DOI: 10.1007/s12288-018-0937-x.