Chapter 17
Laryngeal amyloidosis: Observations of vocal folds kinematics with LVS, HSDP & NBI®

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Abstract

Amyloidosis refers to an unknown pathogenic process in which abnormally folded proteins are deposited in the extracellular space as macroscopic aggregates. Laryngeal deposits of these proteins are extremely rare. In a combined clinical practice of 45 years we have encountered 13 cases. Dysphonia, rather than ventilation, is a primary symptom, yet little is known about this process in these cases. As far as we can discern, no prior (February 2016) reports observations on vocal folds behavior in laryngeal amyloidosis by laryngovideostroboscopy (LVS), high-speed digital phonoscopy (HSDP), or narrow-band imaging (NBI®) of this condition have been identified in the world literature, except papers published or presented by our group at the Pacific Voice Conferences. Our findings showed that LVS identifies the deposits clearly and that mucosal wave may not be disturbed in a well-executed surgery. NBI® exams showed amyloid as unvascularized, and thus benign, in appearance. HSDP studies provide information about the physiological impact of amyloidosis on the larynx, especially regarding voice effects. Conservative piecemeal surgical removal of amyloid deposits secures proper basic laryngeal functions: airway, aspiration prevention, and voice.

Keywords: amyloidosis, larynx, surgery, HSDP, NBI®, LVS, symmetry, mucosal wave, voice quality, outcomes

Introduction

Amyloidosis refers to a condition in which amyloid proteins are deposited abnormally in the extracellular space. Such deposits can occur anywhere in the body, including the larynx. Laryngeal amyloidosis (LA), however, is extremely rare, and as with other locations, the underlying pathogenesis is unclear. The first reported case of LA was described by Borow in 1873 [1]. Since then, we have learned that LA accounts for less than 1% of benign laryngeal tumors [2-4].

LA usually presents with: hoarseness, difficulty breathing, neck pain, and uncommonly with hemoptysis. On visualization LA presents as well-defined focal yellowish mass(es) as shown in Figure 1. Tracheo-bronchial amyloidosis (TBA) has also been reported [5].
Figure 1. White light illumination of A) amyloid-free trachea, B) supraglottic and subglottic LA, and C) infraglottic LA.

Cases

We believe our combined series of 13 cases represents the largest LA report from one clinical group. Surprisingly, the chief complaint in all cases was hoarseness and not shortness of breath. Diagnostic evaluations included Phonatory Function Studies (PhFS), visualization with laryngovideostroboscopy (LVS) using the KayPENTAX system RLS 9100, and acoustics [6]. More recent documentation utilized High Speed Digital Phonoscopy (HSDP) using KayPENTAX Model 9710 HSDI and/or Narrow Band Imaging (NBI®) developed by Olympus Corporation, Tower Model CV-190/CLV-190.

Treatment

Following the initial diagnostic evaluation, all patients with LA underwent microdirect laryngoscopy (MDL) with laser debulking of LA deposits [7-8]. It needs to be noted that multifocal discrete locations of amyloids involving the larynx were common in our cohort. Careful staged removal of glottic involvement unilaterally was performed to reduce anterior commissure scarring and poor vocal outcomes. In addition to surgical debridement, selected patients received Methotrexate® [7].

Removal of lesions involving predominantly the false VF was often associated with voice improvement. For large supraglottic amyloid deposits, this may involve removal of LA tissue to the level of the inner thyroid cartilage perichondrium [7]. LA deposits extending from the false VF into the lateral true VF (floor of ventricle) needed to be at least partially removed to avoid hoarseness from a convex displacement of the VF. Removal of at least 2 mm of the upper edge of a 3 to 4 mm thick submucosal deposit to the thyroarytenoid along with the overlying mucosa on at least one side was necessary to improve hoarseness when LA was present on the undersurface of both true VF. Of the 10 patients described by Dedo and Izdebski [7], seven patients had one to seven prior removals of LA. Of the additional three cases all had two-staged removals.

Objective results showed postoperative voice improvement in all patients discussed here. Results also indicated that partial regrowth may occur in a few months to years after partial LA removal. Follow-up after the first operation was six months to now 25 years with an average of 8.5 years. Four false VF LA patients required re-excison on the same side after the first operation, but none has required a third removal as of yet (2014, updated follow-up) [7].
The value of LVS, HSDP, and NBI® exams

To improve our understanding on how voice production is affected by LA we have more recently conducted LVS, HSDP, and NBI® studies on select patients. LVS is an excellent tool to show the location and magnitude of LA deposits within the larynx and its surrounding structures. LVS is however less accurate in displaying the mucosal wave as the wave in these cases is often aperiodic. HSDP permits very detailed observations of the vibratory cycle, but is less informative about the “dermatologic” details of the LA than LVS. NBI® technology splits the white light (WL) frequencies and uses selective bands to illuminate the surface of interest; this process provides a clearer demarcation between normal and pathological tissue. NBI® technology is also helpful in assessing the malignant potential of any new laryngeal tumor or growth.

To our knowledge, no combined or separate studies using LVS, HSDP, and/or NBI® protocols on laryngeal LA have been published in the world literature (February 2016). Exceptions are the talks our group presented at the last three consecutive Pacific Voice Conferences (2013-2015) and only one paper [5] discussing the use of NBI® to study LA in two cases, but the LA location described in this paper was not in the glottis but rather in the trachea-bronchial region. Therefore, there is no comparative data with which we can contrast our results from LVS, HSDP, and NBI®.

Results from LVS, HSDP, and NBI®

Figures 2 and 3 show a pre- and post-operative case with subglottic LA involvement, respectively, using LVS. Meanwhile, Figure 4 shows the pre-operative and post-operative glottis using HSDP.

Figure 2. Pre-operative view of subglottic LA case using LVS during abduction (left) and phonation (right).

Figure 3. Post-operative view of subglottic LA case using LVS during abduction (left) and phonation (right).
Figure 4. Phonatory glottis: pre-operative (top) and post-operative (bottom) in HSDP mode view.

Although a still photograph cannot demonstrate the mucosal wave, HSDP technology is excellent for demonstrating the often aperiodic wave motion associated with LA. Therefore, we have processed the HSDP file with the Vocalizer® software (Figures 5-6).

Figure 5. Vocalizer® analysis of pre-operative glottic HSDP data.
Vocalizer® processing clearly demonstrated left versus right differences in glottic wave behavior. However actual wave was only marginally improved after the surgery, yet the voice quality was much improved. This is because removal of the LA from the sub-glottis eliminated the LA-formed ridge, which in our opinion caused friction when the air was flowing in the narrowed glottis, hence reducing the signal-to-noise ratio (SN) post-operatively.

Figure 7 shows images of a different LA case—a long-term amyloidosis female patient with frequent recurrences—using white light (WL) and NBI® illumination. Note that both images demonstrate an anterior web and a mildly erythemic, scarred right VF, which is mirrored on the NBI® image by a greenish tinge of the right VF demonstrating the vascular blush of erythema. Finally, note that the LA deposits on WL appear in yellow, while on NBI® they are pink and basically unvascularized, yet surrounded by the more vascularized greenish appearing mucosa.
Summary and conclusions

The etiology of LA remains unclear and the diagnosis is often not considered, as this is an extremely rare condition. Surgical removal is the only efficacious treatment approach. The primary functions of the larynx (e.g., voice, breathing, and airway protection) can be compromised depending on the location of LA deposits and imprudent surgical decision making. Surgical resection should be as complete as possible balancing preservation of laryngeal function. It often follows an indolent course so patients may do well with residual disease having relatively minor symptomatic impact.

Alternative means of LA visualization, such as LVS, HSDP, and NBI® contribute differentially to our understanding of the extent of LA disease and how best to preserve function with surgical treatment.

What is learned from these visual observations, is the fact that the subglottic mass is less disturbing to the phonatory process as it may appear, specifically if the middle and the upper lips of the vocal folds can be set in motion. The subglottic mass appears to be causative of airflow deflection, hence hiss and noise rather than jitter or shimmer will result.

LVS is capable of demonstrating the extent of disease clearly. NBI® verifies involvement as well as the location of discrete deposits, but adds little new information regarding the extent of disease. However, NBI® can reassure the clinician about the non-malignant nature of this process by observing the typical unvascularized appearance of the LA deposits [9]. HSDP demonstrates altered physiological function of the larynx by demonstrating perturbations in the mucosal wave. An aperiodic mucosal wave and resulting harsh dysphonic voice seems to be the result of distorted laryngeal airflow caused by altered tissue compliance and altered airway anatomy from the amyloid deposits.

Thus, the poor voice seen in these patients has a more generalized effect of the disease on the larynx and it appears to spare the muscular and mucosal components of the VF. As a consequence, de-bulking procedures to reduce the amyloid burden in the larynx can result in significant voice improvement as long as the kinematics of the true VF is not compromised during MDL procedure. While these optical imaging techniques help to define LA extent and effects on the voice, we are no closer to understanding why amyloidosis will sometimes selectively involve the larynx.

References

