Laryngeal Amyloidosis: Can it be Determined with Imaging?

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Introduction

Amyloidosis of the larynx (LA) and upper aerodigestive tract is rare, with an incidence of 5-13 per million people per year[1,2.]

LA has non-specific symptoms, resulting in a significant delay between initial presentation and diagnosis[1]. Based on the size and location of the lesion, patients may experience dysphonia, dysphagia, airway obstruction, globus sensation, and/or cough[3].

The differential diagnosis for laryngeal submucosal lesions is broad. Awareness of amyloidosis within the differential diagnosis is essential to alert the pathologist to perform specific staining (Congo red stain with apple-green birefringence on polarized microscopy)[4,5].

The objective in this review is to examine the radiologic features in patients known to have LA, to identify trends suggestive of the presence of LA.

Methods and Materials

A retrospective review of patients with LA from January 2009 to September 2022. Ethics Review Board of the McGill University Hospital Centre (2020-5596).

A fellowship-trained head and neck radiologist reviewed all imaging studies performed, computed tomography (CT) scans and magnetic resonance imaging (MRI) studies.

Demographic information collected: age, sex, co-morbidities, time between presentation and diagnosis, presenting complaints, surgical interventions completed, pathology results, and follow-up time.

Imaging analysis included location of the lesions, extent of the disease, and radiologic features. Specific features are defined as:

- Focal morphology: well-demarcated and isolated lesion.
- Diffuse morphology: ill-defined lesion involving greater than 180 degrees of airway circumference.
- Punctate calcifications: less than 5mm, stippled or focal with a well-defined appearance.
- Diffuse calcifications: greater than 5mm or ill-defined.

#	Age at diagnosis, sex	Time to diagnosis (with symptoms)	Follow-up time	Systemic workup	Number of surgeries	Primary location	Key Imaging findings
1	38, F	2.5 years	13 years	Negative	6	Supraglottic /glottic	CT: no calcifications MRI: diffuse enhancement
2	66, F	6 years	11 years	Negative	3	Glottic	Chest: diffuse tracheobronchial thickening
3	67, M	4 years	7 years	N/A	2	Supraglottic /glottic	MRI: hypointense T1 and T2, diffuse enhancement CT: punctate calcifications, laryngocele
4	27, F	N/A	1 year	Negative	2	Supraglottic /glottic	CT: calcified mass in nasopharynx
5	50, M	2 years	16 years	Negative	2	Glottic/ subglottic	MRI: hypointense T1 and T2, diffuse enhancement CT: post resection, punctate calcifications
6	65, F	4 years	8 years	Negative	4	Supraglottic /glottic	CT: nasopharyngeal involvement
7	47, F	3 years	16 years	Negative	2	Supraglottic	CT: no calcifications
8	61, M	N/A	15 years	N/A	4	Subglottic	MRI: diffuse enhancement, tracheal extension CT: punctate calcifications
9	75, F	N/A	0	N/A	0	Supraglottic	CT: Mucous retention cysts in right base of tongue and vallecula
10	39, F	N/A	4 years	N/A	2	Subglottic	CT: no calcifications
11	35, F	1 year	27 years	Negative	5	Glottic/ subglottic	MRI: hypointense T1 and T2, circumferential thickening, thoracic inlet
12	45, F	6 months	16 years	Negative	1	Subglottic	CT: laryngocele and tracheal extension

Table 1. Patient demographics (M = male; F = female; N/A = not applicable)

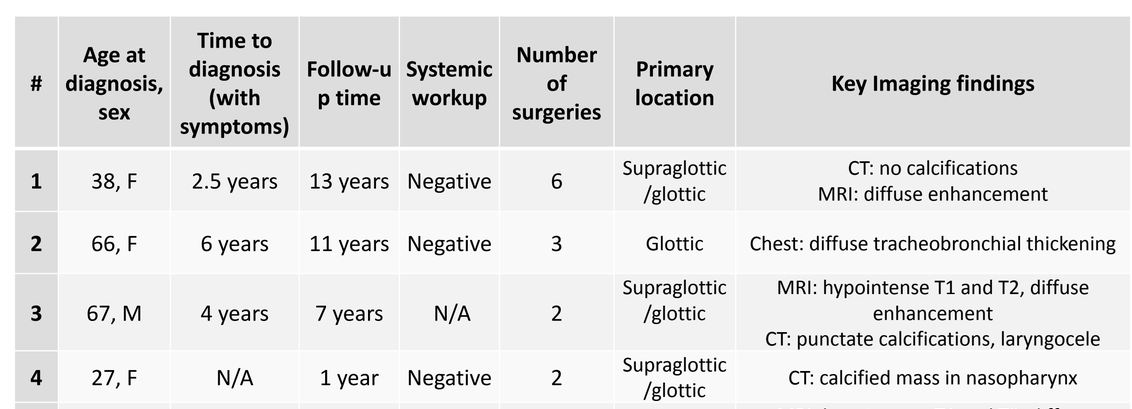
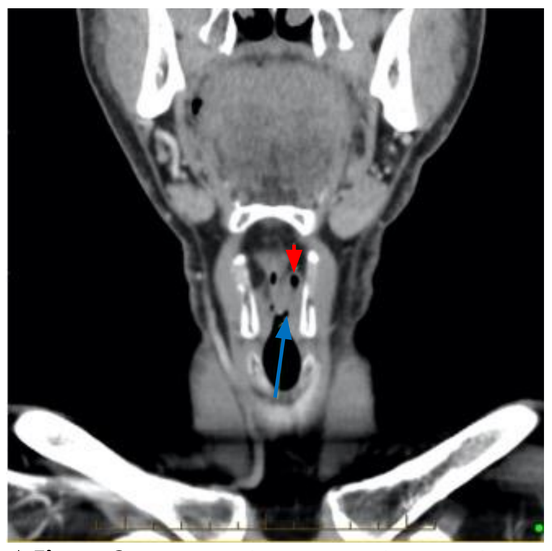


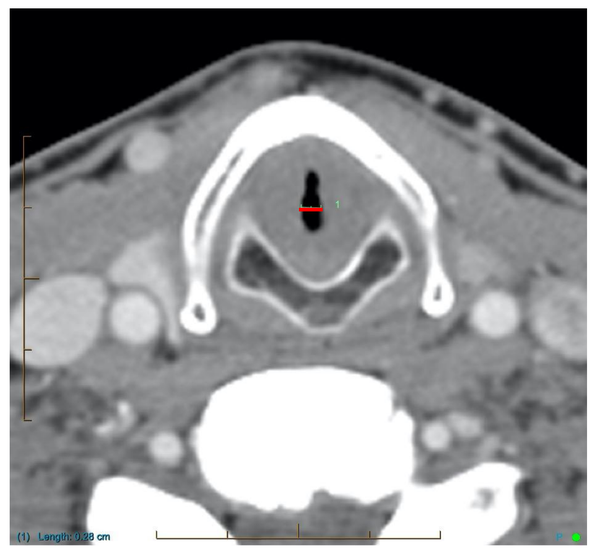
Figure 1. Supraglottic lesion demonstrates typical signal characteristics of amyloidosis with moderate T1-weighted hypointensity (A), marked T2-weighted hypointensity (B), and mild to moderate diffuse contrast enhancement on T1-weighted fat suppressed MR images (C).

Results

- 12 patients were diagnosed with LA. All patients stabilized with intermittent surgical intervention decreasing the burden of disease. Patients were diagnosed on average 2.9 years after initial symptom presentation.
- LA was found in both the supraglottic and glottic regions in 4 cases, both the glottic and subglottic areas in 2 patients, the supraglottic region only in 2 cases, isolated to the glottis just 1 case, and isolated to the subglottic region in 3 cases.
- There was focal laryngeal disease in 7 cases and diffuse laryngeal disease in 5 cases. Multifocal disease within the upper airway was evident in 2 patients (larynx/para-glottic space/nasopharynx and larynx/nasopharynx).
- LA is characterized as a homogeneous and well-defined submucosal soft tissue lesion. Enhancement was only visualized on 4/5 patients who underwent MRI, not on CT. Calcifications were identified in 3/7 patients and were always of punctate morphology, seem on CTs. There were no cases of cartilage invasion.
- Two patients had extra-laryngeal amyloidosis involvement in the nasopharynx. Two patients presented with associated internal laryngoceles.



↑ **Figure 2.** CT scan with contrast in the coronal plane demonstrating a left-sided internal laryngocele (red arrow), with communication with the laryngeal lumen (blue arrow).



↑ **Figure 3.** CT scan with contrast in the axial plane demonstrating severe subglottic narrowing to 3mm (red measurement).

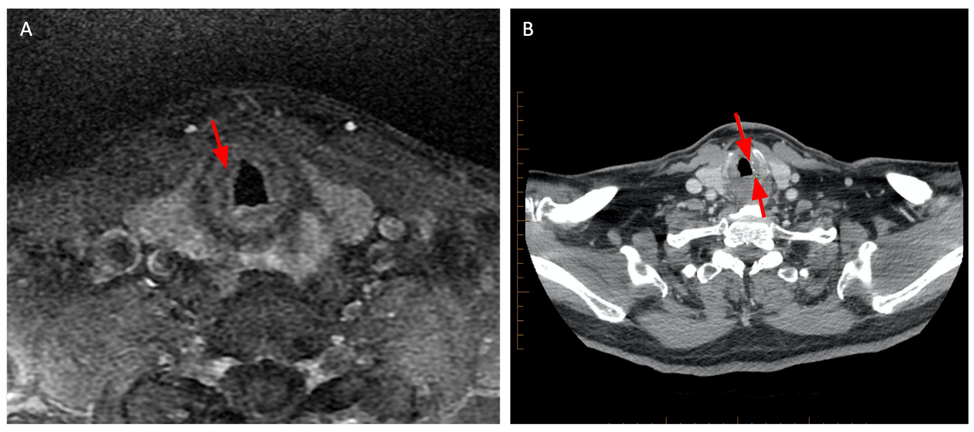


Figure 4. Axial T1-weighted fat suppressed neck MRI at the level of the upper trachea demonstrating tracheal extension (A) and axial CT neck with contrast demonstrating punctate calcifications in a subglottic lesion (arrows) (B).

Discussion

It was challenging to determine just one epicenter as the initial imaging study demonstrated disease in two laryngeal subsites in half of the cases.

There was equal involvement of the supraglottic (n=6) and glottic regions (n=7), as opposed to previous reports of a typical supraglottic LA epicenter[1,6].

MR may be more specific for the initial diagnosis of this pathology as all cases demonstrated similar signal characteristics with iso to hypointensity on T1 and T2-weighted images, and a majority demonstrating contrast enhancement[6-10].

Follow-up imaging is extremely useful to monitor progression, the slow-growing nature of this disease, and the efficacy of de-bulking procedures. This research provides a unique perspective as patients were followed for >11 years.

Conclusions

This case series highlights the consistent imaging features in patients with LA monitored over a long time period of time. MR characteristics are uniform and complement CT findings. Just as “two heads are better than one”, MR assists in obtaining a more prompt and accurate diagnosis of laryngeal amyloidosis.

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