Laryngotracheal Involvement in Systemic Light Chain Amyloidosis

Daniel T. Ginat¹ · Jefree Schulte² · Louis Portugal³ · Nicole A. Cipriani²

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Abstract Laryngotracheal amyloid deposition is an uncommon manifestation of systemic light chain amyloidosis. Diagnostic imaging, such as CT, is useful for suggesting the possibility of amyloidosis and delineating the extent of the lesions for surgical management; however, the diagnosis is confirmed with the histologic finding of amorphous eosinophilic material which stains positively for Congo red and may show apple green birefringence on polarization. These features are exemplified in this sine qua non radiology-pathology correlation article.

Keywords Amyloidosis · Amyloidoma · Larynx · Trachea · Radiology · Pathology

History

The patient is a 40-year-old female with a 10 year history of hoarseness with recent worsening of symptoms, as well as shortness of breath, especially at night. Laryngoscopy demonstrated diffuse supraglottic swelling without evidence of mucosal lesions. The patient was found to have elevated serum free kappa light chains. There was no evidence of cardiac or renal dysfunction. The patient was later found to also have multiple myeloma.

Radiographic Features

CT of the neck with contrast was performed, which revealed diffuse, hyperattenuating enlargement of the supraglottic structures (Fig. 1). There were also multifocal nodular areas involving the tracheal wall (Fig. 2). Punctate calcifications were present in some of the lesions.

Diagnosis

The patient underwent surgical debulking of the supraglottic lesions and tracheostomy tube placement. Histologic sections revealed scant, benign respiratory type epithelium and a proliferation of small capillaries with associated inflammation, consistent with granulation tissue. Acellular, homogeneous, amorphous eosinophilic material was also present in the submucosa in one fragment of tissue (Fig. 3). Congo red stain highlighted the amorphous eosinophilic material with a red to salmon-pink color. Under polarized light, apple-green birefringence typical of amyloid was observed (Fig. 4). Liquid chromatography tandem mass spectrometry detected kappa light chain (AL) amyloid deposition. Fine needle biopsy of abdominal fat was also positive for amyloid.

Treatment

The patient was started on lenalidomide and dexamethasone, followed by bortezomib. The patient also underwent autologous stem cell transplantation. Subsequently, the remaining laryngotracheal amyloidomas regressed, allowing the tracheostomy tube to be removed.

✉ Daniel T. Ginat
dtg1@uchicago.edu

¹ Department of Radiology, University of Chicago, 5841 S Maryland Avenue, Chicago, IL 60637, USA

² Department of Pathology, University of Chicago, Chicago, IL, USA

³ Department of Surgery, Section of Otolaryngology, University of Chicago, Chicago, IL, USA

Fig. 1 Axial (a) and coronal (b) CT images show diffuse swelling of the bilateral false vocal cords, which are mildly hyperattenuating

Discussion

Amyloidosis is the abnormal deposition of amyloid protein in extracellular tissues and can be classified as localized versus systemic disease. Localized amyloidosis restricted to the larynx is rare, however, it should prompt a search for other sites of involvement or circulating light chains, in which case a diagnosis of systemic amyloidosis can be made [1, 2]. Furthermore, the disease can be categorized based on the protein subtype, including antibody light (AL) chain, amyloid A (AA), beta-2microglobulin (beta-2m) amyloidosis related to hemodialysis, and autosomal dominant familial amyloidosis (ATTR type or amyloid transthyretin protein) [3]. In particular, AL amyloidosis is the most common type of systemic amyloidosis and the misfolded amyloid fibrils produced by a bone marrow plasma cell clone enter circulation and deposit in various tissues, where they disrupt the tissue architecture [4]. AL amyloidosis can occur spontaneously, but can coexist with other blood dyscrasias, such as multiple myeloma. However, AL

Fig. 2 Axial CT images (a and b) show multifocal nodular lesions in the tracheal wall (arrows), which contain punctate calcifications

amyloidosis is a molecularly distinct entity from multiple myeloma [5].

Amyloidomas in the region of the head and neck is rare, but most commonly involves the supraglottic and subglottic larynx [6, 7]. CT is useful for delineating the extent of amyloidomas in the upper airway, which can be multifocal as in this case. The lesions tend to manifest as hyperattenuating soft tissue nodules on CT and sometimes contain calcifications. The findings on CT are otherwise not particularly specific and the differential diagnosis based on the imaging findings for laryngotracheal amyloidosis mainly includes papillomatosis and granulomatous diseases. MRI can help evoke the diagnosis, since the amyloid deposits characteristically display intermediate T1-weighted signal intensity and low to intermediate T2-weighted signal intensity, similar to skeletal muscle [6–8]. Furthermore, the amyloid lesions in the neck soft tissues typically enhance [7].

Fig. 3 Hematoxylin and eosin stained sections show benign respiratory type epithelium with associated inflammatory granulation tissue (a). Focal acellular, homogeneous, amorphous, eosinophilic material is also present in the submucosa (b)

Ultimately, the diagnosis is confirmed by tissue sampling. Amyloidosis is characterized by extracellular deposition of homogeneous eosinophilic material, often with a “cracked” appearance. Lymphoplasmacytic inflammation is occasionally present, but usually sparse. The amyloid classically stains positively with Congo red and displays apple-green birefringence under polarized light. The actual amyloid proteins are deposited in the form of fibrils with a beta-pleated sheet configuration [9]. The particular amyloid subtype can be determined based on immunohistochemical or proteomic analysis, such as mass spectroscopy and peptide mass fingerprinting via gel electrophoresis [10, 11]. If the lymphoplasmacytic inflammation is prominent, the differential diagnosis includes amyloid deposition in the context of

Fig. 4 Congo red stain highlights the amorphous eosinophilic material with a red to salmon-pink color (a). Under polarized light, the typical apple-green birefringence diagnostic of amyloid is apparent (b)

extramedullary plasmacytoma, MALT lymphoma, or even neuroendocrine tumors [8]. Amyloid-like fibrinous material is present in vocal cord polyps secondary to vocal abuse; however, Congo red stain is negative [12].

Surgical debulking and tracheostomy tube insertion can address airway compromise resulting from laryngotracheal amyloid deposition. Otherwise, systemic AL amyloidosis can be treated with chemotherapy, including bortezomib and lenalidomide, dexamethasone, as well as autologous stem cell transplantation, which target the amyloid-producing plasma cells [4, 5]. Therapies that directly target amyloid deposits are also being investigated [4].

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no competing interests.

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