

Amyloidosis of the larynx mimicking a malignant neoplasm: report of a case associated with λ light chain restriction

Vassiliki Tzelepi¹, Souzana Logotheti¹, Sofia Spiliopoulou², Dimitra Bantouna¹, Nikolaos Mastronikolis², Vasiliki Zolota¹, Stephanos Naxakis², Maria Melachrinou¹

Abstract

A 65 year old male presented at the ENT outpatients clinic with a two-month history of hoarseness. Laryngoscopic evaluation and CT imaging revealed a submucosal mass involving the false vocal cords. A malignant neoplasm was suspected. Microscopic analysis revealed a hypocellular amorphous eosinophilic material diffusely deposited in the lamina propria. Congo red stain was consistent with amyloid deposition. The plasma cells within the deposition showed λ chain restriction. A diagnosis of laryngeal amyloidosis with λ light chain restriction was rendered. Follow-up of the patient showed no evidence of systemic involvement of a plasma cell neoplasm. Laryngeal amyloidosis is rare and may present clinically and radiographically as a malignant neoplasm. Light chain restriction of the associated plasma cells is usually seen. Controversy exists regarding the nature and pathogenesis of this disease entity.

¹ Department of Pathology, Medical School, University Of Patras, Greece

² Department of ENT, Medical School, University Of Patras, Greece

Corresponding Author:

Vassiliki Tzelepi

Department of Pathology

Medical School

University Of Patras

email: btzelepi@upatras.gr

Introduction

Amyloidosis is a heterogenous disease caused by extracellular deposition of various proteins. Most commonly amyloid deposition consists of fragments of abnormal immunoglobulin light chains (AL-amyloid), usually associated with plasma cell dyscrasias, or acute phase proteins (AA amyloid), usually associated with chronic inflammatory conditions [1,2]. Inherited forms of amyloidosis, for example those associated with mutations in the transthyretin gene are rare, accounting for <2% of the cases [1]. The majority of the cases of amyloidosis are systemic [3]. However, localized cases have been described and usually follow a benign course [4].

Here, we describe a case of a localized laryngeal amyloidosis that was associated with λ light chain restriction but no evidence of systemic plasma cell dyscrasia.

Case Report

A 65-year-old male presented at the ENT outpatients' clinic with a two-month history of hoarseness. The patient was a heavy smoker and a social drinker, with an unremarkable medical history. Laryngoscopic evaluation revealed a nodular submucosal mass that mainly involved the right ventricle and collateral false vocal cord. A CT was ordered and revealed a submucosal mass in the area of the false vocal cords, along with osteolytic-chondrolytic changes with neosteogenetic foci in the thyroid cartilage. The changes were present bilaterally but were most prominent in the right side (Figure 1A). Based on the macroscopic and CT findings, a submucosal soft tissue neoplasm probably malignant

(sarcoma) was suspected and surgical excision of the lesion was scheduled. Multiple white tan fragments were obtained. Microscopic analysis of the fragments revealed that the fragments consisted of mucosa covered by respiratory type epithelium. The epithelium showed areas of squamous metaplasia, but no evidence of dysplasia or ulceration. Beneath the epithelium, a hypocellular amorphous eosinophilic material was deposited that involved diffusely the lamina propria surrounding the normal structures of the area (vessels and glands) (Figure 1AB and 1C). The glands were focally atrophic, but showed no evidence of destruction. A giant cell reaction was focally present at the periphery of the amorphous material. Calcifications were present within the material. Cong red stain showed apple-green birefringent stain under polarized light, consistent with the diagnosis of amyloid deposition (Figure 1D).

A lymphoplasmacytic infiltrate was present both within and outside the amyloid deposition. The plasma cells outside the amyloid deposition showed polytypic expression of κ and λ light chains ($\kappa:\lambda=1:3$), whereas plasma cells within the deposition showed a κ to λ ratio of 1:3, (Figure 1E and 1F), consistent with monotypic λ chain expression [5] indicating that the deposited material consisted of λ chains. CD56 was not expressed by the plasma cells. The lymphocytes were predominantly T-cells. A diagnosis of laryngeal amyloidosis with λ light chain restriction was rendered.

Following surgery, the voice of the patient improved and hoarseness was reduced. Follow-up revealed no evidence of systemic amyloidosis or a plasma cell neoplasm.

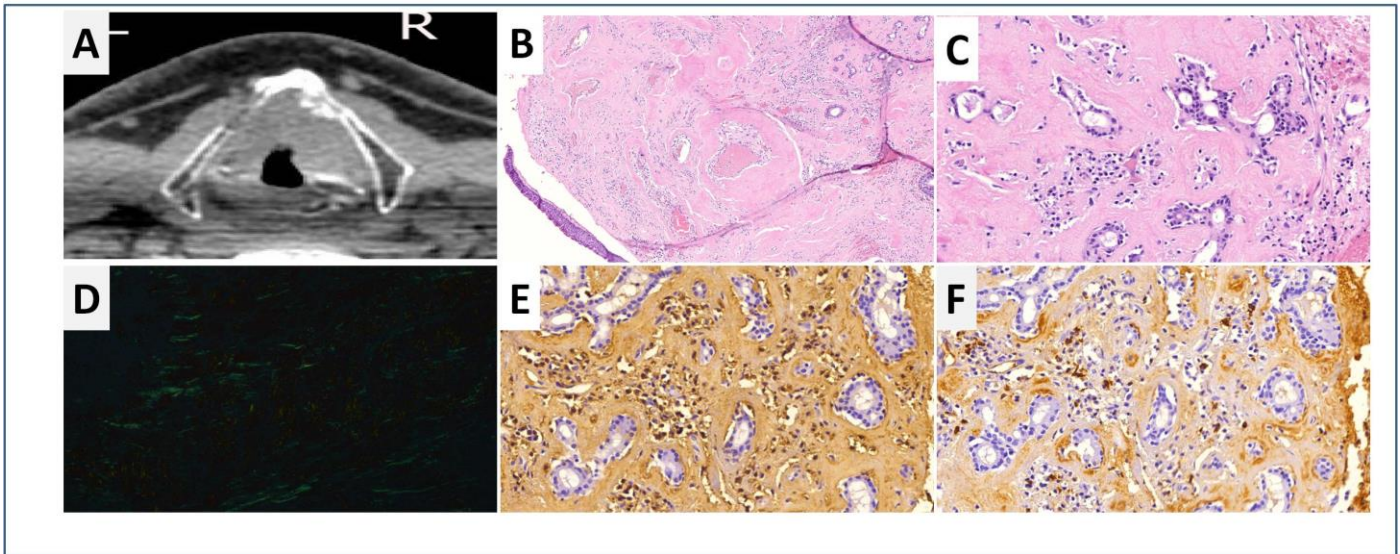


Figure 1. (A) CT image showing a submucosal mass in the area of the false vocal cords. Osteolytic-chondrolytic changes with neosteogenetic foci are noted in the thyroid cartilage. The changes are present bilaterally but are most prominent in the right side. (B-F) Representative histologic images. (B) Diffuse deposition of amorphous eosinophilic material within the lamina propria. Note the epithelium at the left corner (original magnification X5). (C) The material surrounds normal glands without destroying them (original magnification X20). (D) Congo red stain shows apple-green birefringent stain under polarized light (original magnification X40). (E) λ and (F) κ chain immunostaining reveal λ chain restriction (original magnification X20).

Discussion

Around 15% of the cases of amyloidosis are localized to one organ. The urinary and the respiratory tract are the most frequent organ systems involved by localized amyloidosis [6]. Herein, we report a case of primary localized laryngeal amyloidosis that was clinically and radiographically thought to represent a malignant neoplasm, to raise awareness on this disease entity that usually follows a benign course [7].

Laryngeal amyloidosis is rare and usually presents with hoarseness [2,4,8]. In the majority of the cases the larynx is the only affected organ. However, multiple organ involvement has been described in up to 18% of the cases [4]. Biopsy of one other site (i.e the rectum or abdominal fat), serologic studies (i.e. levels of bilirubin,

creatinine, and alkaline phosphatase) and immunoelectrophoresis for the identification of monoclonal proteins along with cardiologic examination (electrocardiogram and cardiac ultrasound) and regular follow-up have been proposed by some investigators to exclude systemic involvement [9]. However, other investigators argue against a systemic work-up, as progression to systemic disease does not seem to occur in patients with laryngeal amyloidosis [10].

Interestingly, light chain restriction is common in laryngeal amyloidosis [2], more commonly involving the λ light chain, as was noted in our case. The pathogenesis of laryngeal amyloidosis has not been fully elucidated. On the basis of the frequent light chain restriction of the plasma cells within the lesion and the identification of abnormal amino acid composition of the light

chains in the laryngeal amyloid [11,12], it has been proposed that local monotypic plasma cells produce excessive amounts of abnormal immunoglobulins resulting in amyloid formation [2]. The origin of these monotypic plasma cells and why they come to the larynx remains elusive, especially since plasma cell myeloma or plasmacytoma has not been described with laryngeal amyloidosis [10].

Conclusion

We present a case of laryngeal amyloidosis. Initial evaluation was suspicious for a malignant neoplasm. Microscopic analysis revealed diffuse amyloid deposition in the right hemilarynx along with λ chain restriction of the associated plasma cells. Systemic work up was undertaken showing no evidence of systemic involvement or a plasma cell neoplasm.

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