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Localized Amyloidosis with Elevated Free Light Chain Ratio Presenting as Hoarseness of Voice: A Case Report

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Abstract

Amyloidosis is a disease characterized by abnormal extracellular deposition of fibrillar proteins in tissues that creates a chronic inflammatory response leading to local tissue injury. The larynx is estimated to be involved in up to 15% of all amyloidosis cases, and accounts for only 1% of all benign laryngeal tumors. Dysphonia is by far the most common primary complaint in laryngeal amyloidosis. A 40 -year-old Ethiopian woman presented with progressively worsening hoarseness of voice of 5 years duration. She had also bilateral knee pain and regurgitation of ingested food over the last 1year. Physical examination, complete blood count, organ function tests, serum electrolyte and other included lab test were unremarkable. Laryngoscopy revealed a 2 cm × 2 cm broad based laryngeal mass and its biopsy result showed an apple-green birefringence, highlighted with a Congo red stain under polarized light microscopy. Kappa free light chain was slightly elevated, & the kappa/lambda ratio was abnormal. This case highlights the significance of high clinical suspicion and histopathology examination in diagnosing such a treatable case.

Keywords: Amyloidosis; Larynx; Hoarseness; Laryngoscopy; Congo red; Ethiopia

Introduction

Amyloidosis is a collective term for the extracellular deposition of abnormal proteins in a single organ (localized amyloidosis) or throughout the body (systemic amyloidosis). Localized amyloidosis can be found anywhere within the body; with the larynx one of the most common locations (14%-15%). When amyloid is localized in the larynx, it is usually the AL type, where the fibril precursor protein is either kappa or lambda light chains, derived from monoclonal immunoglobulins. The amyloid deposits appear as non-specific submucosal swellings usually appearing as nodules or polypoid lesions often with a yellow tinge. Although there are many theories, aetiology of localized amyloidosis remains unclear.

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Dysphonia is by far the most common primary complaint but other symptoms including cough, shortness of breath, foreign body sensation and wheeze are reported. Diagnosis and treatment of the amyloidosis rest upon the histopathology identification of amyloid deposits and immunohistochemical, biochemical, or genetic determination of amyloid type.

Case Presentation

A 40 -year-old female with no history of known medical conditions presented to SPHMMC clinic with 5 years duration of progressive hoarseness of voice that mainly worsened in the last 1 year. She had also bilateral knee joint pain and regurgitation of food content over the last 1 year. She denied history of hemoptysis, weight loss, dysphagia, neck surgery or TB treatment.

Her vital signs during examination were BP: 120/75 PR: 88 RR: 18 Spo2 =95% on atmospheric air. There was no anterior neck mass in the HEENT examination and other physical examinations were unremarkable.

Initial laboratory investigations that included a complete blood count, organ function tests (RFT & LFT), serum electrolytes, urine analysis, VDRL, viral markers for hepatitis B & C, HIV and echocardiography were all normal. A 24-hours urine protein was 24 mg/2400 mL and on Serum free light-chain assay, Kappa free light chain was slightly elevated.

UP on flexible laryngoscope by ENT side A 2 cm × 2 cm broad based laryngeal mass was seen, and under GA the mass was resected and sent for histologic examination.

Biopsy result suggested a classic histochemical finding of amyloidosis, with amorphous deposits demonstrating an apple-green birefringence highlighted with a Congo red stain under polarized light microscopy as shown in the picture.

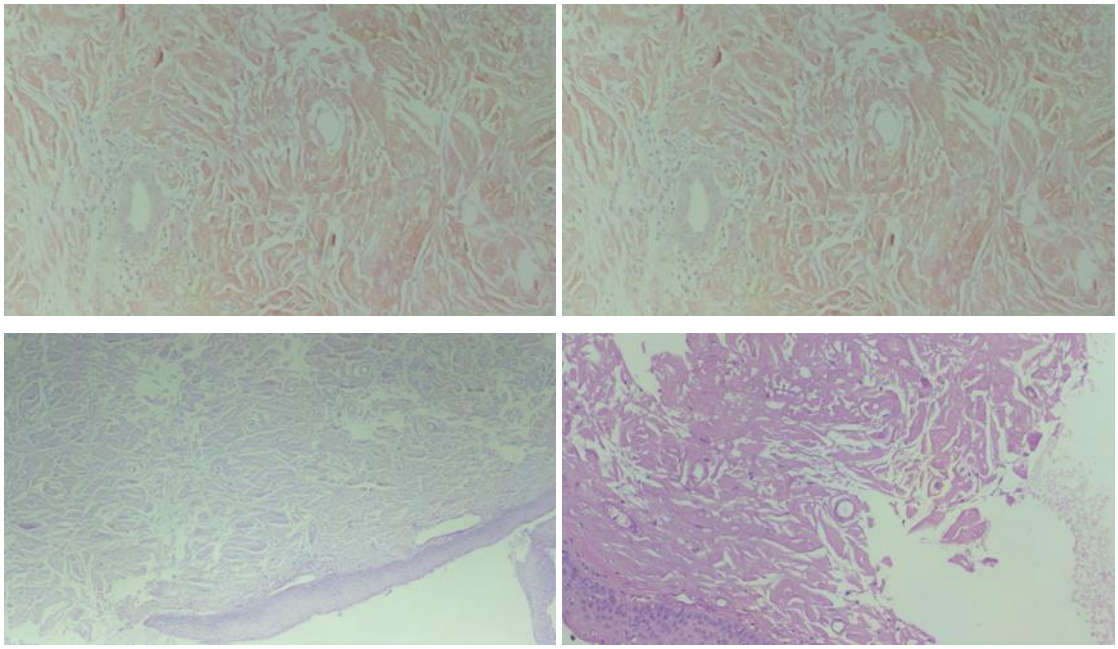

Figure 1: Microscopic images of amyloid deposits using Congo red staining (100X).

Table 1: Serial complete blood count & serum free light chains

	22-12-2023	18-03-2023	20-03-2023	21-07-2024	01-10-2024	30-10-2024
WBC		$3.46x10^3$	$3.9x10^3$	$3.34x10^3$	$4.35x0^3$	$4.3x0^3$
N%		55.50%	56.90%	46.10%	66.30%	59.80%
L%		29.40%	31.70%		22%	30.20%
HGB		15	15.7	15.7	15.6	15.5
HCT		40.80%	42.20%	42.50%	42.80%	42.40%
PLT		$115x10^3$	$202x10^3$	$102x10^3$	$137x10^3$	$121x^3$
Kappa	24.12 ref (3.3-19.4)					8.3
Lambda	23.12, ref (5.71-26.3)					10.8
Kappa/Lambda	1.043 ref (0.26-1.65)					7

Table 2: Serial blood chemistry results.

	18-03-2023	25-09-2024
Cr	0.39	
Urea	12.5	15
AST	13	
ALT	6	

Discussion

We presented a case of laryngeal amyloidosis causing progressively worsening hoarseness of voice and regurgitation of ingested meal. The case intends to emphasize the importance of histopathology in diagnosing this uncommon and treatable condition.

Amyloidosis comprises a heterogeneous group of disorders characterized by the deposition of amyloid protein in various organs of the body. Amyloid deposits are classified according to whether they are systemic or localized, primary or secondary. Diagnosis and treatment of the amyloidosis rest upon the histopathology identification of amyloid deposits and immunohistochemical, biochemical, or genetic determination of amyloid type.[1]

AL amyloidosis can involve any organ system outside the CNS. Laryngeal amyloidosis is a form of AL amyloidosis in most circumstance and only rarely be a hereditary Apo lipoprotein A-I (ApoAI). The larynx is one of the rarer sites where amyloidosis occurs; it is estimated to be involved in up to 15% of all amyloidosis cases and accounts for 0.2%-1.2% of all benign neoplastic tumors of the larynx. It may involve supra-, infra- or subglottic sites, and is frequently multifocal, while it is also typically locally recurrent.[2]

The immunoglobulin nature of laryngeal amyloid is accepted, but the source of the immunoglobulin is unclear. The lesion may develop from a localized monoclonal immunoproliferative disorder, in which the plasma cells, which are intimately associated with the amyloid deposits, are thought to produce the light chain immunoglobulin that is deposited as amyloid, rather than represent an inflammatory infiltrate reacting to the deposited amyloid.[2,3] This intimate association of the lymphoplasmacytic infiltration is different from systemic amyloidosis whereby the plasma cells are spatially separated from the amyloid deposition.[3]

The second theory for the amyloid deposition suggests that a circulating precursor protein is deposited in the stroma after a change in the vascular permeability as a result of local inflammation. In this case the kappa/lambda ratio in the serum free light chains was shown to be elevated, which is an indicator of localized amyloidosis; particularly when supported by tissue biopsy.[3,4]

Symptoms of amyloidosis are nonspecific, and the diagnosis is determined by the severity and laryngeal site involved. It typically presents with dysphonia, but patients can also have dyspnea, stridor, odynophagia, sensation of foreign object in the throat, cough, and hemoptysis. Upper airway obstruction is late manifestation of laryngeal amyloidosis.[4]

Fiber optic examination usually reveal multifocal areas of yellow or yellow-gray submucosal swelling that can also become polypoid and red as the disease progresses; Even though it was a solitary mass in this particular patient. Accurate diagnosis is often delayed for a year more. Diagnosis is initiated by clinical suspicion and should be confirmed by histopathologic examination revealing the hallmark 'apple-green birefringence' with Congo red stain on polarized light microscopy. Imaging may be used to support the diagnosis and determine the boundaries of the lesion, but it is largely nonspecific.[5,6]

When a diagnosis of laryngeal amyloidosis is made, workup should include studies to rule out systemic disease, as well as an accurate assessment of the laryngeal involvement. Multiple myeloma, rheumatic diseases, and tuberculosis are some of the systemic causes that must be considered. Complete blood cell count, erythrocyte sedimentation rate, renal function test, liver enzymes, urinalysis, antinuclear antibody, serum free light chain and serum and urine immune-electrophoresis are some of the ancillary tests that are important. For most cases of suspected localized amyloidosis it is probably not necessary to investigate for systemic disease with biopsies of the lip, rectum, or abdominal fat, because of the low yield. However, fine-needle aspiration of abdominal fat has been shown to be a simple and effective procedure to rule out systemic amyloidosis.[6]

Since the vast majority of lesions of the head and neck, with the exception of macroglossia, represent localized disease, therapy consisting of surgical excision has been far more successful. In the larynx, a conservative approach has been recommended consisting of local excision using laser or micro-laryngeal instruments with conservation of surrounding tissue. Recent literature has advocated CO_2 laser as the treatment of choice. Recurrence is rare, and, if it occurs, can be treated with further conservative excision.[7,8]

Our patient was treated with local excision of the laryngeal mass followed by systemic chemotherapy which resulted in normalization of the elevated free light chain ratio.

Conclusion

Primary laryngeal amyloidosis is a rare presentation of amyloidosis even though common site of AL amyloidosis in the head and neck region. Primary laryngeal amyloidosis can present as a laryngeal mass and subsequent vague upper airway symptomatology.

Histopathologic diagnosis can be made through tissue biopsy using Congo red staining to show an apple-green birefringence. The diagnosis requires a high index of suspicion to complete the necessary investigations and monitor progression of the disease. Definitive treatment of AL laryngeal amyloidosis is local excision of the mass but if it has systemic component can be treated with chemotherapy.

Ethical Approval

According to the review board policy of our institution, ethics approval was not necessary. Written consent was obtained from the patient's family for publication of this case report and associated images.

Acknowledgment

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Disclosure

All authors declare no competing interests of any kind in this publication.

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