

## Case Report

# Laryngeal amyloidosis: a case report

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## ABSTRACT

Amyloidosis is a rare, benign, slowly progressive disease characterized by extracellular accumulation of amyloid in different tissues of the body. It accounts for 0.2-1.2% of benign laryngeal tumors and usually presents as an isolated localized laryngeal amyloidosis, but can also be part of systemic amyloidosis. A 26 years old female with history of gradually developing, persistent hoarseness, and progressive dyspnea since 1 year, worsened over the past three days. Outpatient Department based endoscopy showed bilateral mobile, thickened vocal cords with subglottic edematous thickness. Computed tomography scan showed symmetrical thickening of bilateral vocal cord, causing glottic narrowing about 70% on the AP view and about 50% on the lateral view and no cartilage invasion or lymphadenopathy. Microlaryngoscopy and biopsy of the specimen were performed and histopathology confirmed the diagnosis of amyloidosis with Congo red stain. Patient was managed by surgical excision of the mass and long term follow-up. To rule out systemic amyloidosis patient is referred to rheumatology clinic and hematology clinic for further evaluation and management. Histopathological examination of the involved tissue confirms the diagnosis, and long term follow up is mandatory in the management of amyloidosis.

**Keywords:** Laryngeal tumor, Amyloidosis, Isolated laryngeal mass

## INTRODUCTION

Amyloidosis is a benign, heterogeneous family group of disorders characterized by extracellular proteinaceous deposits with characteristic microscopic, histochemical, and ultrastructural features, in various organs of the body.<sup>1</sup> This process can be localized to one organ or can be a part of systemic involvement.<sup>2</sup>

Localized laryngeal amyloidosis is a rare disease, accounts for 0.2-1.2% of benign laryngeal tumors.<sup>3</sup> It is a subepithelial extracellular deposits of acellular, homogenous, and amorphous eosinophilic material displaying apple green birefringence under polarized light when stained with Congo red dye.<sup>4</sup>

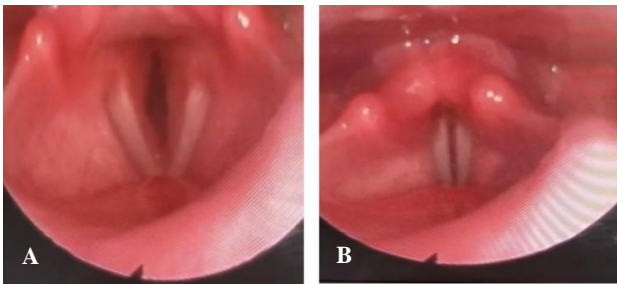
Symptoms are largely dependent on location and size of deposits.<sup>3</sup> Typically, most common manifested symptom

is progressive dysphonia.<sup>4</sup> This common symptom makes the diagnosis of amyloidosis difficult and highlights the need for a high index of clinical suspicion from ENT surgeons. However, deposition sometimes can be extensive leading to alerting symptoms and signs like dyspnea or stridor that requires urgent surgical intervention.

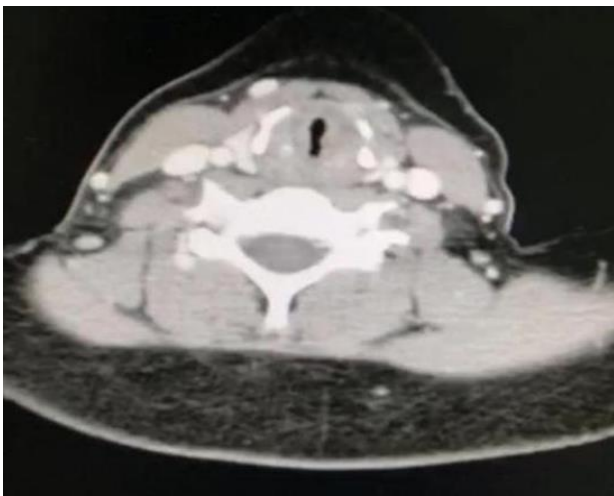
## CASE REPORT

A 26 years old female patient, who is not known to have any medical illness, with history of smoking of Shisha for 10 years, quit 1 year ago, came to ENT OPD with complaint of hoarseness of voice and difficulty in breathing since 1 year. On fiberoptic laryngoscopy showed bilateral thickened and mobile vocal cords (Figure 1). Edematous thickness also seen in the subglottic region, no cervical lymphadenopathy, Rest of

ENT examination within normal limit. Also, the patient has mild cushinoid face as she was on oral steroids since last 6 months. While awaiting for further investigation, she presented with airway compromise to our emergency department with complaining of progressive dyspnea, worsened over the past three days. On examination patients SPO<sub>2</sub> was 90% with CO<sub>2</sub> retention. Secondary respiratory failure was diagnosed, bilevel positive airway pressure was started. Patient was admitted to intensive care unit. Contrast enhanced CT scan of the head neck and chest done, showing symmetrical thickening of bilateral vocal cord, causing glottic narrowing about 70% on the AP view and about 50% on the lateral view and no cartilage invasion or lymphadenopathy (Figure 2). On CT her chest is free from disease.



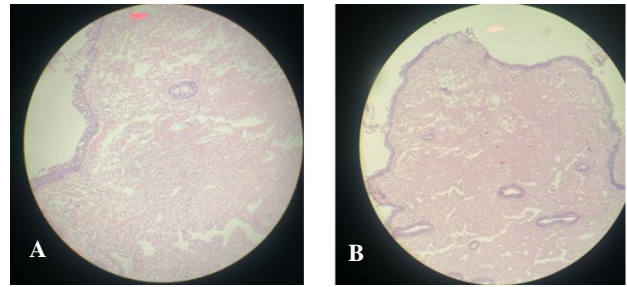
**Figure 1 (A and B): Pre-operative fiberoptic laryngoscopy view of the patient.**



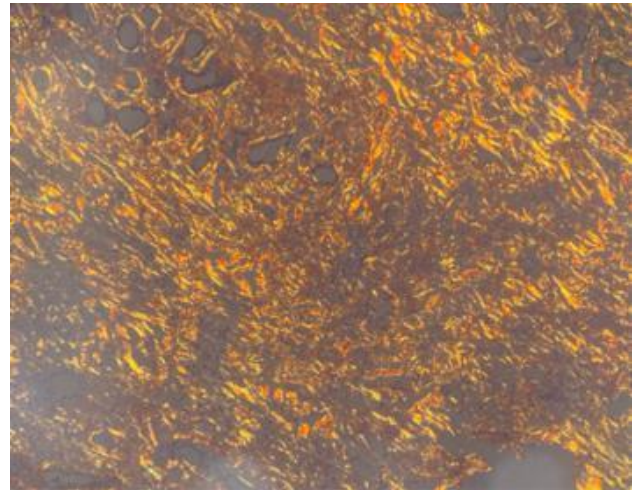
**Figure 2: CT scan of the head and neck region showing symmetrical thickening bilaterally.**

Patient is prepared for surgery after she is vitally stable. Routine laboratory investigations complete blood count, liver function test, kidney function test, coagulation profile, urine routine and microscopy done. All results are clinically acceptable. Patient is planned for direct laryngoscopy and biopsy of the lesion, direct laryngoscopy revealed bilateral thickened vocal cord with subglottic thickness. Biopsy taken and the specimen was sent for histopathological examination. Using CO<sub>2</sub> laser debulking or ablation of thickened vocal cord and subglottic are done. Intra op and immediate post op was

uneventful. Patient was discharged after 48 hours from hospital in clinically stable condition with medication and post-operative instructions regarding vocal hygiene. She was advised for follow up after 1 week in ENT OPD.



**Figure 3 (A and B): Polypoid nodule covered by pseudostratified ciliated columnar epithelium, consist of sheets and nodular mass of amorphous hypocellular eosinophilic material, in both blood vessels walls, and in the basement membrane of mucus blood.**



**Figure 4: Special stain Congo red showing apple green birefringence on polarized microscopic lens.**

Histopathological examination shows prominent acellular, eosinophilic deposits within the stroma. Under polarized light, Congo red staining showed the characteristic apple green birefringence of amyloidosis (Figure 3 and 4). No dysplasia or malignancy was seen, and the diagnosis of laryngeal amyloidosis was made. Patient was followed up in outpatient clinic, repeat fiberoptic laryngoscopy showed an adequate airway with good glottic chink. Patient was referred to rheumatology and hematology clinics to rule out any systemic disease-causing secondary amyloidosis. A long term follow up with frequent fiberoptic laryngoscopy examination is planned for the patient.

## DISCUSSION

Amyloidosis is a rare benign disease characterized by extracellular deposition of proteinaceous material in the

targeted tissue, which has typical staining properties and electron microscopic appearance. Its hallmark is an apple green birefringence under polarized microscopy.<sup>5</sup> Under the electron microscope, amyloid appears as a mass of rigid, non-branching fibrils. X-ray crystallography reveals that these fibrils have a regular, antiparallel, beta-pleated sheet configuration. Amyloidosis is classified clinically into systemic and localized types. Approximately, 10-20% of reported cases are localized.<sup>3</sup>

The immunoglobulin nature of laryngeal amyloid is accepted, but the source of the immunoglobulin is unclear. One of the proposed theory is that, 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. This intimate association of the lymphoplasmacytic infiltration is different from systemic amyloidosis whereby the plasma cells are spatially separated from the amyloid deposition. 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.

Amyloidosis of the head and neck can be either primary isolated disease or secondary to systemic involvement.<sup>5</sup> Sites of localized head and neck involvement by amyloidosis include larynx, nasopharynx, oropharynx, oral cavity, salivary glands, nose, paranasal sinuses, eye, and tracheobronchial tree.<sup>5</sup> Larynx is the most common site of involvement in the head and neck region and is more commonly affected by localized rather than systemic amyloidosis. Localized laryngeal amyloidosis is characterized by monoclonal deposits of the light chain type (AL).<sup>6</sup>

Peak incident of localized laryngeal amyloidosis is between the fifth and the sixth decades of life. Males are predominantly affected with a male to female ratio of 3:1.<sup>1</sup> Clinical presentation is strongly related to site and size of lesion. Most affected site of the larynx is the supraglottis including ventricles and false vocal cords.<sup>4,5</sup> Accordingly, the commonest presenting symptom is hoarseness. However, it may also present with dyspnea, dysphagia, and stridor.<sup>1,5</sup>

Definitive diagnosis of amyloidosis requires tissue biopsy and histological examination with Congo red and immunohistochemical staining which look red or pink in color under normal light and characteristic apple green birefringence under polarized light.<sup>3</sup>

Once the diagnosis of laryngeal amyloidosis has been established, work up should be carried out to exclude systemic involvement. Localized laryngeal amyloidosis has excellent prognosis, in contrast to the poor prognosis

associated with systemic disease.<sup>1,3</sup> Systematic work-up has a wide range of laboratory, imaging, and invasive investigations.

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. The treatment of localized laryngeal amyloidosis is surgical excision. Different approaches have been described in the literature varying from external approach to more conservation endoscopic excision using cold knife or CO<sub>2</sub> laser.<sup>4,5</sup>

Endoscopic CO<sub>2</sub> laser excision has been shown to result in good control of the disease.<sup>3</sup> However, recurrence may occur after long period of time either locally or in multifocal manner, and rarely as a systemic disease.<sup>3</sup> Due to the recurrent slowly progressive nature of the disease, a long term follow up with regular clinic based endoscopic examination is strongly recommended.<sup>3,5</sup>

## CONCLUSION

Laryngeal amyloidosis is a rare, slowly progressive, benign disease. Larynx is the most common site for isolated head and neck amyloid deposition and must be considered in patients with long standing hoarseness that is not improving with maximum medical treatment. Tissue biopsy is required for definitive diagnosis which is confirmed histologically using Congo red stain. When the diagnosis of laryngeal amyloidosis is made, systemic amyloidosis must be ruled out in all cases. Finally, long-term follow up is an important key for the management of the disease.

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