Laryngeal Amyloidosis Case Series: Rare Cause of Hoarseness

Laringeal Amiloidoz Vaka Serisi: Nadir Bir Ses Kısıklığı Nedeni

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ABSTRACT

Background: Amyloidosis is defined as a group of diseases which resulted from abnormal extracellular deposition of insoluble protein, called amyloid. It can either presented as localized or with systemic involvement. Laryngeal amyloidosis is a very rare cause of dysphonia, accounting for only 0.2 to 1.2 percent of all benign laryngeal tumours.
Objectives: To highlight the clinical presentations and raise awareness of laryngeal amyloidosis among otorhinolaryngology surgeons. An index of suspicion must be conveyed to the histopathologist in the request form for them to embark on a specific staining technique.
Method: We discussed two cases of laryngeal amyloidosis, with their presentations, management and the follow up. Both cases were middle aged female. The diagnosis of laryngeal amyloidosis is only by histopathological as clinically it is very ambiguous.
Conclusion: The mainstay of treatment for laryngeal amyloidosis is surgical debulking but it is not curative as complete removal of the diseased tissue is difficult. In addition, the treatment should be directed towards the maintenance of the airway and the improvement of the voice.

Keywords: Larynx, Amyloidosis, Hoarseness, Congo Red

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ÖZET

Giriş: Amiloidoz, amiloid adı verilen çözünmeyen proteinin hücre dışı anormal birikiminden kaynaklanan bir hastalık grubu olarak tanımlanır. Lokalize olabileceği gibi sistemik tutulumla da karşımıza çıkabilir. Laringeal amiloidoz, tüm iyi huylu laringeal tümörlerin yalnızca yüzde 0,2 ila 1,2'sini oluşturan çok nadir bir disfoni nedenidir.
Amaçlar: Klinik sunumları vurgulamak ve kulak burun boğaz cerrahları arasında laringeal amiloidoz farkındalığını artırmak. Belirli bir boyama tekniğine başlayabilmeleri için histopatoloğa istek formunda bir şüphe indeksi iletilmesi gerekir.
Yöntem: İki laringeal amiloidoz olgusunu sunumları, yönetimi ve takibi ile tartıştık. Her iki vaka da orta yaşlı kadındı. Laringeal amiloidoz tanısı klinik olarak çok belirsiz olduğundan sadece histopatolojik olarak konur.
Sonuç: Laringeal amiloidoz tedavisinin temel dayanağı cerrahi olarak kitlenin çıkarılmasıdır ancak hastalıklı dokunun tamamen çıkarılması zor olduğu için küratif değildir. Ayrıca tedavi, hava yolunun korunmasına ve sesin iyileştirilmesine yönelik olmalıdır.

Anahtar Sözcükler: Larenks, Amiloidoz, Ses kısıklığı, Kongo Kırmızısı

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INTRODUCTION

Hoarseness is a common presentation encountered in the otorhinolaryngology clinic. The common causes could be acute laryngitis (42.1%), chronic laryngitis (9.7%), functional dysphonia (30%), benign tumors (10 – 31%), malignant tumors (2.2 – 3%) and neurogenic factors such as vocal cord paralysis (2.8 – 8%) (1). Amyloidosis is a group of diseases that characterized by the deposition of abnormal protein called amyloid in various organs of the body, including the heart, brain, kidneys, spleen and others. It could present in the form of systemic disease which involve multiple organs or limited to certain organs (2). Laryngeal amyloidosis is a very rare cause of dysphonia, accounting for only 0.2 to 1.2 percent of all benign laryngeal tumours (3). Hence, high index of suspicion leading to a specific request to the pathologist is the key to the diagnosis.

CASE REPORT

Case 1

A 51-year-old female presented with hoarseness for four months duration and was not associated with noisy breathing and dysphagia. Perceptual voice assessment using GRBAS revealed overall dysphonia grade 3, main component of strain (roughness=2, breathiness=1, asthenia=1, and strain=3). Rigid laryngoscopy revealed an irregular mass over bilateral false cords which obliterate the membranous vocal cord bilaterally. The mass was seen confined only to the false vocal cords and does not extend to the arytenoid and aryepiglottic folds. Both vocal cords were mobile and moved symmetrically. There was no cervical lymphadenopathy clinically. She underwent laryngoscopy and bronchoscopy under general anesthesia and the findings noted that the growth was confined only to false cords bilaterally. The mass was biopsied and debulking was done with cold instruments. The histopathological examination showed amorphous deposit of homogenous extracellular eosinophilic material, which showing apple-green birefringence under polarized light on staining with Congo-red. Hence, the diagnosis of amyloidosis was confirmed. Two months post-operatively, her voice assessment showed improvement in which the GRBAS score were grade 2, main component of strain (roughness =1, breathiness=0, asthenia=1, and strain=2).

Rigid laryngoscopy showed fullness over bilateral false cords which did not progress during the one-year follow-up as shown in Figure 1. There was also no sign and symptom of systemic amyloidosis observed.

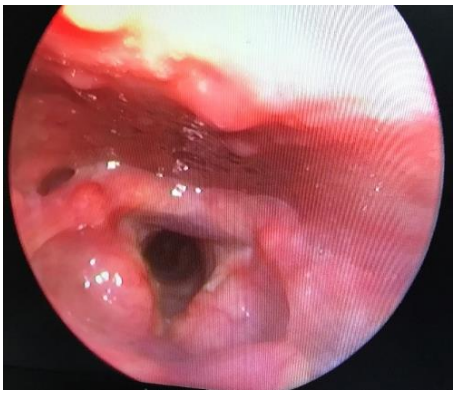

Figure 1. Laryngoscopy shows bulging bilateral false cords.

Case 2

A 62-year-old female complained of hoarseness for two years. Otherwise, she denied dysphagia or noisy breathing. Perceptual voice assessment using GRBAS revealed overall dysphonia grade 3, main component of roughness and strain (roughness=3, breathiness=1, asthenia=1, and strain=3). Flexible laryngoscopy showed diffuse swollen and thickened mucosa of the epiglottis, aryepiglottic folds and false cords (Fig. 2). There was no discoloration, increase in vascularity or ulceration. The mucosa surface was smooth. Under general anesthesia, endoscopic laryngeal microsurgery was performed and tissue biopsy was taken from false cords, epiglottis, post-cricoid and pyriform sinus. The true vocal cords and subglottic mucosa were normal appearance (Fig. 3). Histopathological examination confirmed the diagnosis of amyloidosis. Contrast enhanced computed tomography (CT) of neck and thorax showed diffuse wall thickening involving the epiglottis, aryepiglottic fold, hypopharynx until post cricoid region (Fig. 4 – 5).

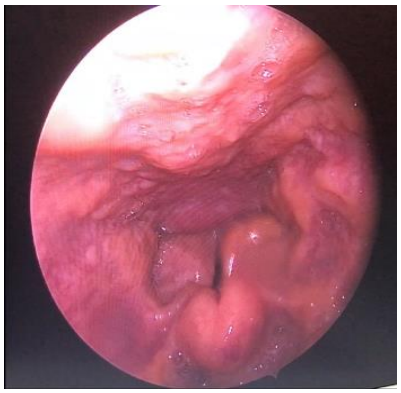

Figure 2. Flexible laryngoscopy showed diffuse swollen supraglottic structures.

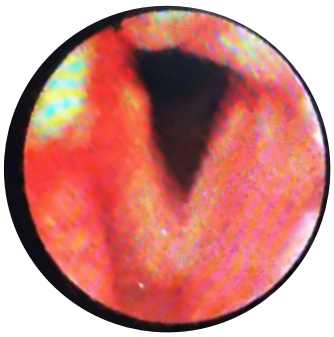

Figure 3. True vocal folds were not involved.

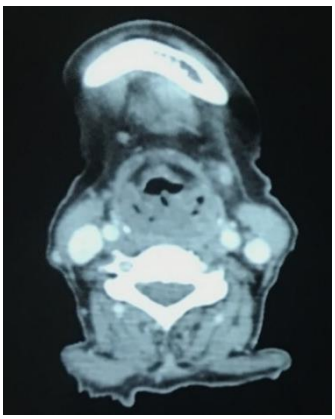

Figure 4. Axial view of CT image.

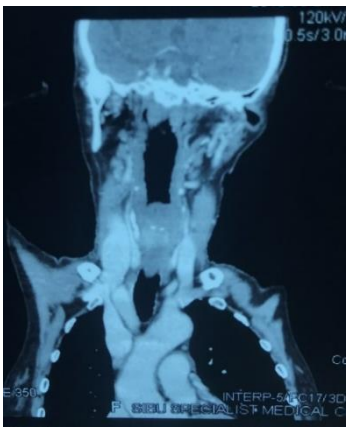

Figure 5. Coronal view of CT

DISCUSSION

Laryngeal amyloidosis is a disease of multifocal nature which there is no specific location in larynx were commonly affected by amyloid deposition and all parts of the larynx could be affected (4). The most common site of laryngeal amyloid involvement was the supraglottis, followed by glottis and subglottis (2,5). It was also common to have involvement of more than one subsite including ventricles, false vocal cords, true vocal cords, aryepiglottic folds, epiglottis, subglottis or upper aerodigestive tract. This was thought to be attributable to the multifocal nature of the disease (6).

Wu X. et. al. has retrospectively studied the laryngeal amyloidosis cases and found that the ratio of male to female about 1: 1.7 with mean age of 51.3 ± 12.6 years (7). Both of the cases we discussed here are middle-aged female and it was similar finding demographically as reported by Wu X et al. Hoarseness is the main presentation, as high as 95% of the cases (6). In extensive cases, it may present with dyspnea, stridor, globus sensation or dysphagia. An extensive growth may cause airway obstruction which is life threatening.

Clinical diagnosis is challenging in laryngeal amyloidosis as its presentations and the irregular growth mimicking carcinoma and chronic inflammation of the larynx such as laryngeal tuberculosis and IgG4 disease. Laryngoscopy, bronchoscopy and esophagoscopy are essential to assess the extension of the disease. Tissue biopsy remained the gold standard diagnostic test of amyloidosis. The surgical team needs to have an index of suspicion and inform the histopathologist their differential diagnosis. Amyloid stains positively with Congo red and characteristically it produces apply-green birefringence under polarized microscopy, which are diagnostic markers.

Amyloidosis can be classified as either primary or secondary as a result of chronic inflammatory condition such as rheumatoid arthritis. Patients diagnosed with laryngeal amyloidosis need to be investigated for systemic involvement including rheumatoid arthritis and multiple myeloma(8). These are normally carried out in collaboration with a rheumatologist. Investigations that can be done to look for circulating immunoglobulin light chain fragments include serum and urine immune-electrophoresis, liver function test, blood urea and electrolytes, serum amyloid P component (SAP) scintigraphy, abdominal fat biopsy and computed tomography thorax. Rarely, patients progress to systemic disease (2,4,6). Our patients had been screened with the tests and no other organs were involved.

The management for the localized laryngeal lesions is debulking procedure endoscopically either by cold instruments or carbon dioxide (CO_2) laser. Excision using CO_2 laser has shown good outcome (9). In addition, CO_2 laser is preferred over cold knife due to its enhanced precision, reduced bleeding, faster healing and reduced scarring (10). However, complete excision of the diseased part would risk the normal phonatory architecture of the vocal cords which making the total resection challenging if the true cords is involved. For patients who are asymptomatic, close observation is an acceptable option (5).

Local recurrence is very common after surgical debulking. Truong et. al. showed that treating laryngeal amyloidosis with radiotherapy using 20Gy in conventional fractionation is effective in arresting progressive airway amyloidosis and allows airway remodeling. It is suggested that obstructive amyloid lesions should be managed with a combination of surgical debulking and radiotherapy (11). However, radiotherapy remains debatable and is not widely accepted now. The side effects and tissue toxicity caused by radiotherapy to esophagus, heart and normal lung parenchyma should be taken into account prior to the treatment. Laryngeal amyloidosis is a benign, slowly progressive disease and rarely fatal. The possible morbidity of every therapy must be weighed against the benefits of the treatment options.

Regular and long term follow up of upper and lower airway is always required. It was recommended to follow up yearly for a duration of at least 7 to 10 years (8,12).

CONCLUSION

The goals of treatment should be directed toward the maintenance of the airway and to improve voice quality. Laryngeal amyloidosis is a rare and is a benign disease. Differential diagnosis should be considered in an atypical mass in the larynx and the index of suspicion should be warranted to the pathologist for a confirmatory diagnosis. In addition, long term follow up is essential as local recurrence is high post-surgical debulking.

Conflict of interest
No conflict of interest was declared by the authors.

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REFERENCES

1. Reiter R, Hoffmann TK, Pickhard A, Brosch S. Hoarseness - causes and treatments. Deutsches Arzteblatt International 2015;112:329–37.
2. Rudy SF, Jeffery CC, Damrose EJ. Clinical characteristics of laryngeal versus nonlaryngeal amyloidosis. Laryngoscope 2018;128:670–4.
3. Chow V, Gardner K, Howlett D. Primary localized laryngeal amyloidosis presenting with dysphonia: a case report. J Surg Case Reports 2012;2012:rjs005.
4. Thompson LDR, Derringer GA, Wenig BM. Amyloidosis of the larynx: a clinicopathologic study of 11 cases. Mod Pathol 2000;13:528–35.
5. Phillips NM, Matthews E, Altmann C, Agnew J, Burns H. Laryngeal amyloidosis: diagnosis, pathophysiology and management. J Laryngol Otol 2017;131:S41–7.
6. Harris G, Lachmann H, Hawkins P, Sandhu G. One hundred cases of localized laryngeal amyloidosis - evidence for future management. Laryngoscope 2021;131:E1912–7.
7. Wu X, Zhang J, Wei C. Risk factors for recurrence of laryngeal amyloidosis treated by microforceps and CO_2 laser. Eur Arch Oto-Rhino-Laryngology 2020;277:521–5.
8. Bartels H, Dikkers FG, Van Der Wal JE, Lokhorst HM, Hazenberg BPC. Laryngeal amyloidosis: Localized versus systemic disease and update on diagnosis and therapy. Ann Otol Rhinol Laryngol 2004;113:741–8.
9. Daudia A, Motamed M, Lo S. Primary amyloidosis of the larynx. Postgr Med J 2000;76:364–5.
10. Deviprasad D, Pujary K, Balakrishnan R, Nayak DR. KTP Laser in laryngeal amyloidosis: five cases with review of literature. Indian J Otolaryngol Head Neck Surg 2013;65(Suppl 1):36-41.
11. Truong MT, Kachnic LA, Grillone GA, Bohrs HK, Lee R, Sakai O, et al. Long-term results of conformal radiotherapy for progressive airway amyloidosis. Int J Radiat Oncol Biol Phys 2012;83:734–9.
12. Hazenberg AJ, Hazenberg BP, Dikkers FG. Long-term follow-up after surgery in localized laryngeal amyloidosis. Eur Arch Otorhinolaryngology 2016; 273:2613-20.