

CASE REPORT

Amyloidosis of the larynx: a case report

Larenks amiloidozu: Olgu sunumu

Özden TULUNAY, M.D.,¹ Gürsel DURSUN, M.D.,² Süha BETON, M.D.,²
Hilal ERİNÇ, M.D.,¹ Hünkar BATIKHAN, M.D.²

A 75-year-old female patient presented with hoarseness and foreign body sensation in the back of her throat of one-month history. Direct laryngoscopy showed bilateral, yellow, hyperemic masses on the left false vocal fold and laryngeal ventricle. Both true vocal folds were mobile. Excisional biopsies of the right false vocal fold and ventricle showed extracellular, insoluble, fibrillar protein accumulation, consistent with amyloidosis. There was no evidence for neoplasm. Serum and urine electrophoreses were negative. The work-up for systemic amyloidosis and multiple myeloma were negative. Treatment was limited to surgical excision. No complications developed within a six-month follow-up period.

Key Words: Amyloidosis/pathology; hoarseness; laryngeal diseases.

Yetmiş beş yaşındaki kadın hasta ses kısıklığı ve boğazının arka bölümünde yabancı cisim duygusu yakınmalarıyla başvurdu. Direkt larengoskopide sol yalancı vokal kordda ve larengeal ventrikülde iki taraflı, sarı, hiperemik kitlelere rastlandı. Her iki gerçek vokal kord hareketliydi. Sol yalancı vokal kord ve larengeal ventrikülden alınan eksizyonel biyopsilerde amiloidoz ile uyumlu ekstraselüler, insolubl fibriller protein birikimleri saptandı. Tümör lehine bir bulguya rastlanmadı. Serum ve idrar elektroforezleri negatif bulundu. Sistemik amiloidoz ve multipl miyeloma yönelik ileri incelemeler negatif sonuçlandı. Tedavi cerrahi ile sınırlandı. Altı aylık takip dönemi sırasında herhangi bir komplikasyon gözlenmedi.

Anahtar Sözcükler: Amiloidoz/patoloji; ses kısıklığı; larenks hastalığı.

Amyloidosis is an acquired or inherited disorder associated with deposition of extracellular, insoluble fibrillar protein. Laryngeal amyloidosis (LA) is an uncommon form of amyloidosis with limited long-term clinicopathological knowledge in the literature. Laryngeal amyloidosis represents 0.5-1% of benign laryngeal disease, increasing with age but occasionally affecting young adults,^[1] and it affects men and women equally. Discrete nodular and diffuse infiltrative types of LA were described in 1919.^[2] Multifocal disease is present in up to 15% of all patients. The dif-

fuse pattern with an intact mucosa is more common, sometimes with a tracheobronchial extension.^[3] The ventricles and false cord folds are affected most frequently, and they exhibit smooth, submucosal nodular to diffuse deposits beneath an intact surface epithelium. Symptomatic laryngeal amyloidosis is usually localized but rarely can be a manifestation of systemic LA type.^[3,4] The amyloid deposits occur most commonly in the supraglottic larynx and usually present with hoarseness or stridor, but can cause a sensation of "fullness" in the throat, choking, and

◆ Departments of ¹Pathology and ²Otolaryngology, Medicine Faculty of Ankara University (Ankara Üniversitesi Tıp Fakültesi, ¹Patoloji Anabilim Dalı, ²Kulak Burun Boğaz Hastalıkları Anabilim Dalı), Ankara, Turkey.

◆ Received - December 10, 2004 (Dergiye geliş tarihi - 10 Aralık 2004). Accepted for publication - February 11, 2005 (Yayın için kabul tarihi - 11 Şubat 2005).

◆ Correspondence (İletişim adresi): Dr. Özden Tulunay. Ankara Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı, 06100 Sıhhiye, Ankara, Turkey.
Tel: +90 312 - 310 83 31 Fax (Faks): +90 312 - 310 83 31 e-mail (e-posta): ozdentulunay@yahoo.com

dysphnoea on exertion.^[3] The disorder is usually relatively benign but can be progressive or recur after treatment. Fatal hemorrhage has been reported.^[5]

We report a female patient diagnosed by a small incisional biopsy, and treated with excisional biopsy.

CASE REPORT

A 75-year-old female patient presented with a one-month history of hoarseness and foreign body sensation in the back of her throat, that was not associated with symptoms or signs of infection. Direct laryngoscopy showed bilateral, yellow, hyperemic masses on the left false vocal fold and laryngeal ventricle (Fig. 1). Both true vocal folds were mobile. An incisional biopsy consisting of 7x3x3 mm tissue was performed which was followed by another excisional biopsy two months later consisting of eleven tissues, the largest was 5x2x2 mm. Microscopically, there was an subepithelial, extracellular, acellular, amorphous and eosinophilic matrix deposition that was often accentuated around minor seromucous glands and vessels (Fig. 2). A sparse inflammatory infiltrate predominantly made up of lymphocytes and plasma cells were noted particularly at the leading edge of amyloid. Foreign body type giant cells also were frequently noted. Deposited material exhibited apple-green birefringence when stained with Congo red and viewed under polarized light, consistent with amyloidosis. Immunoreactivity with p component (Fig. 3), but not with AA and kappa light chain were demonstrated. Seldom and trace lambda light chain immunoreactivity was demonstrated, especially at the central areas of some amyloid deposits. There was no evidence of



Fig. 1 - Hyperemic mass on the left false fold and laryngeal ventricle.

neoplasm. Serum and urine electrophoreses were negative. The work-up for systemic amyloidosis and multiple myeloma were negative. Treatment was limited to surgical excision. The patient did not develop multiple myeloma or an overt B-cell lymphoma six months after the excisional therapy.

DISCUSSION

Since laryngeal amyloidosis may be associated with multifocal or systemic disease, appropriate clinical, radiographic, and laboratory investigation -including serum and protein electrophoreses, chest radiographs, and possibly gastrointestinal biopsy- is recommended to exclude systemic disease. Electron microscopy reveals the characteristic interlacing meshwork of nonbranching fibrils as the protein arranges itself into beta-pleated sheets. The cause of amyloidosis is unknown. Laryngeal amyloidosis is an uncommon indolent lesion that may be associated with multifocal disease (local or systemic). Laryngeal amyloidosis is a slow-progressive disease. Amyloidosis is the deposition of amyloid, an extracellular fibrillar protein with unique ultrastructural, X-ray diffraction, and biochemical properties, in one or more sites in the body. In the head and neck region, deposits may occur in the sinonasal tract, nasopharynx, oral cavity, larynx, or tracheobronchial tree. The larynx is the most common upper respiratory site involved.^[4,6] Within the larynx, amyloidosis affects (in order of decreasing frequency) the true vocal folds, laryngeal ventricle, false vocal folds, aryepiglottic folds, and subglottic space. Multiple sites are frequently affected both in the larynx and throughout the aerodigestive tract, with the trachea and base of tongue being the most common extralaryngeal locations.^[4,7]

Laryngeal amyloidosis is usually a primary, localized process of the AL type, although it can, on rare occasions, be the presenting symptoms of systemic amyloidosis.^[4] Various studies show an equal male-to-female ratio or a 3:1 male predominance, and although it typically presents in middle life, LA has been reported in patients ranging from 8 to 90 years old.^[7] Histologically, amyloid is an homogeneous, acellular, eosinophilic, extracellular infiltrate; lymphocytes, plasma cells, and foreign body giant cells may be seen in the surrounding tissue.^[6] Classically, amyloid can be distinguished from other eosinophilic depositions via its apple-green birefringence when stained with Congo red and viewed

under polarized light (specific but not sensitive). Potassium permanganate distinguishes AL from AA types, and immunohistochemistry can differentiate kappa light chains from lambda chains in AL type amyloidosis. Electron microscopy remains the gold standard for diagnosis, showing a fibrous protein with characteristic rigid, linear, nonbranching fibrils measuring 7.5 to 10 nm in width.^[6]

Hoarseness is the most common presenting symptom. Dyspnea, hemoptysis, dysphagia, throat fullness, and a choking sensation have also been reported. Diagnosis should focus on evaluating the extent of local amyloidosis and on ruling out systemic involvement. Laryngoscopy typically reveals a waxy, translucent, yellow or yellow-gray swelling without ulceration

of the overlying mucosa^[7] as observed in the present case. Some authors recommend a complete endoscopic examination of the entire respiratory tract given the propensity for multifocal LA.^[6] Systemic work-up should assess for multiple myeloma. The differential diagnosis includes vocal fold polyps and ligenous conjunctivitis, and it is important to note that amyloid may occur in association with multiple myeloma, small cell carcinoma, and medullary thyroid carcinoma. Immunohistochemistry can usually clarify this differential. The differential diagnosis should also include metastatic and invasive medullary thyroid cancer. Conservative endoscopic removal of amyloid deposits yields good results, although recurrent or persistent disease is common.

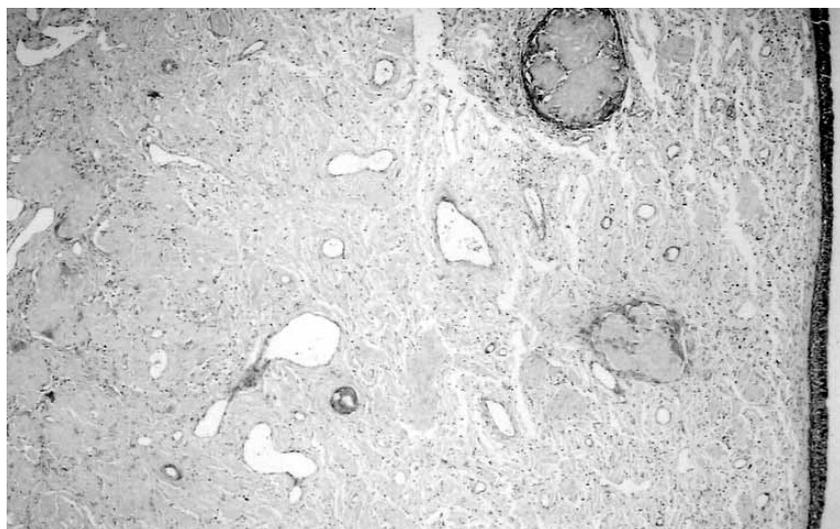


Fig. 2 - Pink amorphous stromal amyloid deposition, surrounding residual blood vessel walls and mucous glands in the submucosa of false vocal fold (H-E x 10).

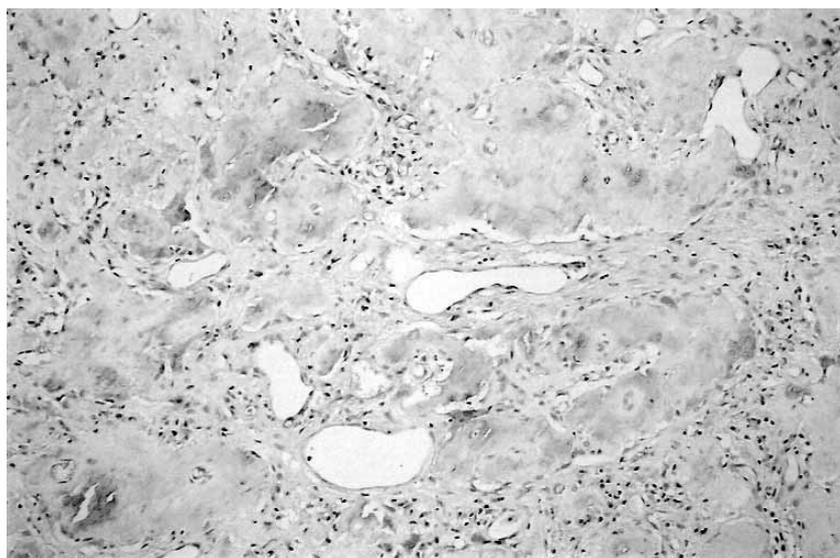


Fig. 3 - Amyloid deposits with a sparse inflammatory infiltrate predominantly made up of lymphocytes and small giant cells, particularly at the leading edge of amyloid, are weakly stained for p component (Peroxidase, x 25).

Treatment for LA is surgical removal. Endoscopic excisional biopsy is usually adequate, although open techniques have been used for extensive disease. Both radiotherapy and medical management are ineffective.^[7]

The prognosis for patients with localized LA is excellent if the lesion is completely excised. Long-term monitoring for local recurrences or subsequent development of systemic disease is important. There has been no report of malignant change in amyloid tumors.

REFERENCES

1. McAlpine JC, Fuller AP. Localized laryngeal amyloidosis, a report of a case with review of the literature. *J Laryngol Otol* 1964;78:296-314.
2. New GB. Amyloid tumours of the upper air passages. *Laryngoscope* 1919;29:327-41.
3. Lewis JE, Olsen KD, Kurtin PJ, Kyle RA. Laryngeal amyloidosis: a clinicopathologic and immunohistochemical review. *Otolaryngol Head Neck Surg* 1992;106:372-7.
4. Talbot AR. Laryngeal amyloidosis. *J Laryngol Otol* 1990;104:147-9.
5. Chow LT, Chow WH, Shum BS. Fatal massive upper respiratory tract haemorrhage: an unusual complication of localized amyloidosis of the larynx. *J Laryngol Otol* 1993;107:51-3.
6. O'Halloran LR, Lusk RP. Amyloidosis of the larynx in a child. *Ann Otol Rhinol Laryngol* 1994;103(8 Pt 1):590-4.
7. Mitrani M, Biller HF. Laryngeal amyloidosis. *Laryngoscope* 1985;95:1346-7.