The Journal of Laryngology & Otology
August 2003, Vol. **117,** pp. 647–650

CO_2-laser treatment of laryngeal amyloidosis

Gaetano Motta, M.D., Francesco Antonio Salzano, M.D.*, Sergio Motta, M.D.†, Stefania Staibano, M.D.‡

Abstract
Four consecutive female patients (age: 14–47 years) with laryngeal amyloidosis, treated with endoscopic CO_2-laser surgery, entered the study. All patients underwent periodic microlaryngoscopies following surgery to confirm the adequacy of the surgical resection. Recurrences or suspected lesions were resected and fibrin deposits were removed to prevent the formation of synechiae or healing adhesions. After two negative microlaryngoscopies, performed two months apart, the patients were followed-up approximately every six months over a period from six months to 18 years, with no evidence of recurrences. The endoscopic CO_2-laser technique is highly effective in the treatment of localized laryngeal amyloidosis.

Key words: Amyloid; Larynx; Laser Surgery

Introduction

The term amyloidosis is used to indicate an extracellular accumulation of homogeneous protein-derived fibrillar and eosinophil material, with well-defined histochemical characteristics.[1]

Amyloidosis can involve various body systems (systemic form) or, more rarely, a single organ (local form). The systemic variant[2] can appear as a complication of an immune disease in which fibrillar proteins derive from immunoglobulin light chains, or can be associated with chronic inflammation/infectious disease, usually leading to a poor prognosis.

Localized amyloidosis can involve a single abdominal organ (liver, kidney, spleen, bladder) or, more rarely, the head and neck region. In the latter rare location, the larynx is most frequently involved. The first case of local laryngeal amyloidosis (LA) dates back to 1875 and was observed by Burow and Newmann.[3] Up to 1990 a little more than 300 cases of the disease had been reported in the literature.[4]

Amyloidosis limited to the larynx or other head and neck sites usually has a favourable outcome. At present, most authors agree that surgery should be the treatment of choice for LA.[5–14] Surgical procedures include external partial laryngectomy or microlaryngoscopy.[10,15,16] Results obtained with CO_2-laser surgery in this series are discussed, in order to define the effectiveness of this procedure in the treatment of localized LA.

Materials and methods

Four patients with localized LA, consecutively admitted at the 'Dipartimento Assistenziale di Otorinolaringoiatria e Scienze Affini' of the University 'Federico II' of Naples from 1982 to 2000, entered the study. In all patients, clinical and laboratory investigation excluded extra-laryngeal involvement. All four patients were females, ranging in age between 14 and 47 years. In all cases a laryngotracheal computed tomography (CT) was obtained to ascertain the localization and extent of laryngeal lesions and to rule out extralaryngeal infiltration.

Resection was performed with endoscopic CO_2-laser surgery, and when possible, with en bloc resection of the lesion with the adjacent tissues. Laser power emission was set between 5–8 Watts in superpulse mode (200 Hz), with 0.27 mm^2 spot impact size.

In the first six months following the initial operation the patients underwent repeated check microlaryngoscopies in order to remove fibrin, prevent the formation of healing adhesions, perform biopsies at the site of excision and to rule out the presence of recurrences, or to resect them.

Subsequently, if two consecutive microlaryngoscopic examinations two months apart ruled out the presence of recurrence, further examinations were performed approximately every six months for three years.

Case reports

Case 1

A 14-year-old female patient was admitted to hospital in October 1982 with dysphonia which had been present for approximately one year. Laryngeal examination showed the presence of a left false cord mass, which was removed some days later by endoscopic CO_2-laser surgery. Histology of the surgical specimen revealed a circumscribed Congo-red positive nucleus of amyloidosis surrounded by healthy tissue, with mild chronic interstitial inflammation. A check microlaryngoscopy was performed to remove fibrin deposits at the site of surgery after approximately 20 days. There has been no evidence of recurrence in 18 years of follow-up, with optimal vocal functional outcome.

From the Department of Otorhinolaryngology, II University of Naples, Naples, the Department of Otorhinolaryngology*, University of Palermo, Palermo and the Departments of Otorhinolaryngology†, and Pathology‡, Ateneo 'Federico II', I University of Naples, Naples, Italy.
Accepted for publication: 9 December 2002.

Case 2

A 21-year-old female patient was admitted to hospital in June 1983 with a history of dysphonia, which had worsened progressively over the previous two years. Laryngeal examination demonstrated the presence of a mass involving the right false cord and adjacent aryepiglottic fold. The lesions were removed by endoscopic CO_2-laser surgery. On histology the typical pattern of LA was identified. The margins were either ill-defined or directly involved by amyloid infiltration. Approximately one month after the first operation, a further mass appeared in the right false vocal cord extending onto an adjacent portion of the epiglottis. It was removed by endoscopic CO_2-laser surgery. On histology, well-circumscribed submucosal amyloid deposits, surrounded by granulation tissue, were documented. There has been no further recurrence in 17 years of follow up, with no vocal functional impairment.

Case 3

A 34-year-old female patient was admitted to hospital with a one-year history of dysphonia. Laryngeal examination showed the presence of two 'pads' covered with mucosa of normal appearance, located in the subglottic region and extending to the anterior commissure. En bloc resections of both lesions were performed with endoscopic CO_2 laser. Histology of the surgical specimen revealed the presence of submucosal amyloid deposits surrounded by healthy tissue. Well-circumscribed fibrin deposits were removed at two further check microlaryngoscopies performed 20 days apart. At the latest follow-up, after 11 years, there has been no evidence of recurrence, with excellent vocal functional results.

Case 4

A 47-year-old female patient was admitted to hospital in March 1994 with dysphonia, which she had had for approximately two years. Laryngeal examination showed various submucosal masses involving the supraglottic, glottic and subglottic regions, especially on the right side (Figure 1). On laryngeal CT, the presence of submucosal hyperdense areas was documented. The bilateral lesions involving the false and true vocal folds were removed by endoscopic CO_2-laser surgery. On histology large deposits of amyloid were detected at the level of resection margins. The infiltration involved the connective tissue immediately below the epithelial layer and extended deeply (Figure 2). Approximately nine months later, some apparently well-circumscribed lesions involving the posterior segment of the right true vocal fold and the subglottic region were removed by endoscopic CO_2-laser surgery. Histology showed the presence of amyloid surrounded by chronic inflammation. In October and November 1995 new lesions of amyloid were incompletely excised from both the true vocal folds and at the level of the epiglottic pedicle. Approximately one month later the patient was again admitted to hospital with worsening dyspnoea. Endoscopic CO_2-laser treatment was performed in order to: 1) vaporize an oedematous flap in the left arytenoid region; 2) resect a synechia at the level of the anterior commissure; 3) and remove some granulations located in the subglottic region. In spite of further repeated laser procedures for recurrent granulations of the false cords and glottal synechia, laryngeal narrowing eventually developed requiring the patient to have a Traissac stent inserted from April 1996 to July 1996. The patient has been left with dysphonia and glottic insufficiency but at the latest follow-up, six years after the first intervention, there was no evidence of recurrence (Figure 3).

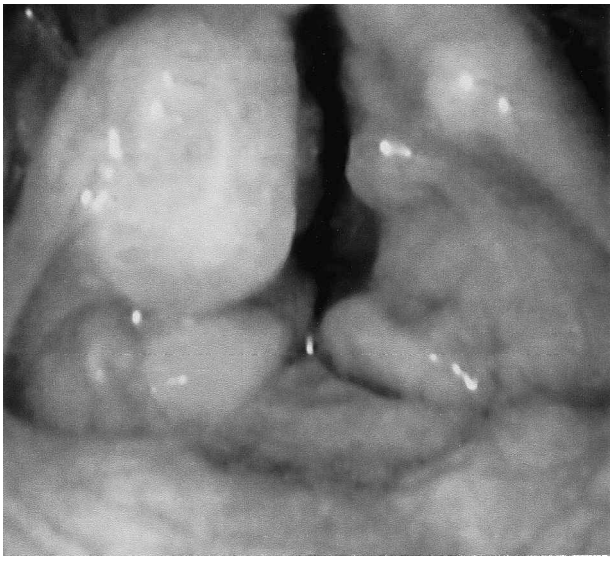

FIG. 1

Pre-operatory fibre-laryngoscopy findings (*Case 4*): submucosal masses involving the supraglottic, glottic and subglottic regions.

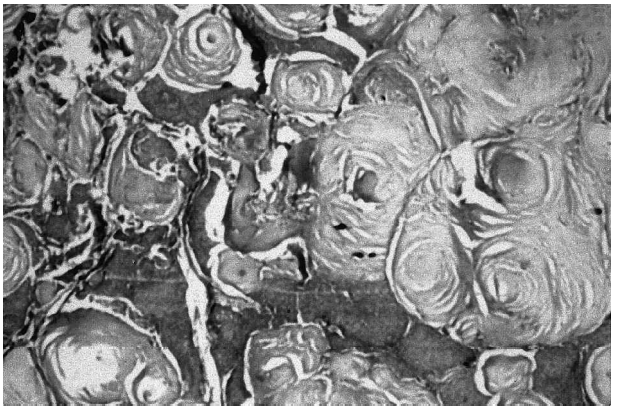

FIG. 2

Presence of extended, deeply diffuse amyloid accumulations (*Case 4*) (H & E; ×250)

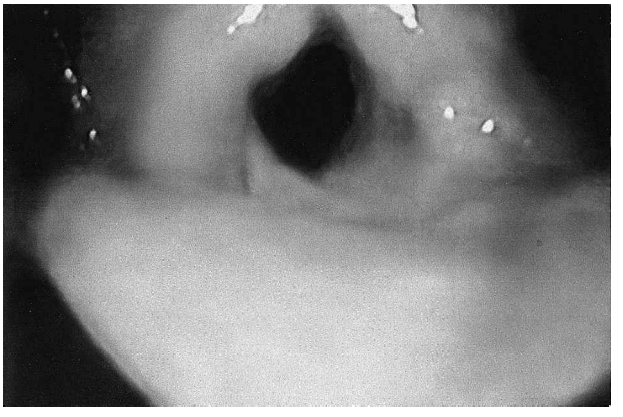

FIG. 3

Fibre-laryngoscopy findings six years after the last intervention (*Case 4*): no signs of recurrence.

https://doi.org/10.1258/002221503768200011 Published online by Cambridge University Press

Discussion

LA represents less than one per cent of all benign tumours of the larynx.[15,17,18] In our series, LA involved women ranging in age between 14 and 47 years. In the literature, a higher incidence in men, especially in the fifth and sixth decade of life, has been reported.[19,20]

Laryngeal involvement can occur at any site within the organ. Earlier reports suggested that the true vocal folds were the most common site to be affected[15,21] but more recent reports have described the supraglottic region and, in particular, the false vocal cords to be most frequently involved.[10,16] This is in agreement with what we observed in our series, where three out of the four subjects (*Cases 1, 2, 4*) showed amyloid lesions at the level of false vocal cords.

In the three patients (*Cases 1, 2, 3*) in whom amyloidosis was relatively superficial, it involved exclusively limited areas of subepithelial soft tissue, while in the patient in whom there was gross involvement of the larynx (*Case 4*), the amyloidosis deeply infiltrated the submucosal connective tissue and showed ill-defined margins.

These pathologic findings have a major impact on the surgical approach to LA. In fact, they demonstrate the need for early surgical treatment, when the lesions are well-circumscribed.

Generally, LA causes the formation of one or more masses covered by apparently healthy mucosa. The diagnosis can be confirmed by histological examination and characteristic histochemical staining with Congo-red.

For a definitive diagnostic assessment, imaging procedures play a major role, CT in particular, documenting the deepness of the submucosal extension, in the absence of superficial lesions or infiltration involving the cartilaginous skeleton.

Treatments of amyloidosis proposed in literature are based on: (1) the use of steroids, immunosuppressants and radiation therapy. These treatments had unsatisfactory results and are now completely abandoned;[4,6,11] (2) treatment of symptomatic lesions only. This clinical approach, still recently supported by Kennedy and Patel,[4] does not seem logical if keeping in mind that the patient is submitted to follow-up examinations for very long periods (five to 10 years) and subsequent surgery is not ruled out. Furthermore, in case of late operations with definitely more extended lesions, surgical resection of the lesions is more complex, the patient is exposed to a higher risk of recurrence and undesirable functional sequelae.

At present, most authors[9,20,22] agree on surgical treatment. However, the type of surgery to be performed remains controversial.

Kennedy and Patel[4] suggested the need for an external approach to remove the entire lesion radically, reporting their experience with five cases of localized LA. Two of them, after biopsy, did not receive any treatment because their symptoms were not severe enough (hoarseness, dysphagia, sore throat), while three patients with significant symptoms underwent surgery. Initially, endoscopic CO_2-laser surgery was performed but it did not allow radical excision. Subsequently, in two cases, an external approach was performed: recurrent disease was detected in one of those four months after and resected with CO_2-laser. According to the authors, an external lateral supraglottic approach would be the most suitable procedure for LA, as the continuity of internal supraglottic structures and anterior commissure is ensured. Moreover, the authors' procedure would imply lower risks and costs as compared to endoscopic surgery that requires repeated admissions for microlaryngoscopy during follow-up.

On the contrary, other authors[8,9,13,14,20,23] strongly support endoscopic CO_2-laser surgery, pinpointing the advantages of this procedure, in terms of functional outcomes, as compared to conventional external approaches.

In our opinion, LA must be treated surgically with the most suitable techniques. In three of the study subjects, radical resection was feasible and a definitive clinical recovery was achieved. Obviously, in case of extended laryngeal involvement, as for *Case 4* in our series, the cure of LA can require a series of undoubtedly complex surgical procedures. Regarding this, it should be noted that the lesion margins are usually ill-defined and the need for surgical revisions cannot be ruled out *a priori*, even with external surgical approaches.

In light of our experience, we believe that endoscopic CO_2-laser surgery is highly effective in the treatment of LA. In fact, radical resection is feasible with reduced trauma, excellent post-operative functional outcomes and prompted surgical revisions, based on easier follow-up examinations, and in less extended cases, shorter hospital stay is possible with subsequent lower public health costs.

Conclusion

Endoscopic CO_2-laser surgery allows a radical resection of localized laryngeal amyloidosis. The need for surgical revisions cannot be ruled out, especially in more extended forms. Surgery must be followed by careful check microlaryngoscopies to remove fibrin, prevent the formation of healing adhesions and confirm the radicality of surgery with biopsy sampling.

References

1 Loehrl TA, Smith TL. Inflammatory and granulomatous lesions of the larynx and pharynx. *Am J Med* 2001;**111** (suppl 8):113–7
2 Husby G. Nomenclature and classification of amyloid and amyloidosis. *J Intern Med* 1992;**232**;511–2
3 Burrow A, Neumann L. Amyloid degeneration von larynxtumoren, canule sieben jahre lang getragen. *Arch Klin Chir* 1875;**18**:242–6
4 Kennedy TL, Patel NM. Surgical management of localized amyloidosis. *Laryngoscope* 2000;**110**:918–23
5 Caldarelli DD, Friedberg SA, Harris AA. Medical and surgical aspects of the granulomatous diseases of the larynx. *Otolaryngol Clin North Am* 1979;**12**:767–81
6 D'Arcy F. Localised amyloidosis of the larynx. *J Laryngol Otol* 1972;**86**:929–31
7 Fernandes CM, Pirie D, Pudifin DJ. Laryngeal amyloidosis. *J Laryngol Otol* 1982;**96**:1165–75
8 De Vergas Gutierrez J, Mingorance Lopez A, Romero Castellano L, Garcia Fernandez A, Brandariz Castelo JA, Marino Espuelas J. Localized laryngeal amyloidosis. Treatment with CO_2 laser. *Acta Otorrinolarngol Esp* 1995;**46**:381–3
9 McIlwain JC, Shepperd WH. Laser treatment of primary amyloidosis of the larynx. *J Laryngol Otol* 1986;**100**:1079–80
10 Raymond AK, Sneige N, Batsakis JG. Pathology consultation amyloidosis in the upper aerodigestive tracts. *Ann Otol Rhinol Laryngol* 1992;**101**:794–6
11 Heiner ER. Primary amyloidosis of the larynx. *Arch Otolaryngol* 1968;**87**:413–5
12 Schindel J, Ben-Bassatt H. Amyloid tumor of the larynx, case report with electron microscopy study. *Ann Otol Rhinol Laryngol* 1972;**81**:438–43
13 Simpson GT, Strong MS, Skinner M, Cohen AS. Localized amyloidosis of the head and neck and upper aerodigestive and lower respiratory tracts. *Ann Otol Rhinol Laryngol* 1984;**93**:374–9
14 Talbot AR. Laryngeal amyloidosis. *J Laryngol Otol* 1990;**104**:147–9

https://doi.org/10.1258/002221503768200011 Published online by Cambridge University Press

15 Mitrani M, Biller HF. Laryngeal amyloidosis. *Laryngoscope* 1985;**95**:1346–7
16 O'Halloran LR, Lusk RP. Amyloidosis of the larynx in a child. *Ann Otol Rhinol Laryngol* 1994;**103**:590–4
17 Hellquist H, Olofsson J, Sofjer H, Odkvist LM. Amyloidosis of the larynx. *Acta Otolaryngol* 1979;**88**:443–50
18 McAlpine JC, Fuller AP. Localized laryngeal amyloidosis: a report of a case with review of the literature. *J Laryngol Otol* 1964;**78**:296–314
19 Graamans K, Lubsen H. Clinical implications of laryngeal amyloidosis. *J Laryngol Otol* 1985;**99**:617–23
20 Walker PA, Courey M, Ossof RH. Staged endoscopic treatment of laryngeal amyloidosis. *Otolaryngol Head Neck Surg* 1996;**114**:801–5
21 Ryan JR, Pearson BW, Weilland LH. Laryngeal amyloidosis. *ORL* 1977;**84**:872–7
22 Woo KS, Van Hasselt CA, Waldron J. Laser resection of localized subglottic amyloidosis. *J Otolaryngol* 1990;**19**:337–8
23 Gaillard J, Haguenauer JP, Pignal JL. L'amylose laryngeé. A propos de 2 cas d'amylose sous-glottique traites par làser. *J Français d'Oro-Rhino-Laryngol* 1986;**100**:1079–80

Address for correspondence:
Sergio Motta, M.D.,
Via M. da Caravaggio 119,
80126 – Naples,
Italy.

Fax: 081 5752552
E-mail: sermotta@yahoo.it

Sergio Motta, M.D., takes responsibility for the integrity of the content of the paper.
Competing interests: None declared