Exertion Dyspnea and Stridor: an Unusual Presentation of Localized Laryngeal Amyloidosis

David Ergas MD[1], Yigal Abramowitz MD[1], Yonatan Lahav MD[2], Doron Halperin MD[2] and Zev Moshe Sthoeger MD[1]

Departments of [1]Medicine B and [2]Ear/Nose/Throat, Kaplan Medical Center, Rehovot, Israel
Affiliated to Hebrew University-Hadassah Medical School, Jerusalem, Israel

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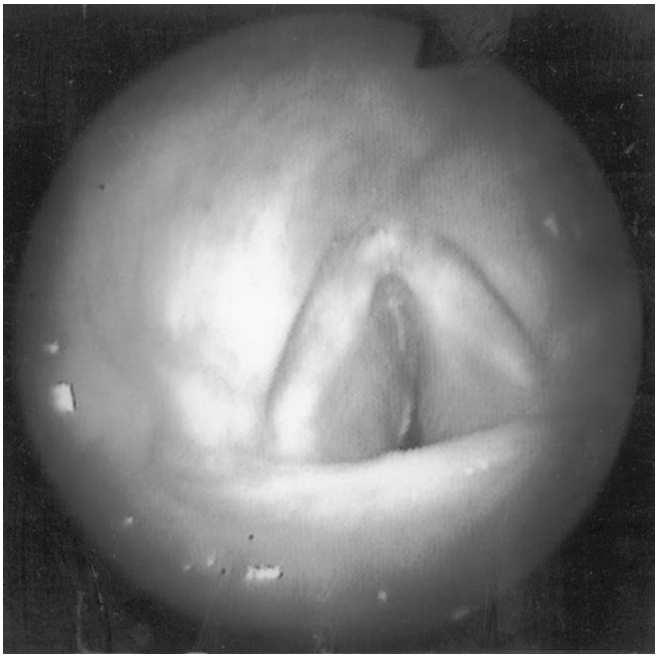
Amyloidosis is characterized by the extracellular deposition of abnormal insoluble fibrillar proteins in organs and tissues. The amyloid protein takes up Congo red stain and exhibits an apple-green birefringence under polarized microscopy [1]. Amyloidosis is usually a systemic disease with multiorgan involvement and a grave prognosis. Thus, detection of amyloid protein in any tissue usually leads to a thorough search for systemic involvement. Nevertheless, focal forms of amyloidosis with solitary organs but no systemic involvement rarely occur. The latter forms have a much better prognosis [1,2]. We describe here a patient with recurrent laryngeal amyloidosis without systemic involvement.

Patient Description

A 63 year old woman with a 3 month history of progressive dyspnea on exertion and an episodic non-productive cough was admitted. Her medical history included well-controlled hypertension, migraine and parathyroidectomy due to adenoma. On examination, inspiratory stridor was present while at rest. The stridor increased after mild exertion. There was no change in her voice. The rest of the examination was normal. Routine laboratory tests including erythrocyte sedimentation rate, urinalysis and chest X-ray were all normal.

Direct laryngoscopy demonstrated an irregular subglottic lesion that originated immediately under the true vocal cords and descended 3 cm to the subglottic area. Biopsy from the lesion disclosed chronic inflammation, fibrosis and atypia of epithelial cells but no signs of malignancy. There was prominent sedimentation of a homogenous eosinophilic material with a typical apple-green birefringence under polarizing microscope after staining with Congo red. Stain for AA amyloid was negative. Debulking of the lesion was performed to relieve mechanical airflow obstruction, with complete resolution of symptoms. An extensive workup for systemic amyloidosis including serum and urine electrophoresis, bone marrow biopsy, subcutaneous fat aspiration, cardiac echo, bronchoscopy, chest computed tomography and abdominal ultrasound were all normal. Serum beta-2 microglobulin was mildly elevated at 3259 ng/ml (normal 0–1900).

The patient was asymptomatic for 1 year following the operation, after which her dyspnea recurred accompanied by a mild hoarseness. Concomitantly, the level of serum β2-microglobulin was further elevated (4453 ng/ml). Laryngoscopy revealed bilateral subglotic submucosal lesion compatible with a mild recurrence of her laryngeal amyloidosis that did not require re-operation. Two months later, the patient developed severe dyspnea with stridor. Repeated laryngoscopy demonstrated severe subglotic stenosis [Figure]. At that time, extensive workup was again negative for systemic disease. The patient was re-operated using a CO_2 Laser. Laryngeal tissue obtained was infiltrated with a Congo-red stained material. Following the second operation a clinical improvement was observed although residual exertional stridor persisted. Similarly, the β2-microglobulin levels declined but remained elevated (3200 ng/ml). Four months later the patient underwent tracheostomy due to another local recurrence. Eighteen



Direct laryngoscopy before re-operation shows recurrent disease (laryngeal amyloidosis). Immediately beneath the vocal cord there is bilateral submucosal encroachment on the lumen, leaving only a minute orifice.

months after the tracheostomy she is in a stable condition without any respiratory complaints.

Comment

Amyloidosis of the larynx is quite an uncommon disease, accounting for 0.2–1.2% of benign tumors of the larynx [3]. Burow and Neumann [2] reported the first case in 1875. Most patients with laryngeal amyloidosis present with progressive hoarseness. All 11 patients in the clinical series published by Thompson et al. [3] and 18 of 22 patients in the series published by Lewis et al. [2] had a progressive hoarseness as their chief complaint. Other common clinical features include stridor, fullness in the throat and dysphagia [2–4].

Amyloid in the larynx and trachea is formed by local deposition of monoclonal light chains, probably from a focal plasma cell clone. Of the 22 cases studied by Lewis et al. [2], monoclonal lambda light chains were detected in 12 and kappa chains in 5. Despite its monoclonal origin, amyloidosis of both the larynx and the tracheobronchial tree, with rare exceptions, takes a localized benign form. In a prolonged follow-up of 43 patients with amyloidosis of the larynx and trachea, none of the patients developed systemic amyloidosis, B cell lymphoma or multiple myeloma [2,3,5]. Nevertheless, systemic workup is considered mandatory in every patient. Given that systemic involvement in patients with symptomatic amyloidosis of the airways is so rare, we believe that systemic workup should be limited to urinalysis, serum and urine protein electrophoresis and bone marrow aspiration if there are no clinical signs of systemic involvement.

β2-microglobulin is elevated in sera of patients with systemic AL amyloidosis. There is a negative correlation between the levels of β2-microglobulin and the prognosis of the disease. In our patient, the levels of sera β2-microglobulin also correlated with disease progression demonstrating reduction of β2-microglobulin levels following surgery. Thus, the levels of the β2-microglobulin in the sera may have a value in follow-up of patients with localized laryngeal amyloidosis.

Treatment of laryngeal amyloidosis usually consists of surgical excision [2]. Although systemic progression is rare, local recurrences of the disease, as in our patient, are quite common. More than 50% of patients suffer from recurrent or multifocal local disease, requiring repeated surgical procedures [2,3]. Laser therapy and local irradiation are other therapeutic options for those patients.

Finally, the patient described here had an unusual presentation – namely, exertional dyspnea and episodic cough without hoarseness. Such a presentation is more characteristic of tracheobronchial amyloidosis [5] and probably reflects the proximity of her lesion to the trachea.

References

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Correspondence: Dr. Z. Sthoeger, Head, Dept. of Medicine B, Kaplan Medical Center, P.O. Box 1, Rehovot 76100, Israel.
Phone: (972-8) 944-1357
Fax: (972-8) 944-1826
email: zev_s@clalit.org.il