LOCALIZED VOCAL CORD AMYLOIDOSIS

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Localized laryngeal amyloidosis is an uncommon diease with limited long-term follow-up studies. The precise etiology and pathogenesis are not entirely clear. We present a case of localized laryngeal amyloidosis. 35 years old man suffered from hoarseness during the last six months. Laryngoscopic examination showed nodular infiltration of bilateral vocal cords. Amyloidosis was confirmed by the characteristic Congo red staining of biopsies. The search for other localizations of amyloidosis was negative. No evidence of systemic amyloidosis or plasma cell proliferation was found in this patient. There were no recurrences during the nine-months follow-up.

Key words: Amyloidosis, localized, larynx, vocal cords.

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INTRODUCTION

Amyloidosis is a disorder in which an insoluble proteinaceous material is deposited in the extracellular matrix of tissues. The deposits may be localized one organ or may be systemic. Localized amyloidosis is characterized by the deposition of amyloid fibres in a particular site or organ system in the absence of systemic involvement (1). Amyloidosis of the respiratory tract is rare. However, the larynx is the commenest site within the upper airways to be affected. The common presentation of the patients are long-standing hoarseness or dyspnea (2). The lesions may involve vocal cords, anterior commissure, and ventricle (3). We are reporting a case of localized vocal cord amyloidosis in a 35 year old man.

CASE

A 35 year-old man presented in September 2005 to a private clinic with a 6-months history of hoarseness. On laryngoscopic examination, bilateral nodular involvement of the vocal cords was noted. Deep punch biopsy was performed. Congo red stain was positive for amyloidosis which persisted after potassium permanganate treatment (Figure 1). Polarization microscopy revealed the typical green birefringence of amyloid. The patient had been referred to our Rheumatology Clinic for evaluation of sytemic primary amyloidosis.

On admission, body temperature was 36.6 C, and pulse was 80/min, his blood pressure was 112/70 mmHg. He had no history of fatigue, weight loss, purpura, carpal tunnel syndrome or gross bleeding. In physical examination, there were no edema, purpura, joint symptoms, macroglossia, organomegaly or lymphadenopathy. His heart and pulmonary auscultation were normal. In neurological examination, he had no peripheral or autonomic neuropathy.

Laboratory investigations revealed: erythrocyte sedimentation rate 10 mm/h, serum CRP 0.1 mg/dl (normal, <0.8 mg/dl), white blood cell count 7200/mm3, haemoglobin 12.7 g/dl, haematocrit 40 %, platelets 225000/mm3, urea 31 mg/dl, creatinine 0.8 mg/dl. AST, ALT, CPK, ALP, LDH, Na, K, Ca, P, uric acid and TSH levels were normal. Urinalysis was unremarkable. Serum albumin and globulin levels were 4.5 g/dl and 3.2 g/dl, respectively. There was no sign of a monoclonal gammapathy on serum protein electrophoresis. Serum and urine immun electrophoresis for free light chains were negative. Chest X-ray and abdominal ultrasonography were unremarkable. Laryngeal magnetic resonans imaging failed

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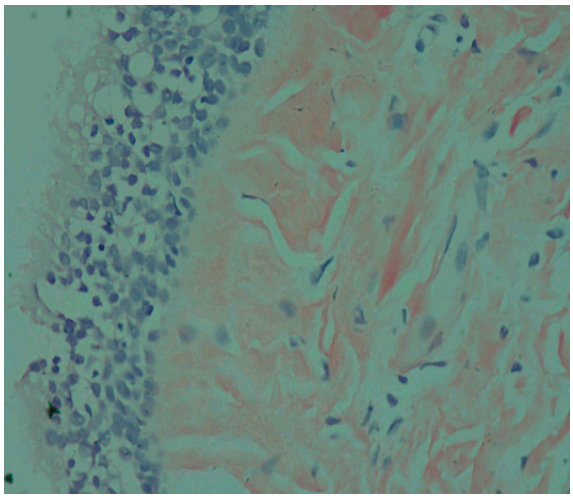

Figure 1. Submucosal diffuse amyloid deposition revelaed by Congo red-staining (Kongo x400).

to demonstrate evidence of extravocal cord amyloidosis. In two-dimensional echocardiographic examination, there was no increased myocardial echogenicity. Upper gastrointestinal endoscopic examination revealed a normal gastric mucosa with unremarkable histopathological findings. No evidence of systemic amyloidosis or an overt B-cell lymphoma was found in this patient. There were no recurrences during the nine-months follow-up.

DISCUSSION

Amyloidosis is a generic term for a heterogeneous group of disorders associated with extracellular deposition of protein in an abnormal fibrillar form. A current concept of amyloid formation is that specific proteins are transformed in such a way that they become insoluble and then aggregate along with other biologic substances to form proteolytically resistant tissue deposits. It can be deposited locally where it has no clinical consequences or may involve virtually any organ system of the body leading to severe pathophysiologic changes. There are many different types of amyloidosis and each type, characterized by a spesific class of proteins must be considered a separate disease. It is important for the physician first to recognize that a patient's ilness is due to amyloidosis and then to determine which disease the patient has, so that appropriate madical evaluation and intervention can be planned (4).

There are a number of types of amyloidosis that are localized to specific tissues or organs and these may be either sporadic or genetically determined. Amyloid may occur in localized deposits, resembling tumors. The lung, skin, larynx, eye, and bladder are common sites (2).

Amyloidosis localised to the respiratory tract was recognised by Lesser in 1877 (2). Amyloid deposits in the larynx or tracheal-bronchial tree may occur in a sporadic fashion. Symptomatology will include hoarseness if the amyloid deposits involve the larynx, or respiratory obstruction, nonproductive cough, and hemoptysis if the trachea or bronchi have significant amounts of amyloid deposition. Pulmonary function abnormalities depend on the location of involvement with proximal deposition typically causing obstructive physiology and mid/distal disease demonstrating normal airflow rates and air trapping (5).

Laryngeal amyloidosis is relatively uncommon, accounting for only 0.5-1 % of benign laryngeal disease. It increases with age but occasionally affects young adults. It can present as a nodular tumor or diffuse subepithelial deposition forming a bulging mass, the diffuse pattern with an intact mucosa being more common (2). The amyloid deposits occur most commonly in the supraglottic larynx. The lesions may involve vocal cords, anterior commissure, and ventricle. Patients usually present with hoarseness or stridor, but can cause a sensation of "fullness" in the throat, choking, and dyspnea on exertion (1,2). The patient under discussion also presented with hoarseness of six months' duration.

The diagnosis of laryngeal amyloidosis is made by a high degree of suspicion on the basis of the history and a typical pale yellow appearance of the deposits on direct laryngoscopic examination (1,2). When such lesions are seen, an adequate deep punch biopsy should be obtained. The definitive diagnosis of amyloidosis depends on the histologic examination of tissue infiltrated with amyloid. The Congo red stain, which is the most commonly used to demonstrate amyloid deposits, gives a typical apple-green birefringence to the amyloid deposits, when viewed by polarisation microscopy. A modified potassium permanganate stain will allow reasonably accurate differentiation of the AA type from AL amyloid. An immunohistochemical test for AA amyloidosis using spesific anti-AA antiserum is reliable. Antiserum to K or L light-chain protins may be used but this is not as reliable as anti-AA staining (1). Amino acid sequence studies of laryngeal amyloid have shown that the amyloid fibrils are derived from amyloid

immunoglobulin light chain (6,7). In this case report, amyloidosis was confirmed by the Congo red staining of the biopsy specimen. Immunohistochemical staining could not be performed.

Symptomatic laryngeal amyloidosis is usually localised but can rarely be a manifestation of systemic AL type; or localized laryngeal amyloidosis may turn out to be systemic AL amyloidosis several years later (8). Systemic amyloidosis should be suspected whenever there are functional abnormalities in more than one organ system (2,4). Potential for an underlying disease, further medical evaluation for systemic disease, including measurement of free light chains should be performed. In this case, there were no clinical sign suggesting systemic amyloidosis. Protein electrophoresis did not reveal the presence of monoclonal gammapathy. Serum and urine immune electrophoresis for free light chains were negative.

After an appropriate examination to rule out systemic involvement, each patient therefore requires thorough evaluation to determine their optimal management. Management depends on the severity of the symptoms in regard to the individual patient, and some case, can be conservative observation. Biopsies during direct laryngoscopy can play both a diagnostic and therapeutic role. If disease is causing significant symptoms or showing signs of increasing in size, surgical intervention must be carried out. Preservation of the voice and airway should be the aim in all patients. Microlaryngoscopy with a carbon dioxide laser or cold endoscopic excision of the mass should be the first line of therapy. The carbon dioxide laser technique is better in the treatment of laryngeal amyloidosis (9,10). Regarding the present case, a deep biopsy of the vocal cords during direct laryngoscopy resulted in complete resolution of the symptoms.

The clinical significance and prognosis of respiratory tract amyloidosis vary substantially depending on its aetiology and anatomical distribution. Laryngeal amyloidosis generally behaves as a benign disorder but can be progressive or recur after treatment. Regular follow-up with laryngoscopy is indicated for early detection of recurrence, and multiple surgical procedures may be required to control symptoms (2,11). In the present case, laryngoscopic examination performed 9 months later was normal.

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