

HOARSENESS AS PRESENTING SYMPTOM OF PEDIATRIC LARYNGEAL AMYLOIDOSIS

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Abstract- Amyloidosis of the upper aerodigestive tract is rare in the pediatric age group. We present two cases of pediatric laryngeal amyloidosis. Both of them had hoarseness as the presenting symptom. Diagnostic evaluation included flexible nasopharyngoscopy, rigid laryngoscopy, biopsy, computed tomography scan and laboratory tests. The results of Congo red staining of the specimen were characteristic of amyloid. The most common area of reported laryngeal involvement have been the vestibule, followed by the false cords, the aryepiglottic folds and subglottic region. In our cases, the masses were limited to supraglottic larynx. Management depends on the severity of the symptoms regarding the individual patient.

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INTRODUCTION

Amyloidosis is deposition of amyloid which is an extracellular fibrillar protein with unique ultrastructural, X-ray diffraction and biochemical properties in one or more sites in body (1-6). Virchow in 1851 was the first to use the term amyloid because of its starch like reaction when treated with iodine and sulfuric acid (1). Laryngeal amyloid was first recognized in 1875. Deposits of amyloid in the larynx are rare, accounting for between 0.2 and 1.2% of benign tumors of the larynx (4). However the larynx is the most common site for isolated amyloid deposits to occur in the head and neck (3). Amyloidosis has male to female ratio ranging from 1/1 to 3/1 in different studies (7, 8). It typically presents in middle life.

Here we report 2 cases of pediatric laryngeal amyloidosis.

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CASE REPORTS

The patients included two children, one male and one female. Both patients experienced progressive hoarseness and duration was from 4 to 36 months. Patients had negative systemic work up which included physical examinations, laboratory tests, radiological studies and biopsies. In both of them, amyloid deposition occurred in the false cord submucosally.

Case 1

A ten-year-old girl presented with four-month history of hoarseness. She had also dyspnea in sleep. There were no other symptoms like dysphagia, odynophagia, cough or having sputum. Indirect laryngoscopy revealed a large mass located submucosally in the supraglottic area. The mass was limited to the right false vocal cord and aryepiglottic fold sparing true vocal cords. Other otorhinolaryngologic examinations were normal. Routine laboratory, rheumatoid and liver function tests were normal. High-resolution computed tomography (CT) was used to evaluate extension of the laryngeal involvement (Fig 1).



Fig. 1. Axial computed tomography (CT) revealing right supraglottic involvement.

Biopsy revealed an amorphous, eosinophilic hyaline material that exhibited apple-green birefringence when stained with Congo red and viewed under polarized light. Biopsies from gingiva, skin and abdominal fat ruled out systemic involvement. The patient underwent microscurgically CO₂ laser debulking of the mass with improvement in her symptoms.

Case 2

A 15 year-old boy presented with hoarseness since 3 years and exacerbation during the past three months. Indirect laryngoscopy revealed a large right side false cord mass located submucosally. Axial CT scan showed the same findings (Fig. 2).

Laryngoscopy revealed extension of the mass into the ventricle and right true vocal cord. Biopsy demonstrated fragments of tissue including seromucous gland containing stratified squamous and columnar epithelium within the submucosa of both portions. Congo red stain under polarized light showed birefringence characteristics (Fig. 3). The work up for systemic amyloidosis and multiple myeloma was negative. The biopsy of rectal mucosa was normal.

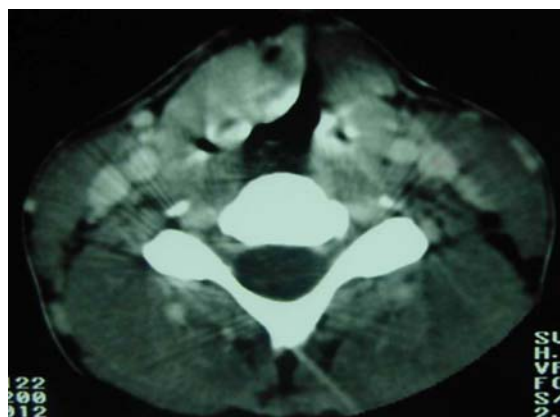


Fig. 2. Axial CT showing a large right side false cord mass.

DISCUSSION

The term amyloid encompasses a family of different types of extracellular fibrillar protein deposits (1-8). Clinically it can be divided into two categories: primary amyloidosis, in which there is spontaneous development of amyloid deposits, and secondary amyloidosis in which the condition is found in conjunction with some other systemic diseases such as rheumatoid arthritis or tuberculosis (3-6). Primary amyloidosis can be subcategorized further into localized and generalized forms (1, 3, 4, 7, 8). The larynx is rarely involved with amyloidosis with approximately 300 cases reported thus far (1, 3). The most common area of laryngeal involvement is the vestibule, followed by the false cords, the aryepiglottic folds and subglottic region (2). In literature the age ranges from 8 to 80 years with a peak in fifth decade (1, 6). The sex ratio is 3 males to 1 female (1, 7, 8).

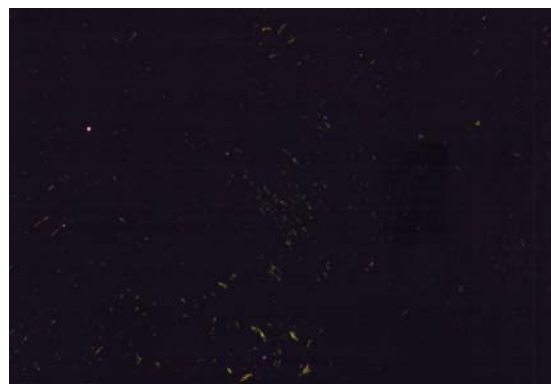


Fig. 3. Birefringence characteristics by Congo red stain under polarized light.

Hoarseness is the most common presenting symptom (1, 3). Dyspnea on exertion is occasionally reported and hemoptysis, dysphagia and throat fullness are rare symptoms (8). Diagnosis should focus on evaluating the extent of local amyloidosis and ruling out systemic involvement (1, 3-8). Systemic work up should contain assessment of collagen vascular diseases, tuberculosis, multiple myeloma including rheumatoid factor, antinuclear antibody, purified protein derivative, chest radiography, urine/serum protein electrophoresis (7, 8). Amyloidosis associated with familial syndromes and endocrinopathies, and needs to be investigated (7, 8). A number of reports have demonstrated a relationship between extramedullary plasmacytoma of the larynx and localized laryngeal amyloidosis. For most cases of suspected localized amyloidosis, it is probably not necessary to investigate for systemic disease with biopsies of the lip, rectum, or abdominal fat, because of the low yield (1, 3, 7, 8). However, there have been documented cases of laryngeal amyloidosis with systemic involvement (primarily in the upper respiratory tract and stomach) (1). Fine needle aspiration of abdominal fat has been shown to be a simple and effective procedure to rule out systemic amyloidosis (1, 3).

Both our cases revealed negative laboratory results for blood and urine tests and radiological studies to eliminate systemic causes. Results of rectal biopsy were negative for amyloid. Laryngeal amyloidosis is almost always evaluated initially at the time of biopsies by direct laryngoscopy. Amyloid is mostly a submucosal disease, so it could be better defined by radiological scans (3). Axial CT scans were performed in both of our patients and revealed supraglottic involvement (Fig. 1, 2). Treatment for isolated laryngeal amyloidosis is based on observation or surgery. Endoscopic excisional biopsy (via either cold knife or CO₂ laser) is usually adequate (4). Both radiotherapy and medical management (local or systemic steroids, chemotherapy) are ineffective (1, 3). A new therapeutic approach for amyloidosis involving an experimental small molecule drug called R-1-[6-[R-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl] pyrrolidine-2-carboxylic acid (CPHPC) that depletes serum amyloid P component (SAP) has been developed by

Pepys *et al.* (1, 11). SAP typically binds to amyloid fibrils and makes them resistant to degradation. CPHPC interferes with SAP binding to amyloid fibrils and leads to rapid clearance of SAP by the liver (1).

The prognosis for patients with localized laryngeal amyloidosis is excellent. There has been no report of malignant change in amyloid tumor (1, 2). In conclusion, we had two children with hoarseness and laryngeal amyloidosis. In children, the perceptual evaluation of voice is of obvious importance. Endoscopy with a transnasal flexible scope makes it possible, in practically all cases, to identify the morphodynamic changes (9). The most common causes for dysphonia in children are infections, anatomical, congenital, inflammatory, neoplastic, neurologic or iatrogenic in nature (10). We recommend considering laryngeal amyloidosis in differential diagnosis of pediatric hoarseness. Laryngeal amyloidosis usually indicates localized disease with which systemic involvement is uncommon. However, a full medical evaluation for systemic disease should be performed. Management depends on the severity of the symptoms regarding the individual patient. Some cases can be followed by conservative observation. If the disease is causing significant symptoms or showing signs of an increase in size, surgical intervention must be carried out (3). It could be facilitated by use of CO₂ laser, which has been applied in our cases.

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