

Full Length Research Paper

Narrowing of the upper airway due to amyloidosis: A case report

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A 37 year-old woman was referred to our hospital complaining of dyspnea and bilateral swelling of the submandibular region which were developed 6 months ago. Although the submandibular glands seemed to be diffusely enlarged, with suspicion to amyloidosis, an incisional biopsy of one gland stained with Congo red was performed but normal glandular tissue was found. As a result, abdominal fat pad biopsy was done to confirm the diagnosis. Further review of MRI data indicated that the submandibular swelling was due to down-shifting of the submandibular glands brought about by enlargement of the tongue and floor-of-mouth muscles. Abdominal fat pad biopsy showed deposition of amyloid fibrils. Findings were consistent with amyloidosis. In this case the most remarkable findings were swelling in submandibular area secondary to down-shifting of the submandibular glands and macroglossia which had partially compromised the airway. Abdominal fat pad biopsy is easier and less invasive than other methods and shows amyloid fibril deposition in 70 to 80% of cases.

Key words: Amyloidosis, macroglossia, submandibular gland.

INTRODUCTION

Amyloidosis is a generic term referring to extracellular tissue deposition of amyloid fibrils composed of low molecular subunits of a different variety of proteins. Major types of amyloidosis include: AA amyloidosis (secondary), AL amyloidosis (primary), dialysis-related amyloidosis, heritable amyloidoses, age-related (senile) systemic amyloidosis and organ-specific amyloid (Gorevic, 2009). Amyloidosis in the head and neck is a rare and benign condition that is usually considered as a form of localized amyloidosis. It can involve the orbit, sinuses, nasopharynx, oral cavity, salivary glands, and mostly larynx and thyroid (Tas et al., 2007). Amyloidosis complications in the head and neck include: compromising the airway (Sreetharan et al., 2003), epistaxis (Prasad et al., 2009) and chronic ocular discomfort (Chaturvedi et al., 2000). We present here an interesting case of amyloidosis in which deposition of fibrils led to narrowing of the upper airway and swelling in

submandibular area.

CASE REPORT

In April 2009, a 37 years old woman was referred to our hospital complaining of bilateral swelling of submandibular region which was started 6 months ago. She also was suffering from bilateral postero-lateral ulcers in her tongue due to self biting. In addition, she mentioned recurrent episodes of difficulty in breathing since 2 months ago. Bilateral edema of lower limbs, as well as pain in knees and interphalangeal joints were also developed. She has experienced petechiae and purpura in the neck and papular lesions in upper eyelids since 5 months before admission. Six recurrent spontaneous abortions in the second trimester were mentioned. She reported a weight loss of about 10 kg during the last 6 months probably due to tongue enlargement and dysphagia to solid foods, without concomitant night sweating or fever. In our physical examinations, vital signs were in the normal range. In the head and neck examination macroglossia

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Figure 1. Macroglossia and lateral scalloping of the tongue from impingement on the teeth.

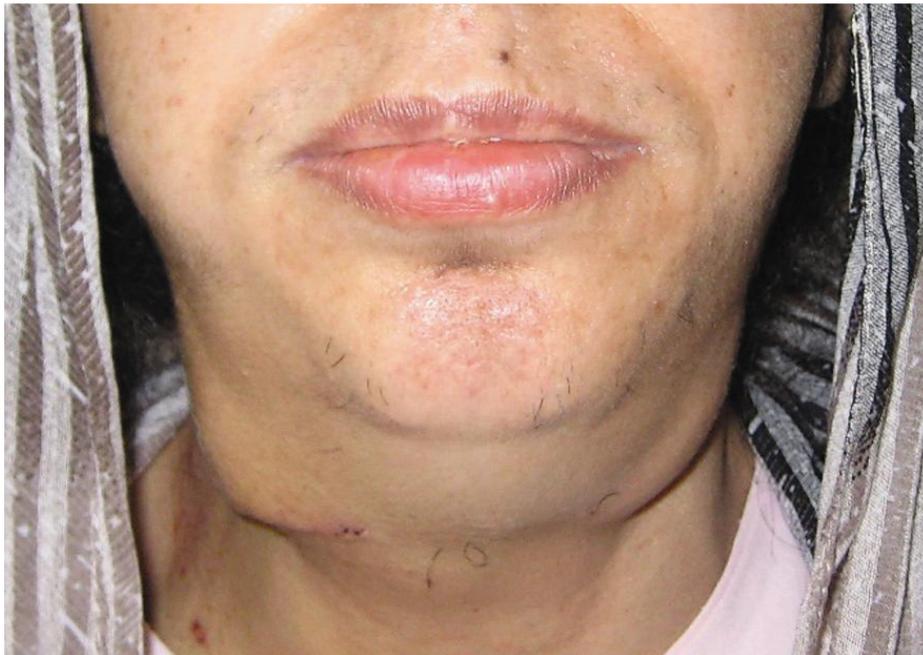


Figure 2. Bilateral enlargement of submandibular region.

examination macroglossia and lateral scalloping of tongue were obvious (Figure 1) and both submandibular glands seemed to be diffusely enlarged (Figure 2). The base of tongue was enlarged and narrowed her airway consequently (Figure 3). Incisional biopsy and Congo red

staining of one submandibular gland was done and the pathology was surprisingly negative. As she was suspected to have a rheumatologic disease, rheumatic factor, C-reactive protein, anti nuclear antibody (ANA), anti ds-DNA, complements, anticardiolipine antibodies,

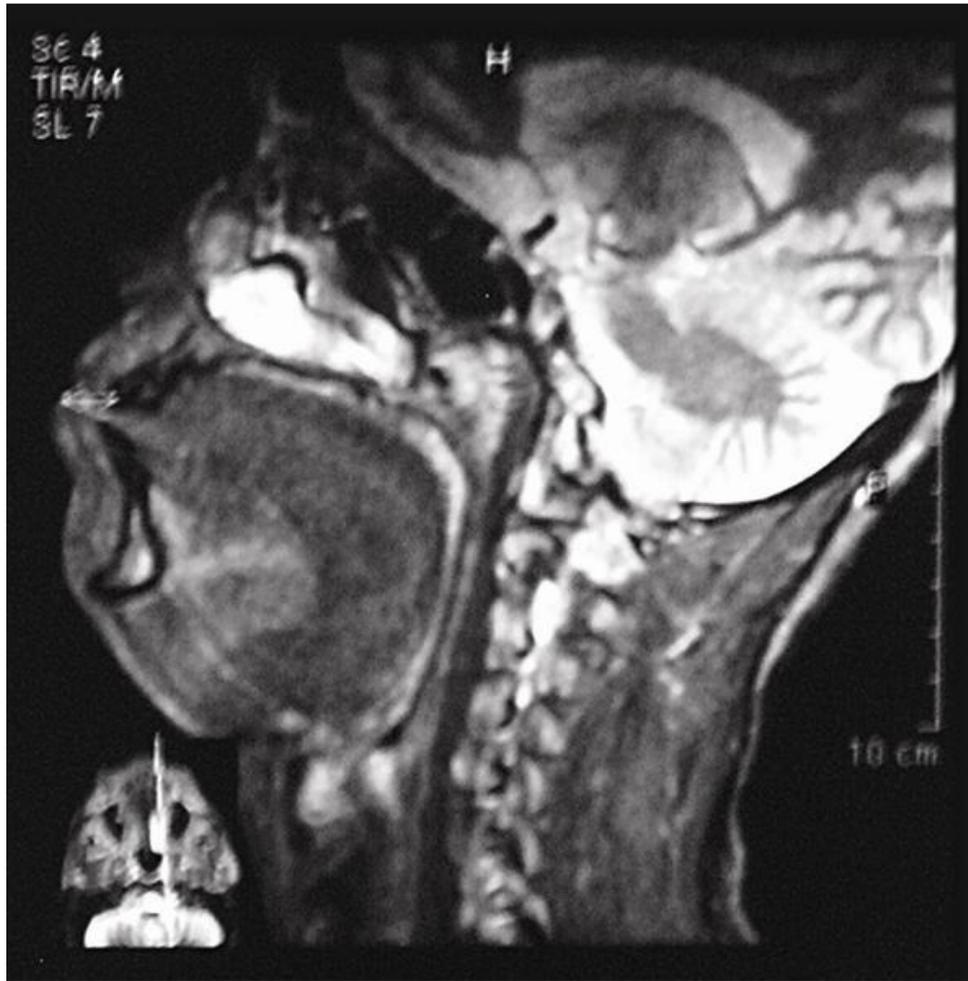


Figure 3. Narrowing of the upper airway due to base of tongue enlargement.

anti SS-A, anti SS-B and ACE levels were evaluated. However, all mentioned tests were in the normal range. Moreover, to rule out Sjögren's disease, we biopsied lower lip minor salivary glands and the result was also negative. However, erythrocyte sedimentation rate (ESR) was higher than normal; about 32 mm/h.

Chest x-ray showed mild pleural effusion. In spite of lower limb edema, no evidence of heart failure or cardiomyopathy was found on echocardiography. The patient had normal blood urea nitrogen and creatinine. A 24 h urine collection manifested 9625 mg of proteins in urine. Sonography and computed tomography of kidneys only showed an angiomyolipoma in the upper pole of the left kidney. Serum protein electrophoresis was normal but in urine protein electrophoresis alpha-2-globuline was significantly higher than the normal range. Further review of MRI data indicated that submandibular swelling was due to down shifting of the submandibular glands brought about by enlargement of the tongue and floor-of-mouth muscles. Therefore, the horizontal axis of the submandibular glands seemed to be changed to a vertical

position (Figure 4). Although the submandibular gland samples stained with Congo red showed a negative result, abdominal fat pad biopsy with H&E and subsequent Congo red staining showed deposition of amyloid fibrils (Figure 5; a and b). Bone marrow aspiration and biopsy results ruled out the probable diagnosis of multiple myeloma and the patient was admitted in the hematologic department for treatment of primary systemic amyloidosis. Treatment was included applying a salt-restricted diet, prednisone and melphalan given for 12 months. During the follow-up period, peripheral edema and dyspnea were significantly improved. However the swelling of the floor-of-mouth and submandibular region decreased moderately.

DISCUSSION

AL amyloidosis is due to deposition of proteins derived from immunoglobulin light chain fragments which can occur alone or in association with multiple myeloma or,



Figure 4. Down-shifting of submandibular glands due to macroglossia and pseudohypertrophy of floor of mouth muscles.

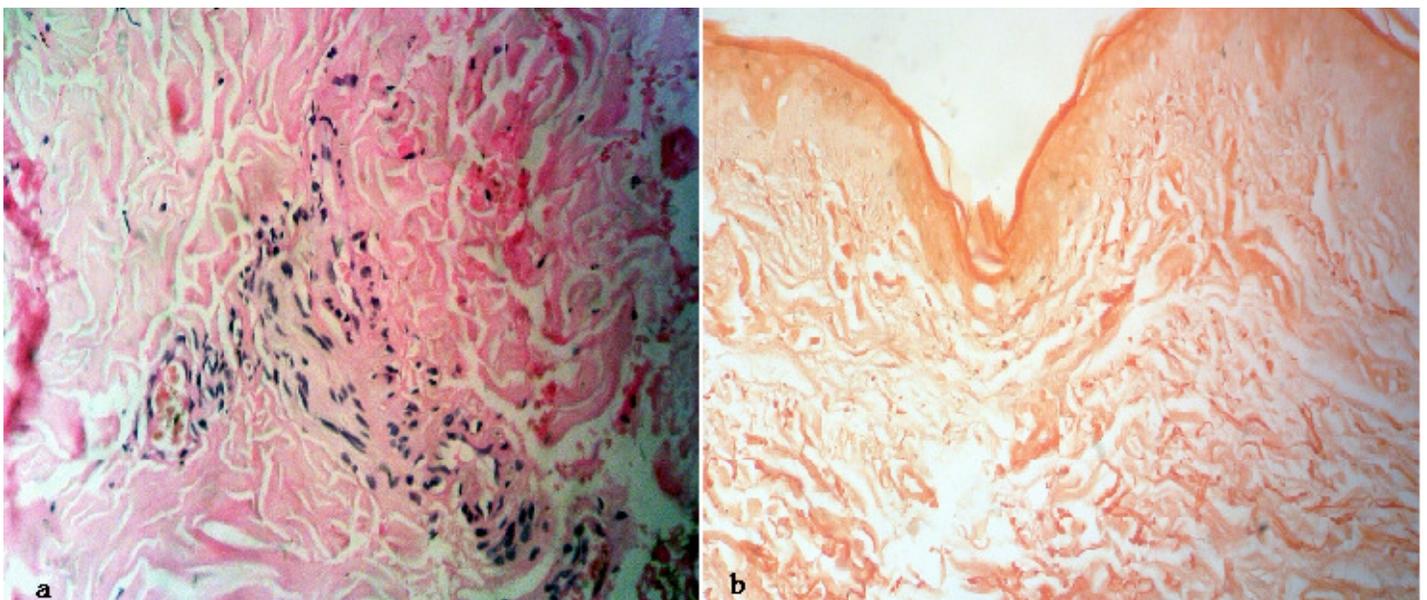


Figure 5. Abdominal fat pad biopsy with H&E (a) and subsequent Congo red; (b) staining showed deposition of amyloid fibrils.

less often, Waldenstrom's macroglobulinemia (Gorevic, 2009). Major clinical presentations are asymptomatic proteinuria or nephrotic syndrome, symptoms of heart failure, hepatomegaly with or without splenomegaly, mixed sensory and motor peripheral neuropathy and/or autonomic neuropathy, visible enlargement of muscles, macroglossia, lateral scalloping of the tongue from impingement on the teeth (characteristic of AL amyloidosis), arthropathy, bleeding diathesis, tracheobronchial infiltration, pleural effusions, parenchymal nodules (amyloidomas), pulmonary hypertension, easy bruising, subcutaneous nodules or plaques and purpura (Falk and Comenzo, 1997). As a screening test, serum electrophoresis is not enough and 25% of patients show no abnormality, while in 90% of cases serum and urine immunofixation test is able to detect monoclonal light chains. Demonstration of amyloid deposits in biopsy specimens is the only means to confirm the diagnosis of amyloidosis. In experienced hands, nonsurgical biopsies of the rectal mucosa, abdominal fat pad or labial salivary glands provide the diagnosis in 80 to 85% of cases (Hachulla and Grateau, 2002). Although Congo red staining of abdominal fat aspirates requires training to avoid sampling difficulties, abdominal fat aspiration is a highly reliable screening procedure for the diagnosis of AL amyloidosis, AA amyloidosis and familial amyloidotic neuropathy (FAP) (Masouye, 1997). There are some reports about submandibular gland enlargement due to amyloidosis (Mateo-Arias et al., 2003; Finkel et al., 2006), but the negative result of biopsy in our case and further imaging studies showed that the submandibular swelling was due to macroglossia and muscular enlargement of the floor-of-mouth. Involvement of the tongue is not uncommon in primary amyloidosis. In 22 to 26% of patients suffering from amyloidosis, amyloid deposition in the tongue can result in an enlarged tongue (Dominey et al., 1990). Although the larynx is the most commonly affected site in the head and neck, there was no evidence of hoarseness or laryngeal dysfunction on fiberoptic evaluation in our case.

Another remarkable finding was a macroglossia which had partially compromised the airway. Although there is a case report of amyloid deposition in renal angiomyolipoma (Toyoda et al., 2002), the exact association between these 2 diseases and a cause and effect relationship is not cleared. The aim of therapy in systemic AL amyloidosis is to reduce the amyloid-forming monoclonal light chains, measured with the serum free light chain assay, by suppressing the underlying plasma cell dyscrasia, while using supportive measures to sustain organ function. Amyloid deposits can be resorbed and organ function restored if the amyloid-forming precursor light chain could be eliminated. The most effective treatment for systemic AL is risk-adapted melphalan with peripheral blood stem cell transplant. However, oral melphalan and dexamethasone is the most effective therapy for patients who are not stem cell transplant

transplant candidates although it carries a risk of myelodysplasia and leukemia. With therapy, a majority of patients can achieve long-term durable remissions with stabilization or recovery of organ function. The use of novel antibody-based approaches for imaging amyloid and possibly for accelerating removal of deposits is under active investigation (Comenzo, 2007).

COMPETING INTERESTS

The authors declare that they have no competing interests. All patient's photos have been reported by her permission.

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