CASE REPORT

MACROGLOSSIA ASSOCIATED WITH PRIMARY SYSTEMIC AMYLOIDOSIS – CASE REPORT WITH UNUSUAL CLINICAL PRESENTATION

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Background: Amyloidosis is characterised by the deposition of fibrillar insoluble proteinaceous material called amyloid in the extracellular spaces. It may present as localized form which is rare and systemic form. Systemic amyloidosis involves many organs like kidney, heart and liver. Manifestations of both types may vary based on the age of onset, degree and extension of the deposition. Understandably, the diagnosis is challenging but the early identification of the condition and the type of amyloidosis can increase the efficiency of treatment. Positive Congo red staining is the gold standard for demonstration of amyloid in tissue sections. Here we are presenting a case of a 77-year-old female patient who presented with the complaint of difficulty in swallowing for 2 years due to bilateral symmetrical enlargement of the tongue which was subsequently diagnosed as systemic amyloidosis.

Keywords: Macroglossia, Amyloidosis, Primary amyloidosis, Light chain amyloidosis

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INTRODUCTION

Amyloidosis is a rare, progressive disorder characterized by extracellular deposits of amyloid protein in the different tissues or organs which frequently affects the kidney, heart, liver, spleen, nervous system and gastrointestinal tract. Various types of amyloidosis are described based on distribution as systemic or localized and precursor protein that forms the amyloid fibrils. There are various proteins demonstrated in the form of insoluble amyloid fibrils. Among these, most common are immunoglobulin light chain protein (AL) and familial transthyretin protein (ATTR). Systemic form is subclassified as primary, secondary, hereditary and amyloidosis associated with multiple myeloma.[1] Incidence of AL amyloidosis is estimated as 9 cases per million. In head and neck region, the most common sites are tongue (63%), larynx (19%) and the frequency of manifestations ranges from 12–90%.[2] Different classes of immunoglobulin light chain are capable of causing AL amyloidosis, in this monoclonal lambda light chain is the frequent one, usually involving kidneys and heart. In cardiac involvement, there is diffuse deposition of amyloid fibrils in the cardiac interstitial space producing significant thickening of both ventricles with associated stiffness and narrowing of smaller vessels leading to ischemia/ infarction.

CASE REPORT

A 77-year-old female patient reported with the complaint of difficulty in swallowing for 2 years. She related it to gradual enlarging of her tongue which was otherwise asymptomatic. Initially it resulted in loosening of her complete denture. Gradually, she developed difficulty in speech and swallowing along with reduced salivation. She gave a dental history of uneventful total teeth extraction 25 years back after which she was using upper and lower removable complete denture. Her medical history was significant for hypertension, type 2 diabetes mellitus, hyperlipidaemia for which she was under medication. Her family and personal histories were non-contributory. On general examination, she was poorly built and nourished with history of weight loss for 4 months, generalized pallor and pitting type of pedal oedema on both the ankles. Her vital signs were with in normal limits.

On extraoral examination, there was a diffuse soft tissue swelling in the submental and submandibular region bilaterally. Overlying skin was normal in colour with no secondary changes such as ulcers or fistula, and was pinchable. Swelling was non-tender, non-pulsatile, firm in consistency and did not move with deglutition.

Intraorally, the patient was found to be completely edentulous with diffuse enlargement of the entire tongue. The colour appeared to be pale pink without depapillation over the dorsum of tongue. There were no ulcerations, pulsations or swellings over the tongue. On palpation it was non-tender, firm in consistency and no pulsations were felt over the mass. Tongue movements were within normal limits. Saliva of patient was thick and ropy and tongue blade sign was positive suggestive of hyposalivation.

Differential diagnosis considered were macroglossia secondary to amyloidosis, hypothyroidism, idiopathic muscular hypertrophy and malignant tumours of base of tongue.

Routine blood investigations revealed anaemic status of patient with the haemoglobin level of 8.9gm/dl and all other values were within normal range. Laboratory investigations of serum free kappa light chain estimation showed elevated value of 379 mg/L (normal range 3.30–19.40 mg/L). Free Lambda light chain level was with in normal limits-17mg/L (normal range 5.71–26.30 mg/L). Serum Kappa Lambda ratio was also elevated- 17 (normal range 0.26–1.65). Level of serum Lactate dehydrogenase was 256.7U/L (normal range 125–220 U/L) and protein creatinine ratio was increased to 0.61 (normal range <0.15). Serum protein electrophoresis revealed normal pattern, Antinuclear antibody estimation was negative in 1:100 dilutions and bone marrow aspirate smear showed normocytivc normochromic anaemia with mild relative lymphocytosis. Serological test for Hepatitis B and C were negative. Echocardiogram findings were suggestive of low to moderate mitral regurgitation, mild tricuspid regurgitation, mild pulmonary arterial hypertension and concentric left ventricular hypertrophy.

Lateral cephalogram and computed tomography confirmed the bilateral symmetrical enlargement of the tongue. Incisional biopsy was done under LA on both the sides of lateral border of tongue. Haematoxylin and eosin-stained sections demonstrated fibromuscular tissue lined by stratified squamous epithelium with sub-epithelium showing skeletal muscle with focal vacuolation, degeneration and eosinophilic material. A special staining with Congo red was performed which showed a faint apple green birefringence in the degenerated muscles under polarising light microscopy suggestive of Amyloid deposits.

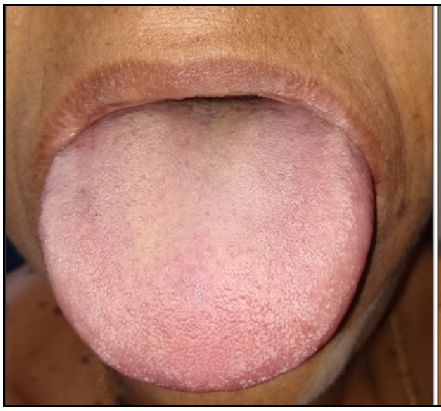

Figure-1: Intraoral view showing bilateral symmetric enlargement of tongue

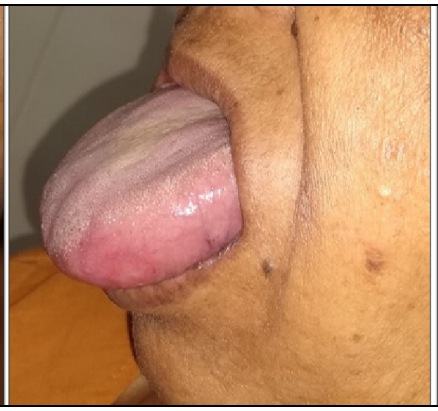

Figure-2: Lateral view of tongue shows thickening of enlarged tongue

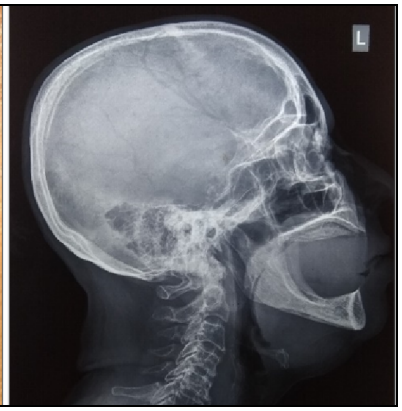

Figure-3: Lateral cephalogram shows the significant symmetrical increase in tongue volume

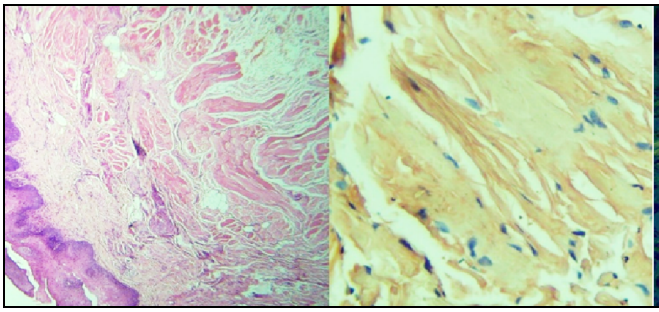

Figure-4: Haematoxylin and eosin stain (magnification 10x) showing a fibromuscular tissue lined by stratified squamous epithelium with sub epithelium shows skeletal muscle with focal vacuolation and degeneration.
Congo red stain (magnification 40x) showing peach-coloured amyloids in the connective tissue

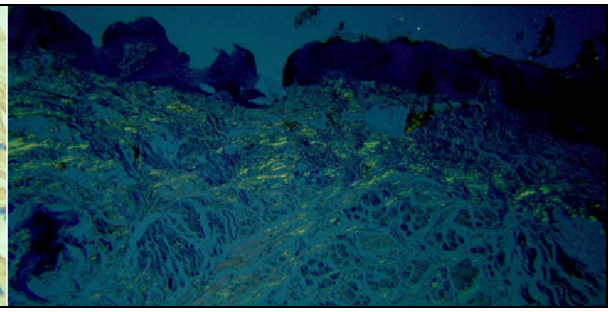

Figure-5: Faint apple green birefringence under polarising light in the degenerated muscle

DISCUSSION

Amyloidosis is characterized by an abnormal extracellular deposition of amyloid in different tissues and organs. Rudolph Virchow then coined the word "amyloid" in 1854 to describe tissue deposits that stained like cellulose when exposed to iodine.[3] The amyloid fibrils are rigid, proteolysis resistant structures, typically less than 10 nm in diameter with a characteristic apple green birefringence with Congo-red staining under polarized light microscopy. Bennhold introduced Congo red staining in 1922, it remains the gold standard diagnostic procedure for amyloidosis.[4] Two main types of amyloidosis are systemic and localized amyloidosis. Systemic amyloidosis subcategorized into four types as primary, secondary, hereditary and associated with multiple myeloma. In the primary amyloidosis immunoglobulin or light chain related amyloidosis is the most common one (AL).[1] AL amyloidosis is caused by deposition of fibrils composed of monoclonal immunoglobulin light chains and is associated with clonal plasma cell or other B-cell dyscrasias.[5] AL amyloidosis shows slight male predominance with average of 65years, only 10% of cases occur in those under the age of 50 years.[1] It was commonly affects the kidney which manifests as a heavy proteinuria and decreased glomerular infiltration rate. Second common involvement occurs in the heart (40%). Involvement of these two organs leads to death. Mean survival of primary systemic AL amyloidosis is up to 15 months. Here we are presenting 72-year-old women with painless gradual enlargement of tongue with the presenting symptoms of dysphagia, weight loss and fatigue. Echocardiogram findings were suggestive of as primary amyloidosis involving heart.

There are more than 30 proteins identified to form amyloid fibrils in vivo, which cause disease by progressively damaging the structure and function of affected tissues. Amyloid deposits also contain minor non-fibrillary constituents, including serum amyloid P component (SAP), apolipoprotein E, connective tissue components (glycosaminoglycans, collagen), and basement membrane components (fibronectin, laminin).[5] In this present case, increased serum kappa free light chain level and kappa-lambda ratio were found. In Congo-red staining showed a faint apple green birefringence under polarising light in the degenerated muscle.

Here macroglossia due to amyloidosis was confirmed by histopathologic and Congo red staining. In suspected cases of amyloidosis diagnostic work up consists of haematological, urine analysis, radiographic examination and tissue biopsy followed by Congo red staining and examination under the polarising light microscope. Treatment of amyloidosis varies according to the variants and also the severity. In this patient it was diagnosed as primary systemic amyloidosis due to the deposition of immune light chains. Cardiac involvement was evaluated by echocardiogram findings. Usually, amyloid deposition in heart may results congestive heart failure (CHF) and conduction system abnormalities. Treatment for systemic AL amyloidosis relies largely on chemotherapy, with dosage depending on the age of the patient and the extent of disease.[1]

Warfarin was not started for this patient due to high HAS-BLED (acronym-hypertension, Abnormal liver/ renal failure, Stroke history, bleeding history, Labile INR, Elderly, Drug/ alcohol usage) score. Prognosis is considered poor for AL type of amyloidosis. There will be marked elevation of the biomarkers include brain natriuretic peptide (BNP) and cardiac troponin, even at an early stage which may aid in diagnosis. Involvement of the heart is the commonest cause of death in AL amyloidosis and without cardiac involvement, patients have a median survival of around 4 years.[5]

CONCLUSION

In order to reduce the morbidity and mortality of patients with amyloidosis, early diagnosis and active intervention is needed. Additionally, further research regarding newer treatment modalities is required to improve the survival rate and quality of their life.

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