University J Dent Scie 2024; Vol. 10, Issue 4

Macroglossia Secondary to Amyloidosis: A Case Report

Abstract:
Macroglossia is a considered a pathognomonic sign of AL amyloidosis. In the absence of an infective or neoplastic/infiltrative etiology, a clinician must be quick to divert his/her attention to amyloidosis as a cause. Ruling out concurrent multiple myeloma in such cases is also of paramount importance. Prompt diagnosis would lead to early institution of appropriate therapy. We present a case of macroglossia secondary to amyloidosis.

Key-words: AL Amyloidosis, Macroglossia, Multiple Myeloma.

Introduction:

A clinician might, on a rare occasion, encounter a patient presenting with an excessively enlarged tongue, also termed macroglossia. Macroglossia can be congenital or acquired, and the literature describes macroglossia attributed to many different causes including, vascular malformation, neoplastic infiltration, Down's syndrome, mucopolysaccaridosis, Beckwith–Wiedemann syndrome, actinomycosis, myxedema, angioedema, and amyloidosis[1,2,3,4].

Amyloidosis is the term for a group of protein misfolding disorders characterized by the extracellular deposition of insoluble polymeric protein fibrils in tissues and organs[5]. The two main types of amyloidosis are *systemic* and *localized*. The systemic form is subclassified as primary, secondary, hereditary, and amyloidosis associated with multiple myeloma. Amyloidosis is designated as primary when no cause can be identified and secondary when it occurs in conjunction with a chronic disease such as tuberculosis, rheumatoid arthritis, Crohn's disease, etc[6].

The most common type; immunoglobulin light chain amyloidosis (AL), is caused by the production of misfolded light chains by clonal plasma cells[7].Despite the etiological heterogeneity of systemic amyloidosis, the clinical manifestations of the different forms of amyloidosis largely overlap and depend upon the effected organ. Macroglossia is a feature in 20–26% of patients with primary systemic AL amyloidosis[8].

Here, we report a case of a 63 year old man presenting with macroglossia, which was diagnosed as secondary to amyloidosis.

Case Report:

A 63 year old man reported to the outpatient department of Oral and Maxillofacial Surgery at Dr. R. Ahmed Dental College and Hospital, Kolkata, with a complain of enlarged tongue since the last 2 years(Fig 1).

The patient complained of inability to chew food or swallow, and speech problems. The patient did not have any breathing difficulties. He also reported pain in his tongue. The patient

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Received : 11 July, 2024, **Published :** 31 Dec., 2024

How to cite this article: Uddin, Inam. (2024). Macroglossia Secondary to Amyloidosis: A Case Report. UNIVERSITY JOURNAL OF DENTAL SCIENCES, 10(4).

Access this article online

Website: www.ujds.in

Quick Response Code

DOI: https://doi.org/10.21276/ujds.2024.10.4.10

had visited multiple hospitals and had underwent multiple investigations including radiological assessment including MRI and PET scans, incisional biopsy of the tongue with histopathological evaluation, and examination under anaesthesia (EUA), but remained without diagnosis or appropriate therapy.

Routine laboratory investigations and medical history of the patient were unremarkable, except an elevated serum alkaline phosphatase level of 178 U/L, a slightly reduced serum albumin level of 3.2 gm/dl, and a slightly raised serum creatinine level of 1.3 mg/dl. Previously performed plain and contrast enhanced MRI had revealed 7.2*7 cm bulky and enlarged tongue and its base without diffusion restriction. The appearance of the tongue was homogeneous and no abnormal enhancement suggested a hypertrophied tongue (Fig 2).Previously performed whole body FDG-PET scan had revealed absence of any metabolically active lesion. Previously performed histopathological evaluation of incisional biopsy of the tongue had revealed normal tissue and was labeled descriptive.

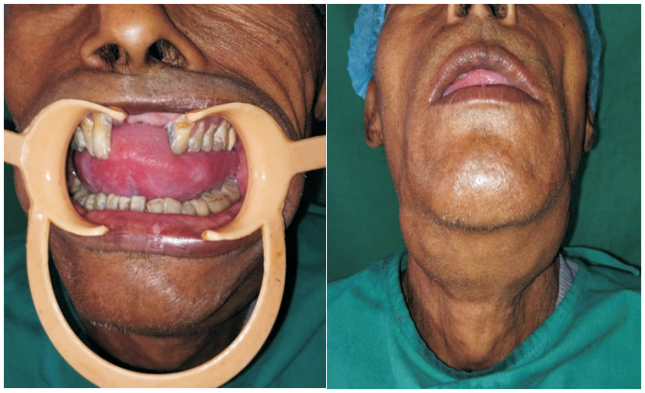

Fig 1. Clinical Presentation of the patient showing an enlarged tongue (left), and swelling in the submental and bilateral submandibular region (right).

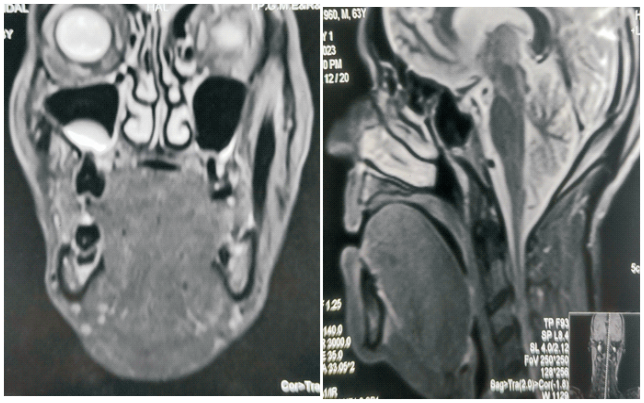

Fig 2. Coronal and sagittal sections of MR imaging revealing a hypertrophied tongue.

A serum protein electrophoresis was perfomed which revealed a small M-peak in the gamma region suggesting gammopathy. X-ray skull AP view, and lumbosacral spine AP and Lateral view revealed absence of osteolytic lesions. The family history of the patient was non contributory.

Based on the patient's history, clinical examination, and the results of previous and current radiological, laboratory and histopathological assessment, a provisional diagnosis of macroglossia, secondary to amyloidosis, was made.An abdominal fat biopsy was performed for the patient under spinal anaesthesia(Fig 3).

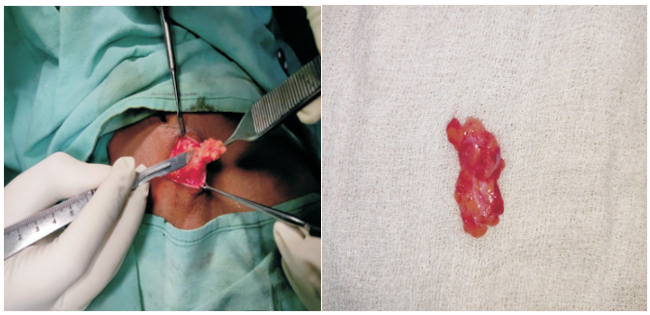

Fig 3. Abdominal fat biopsy after placing a periumbilical incision (left). Specimen after incisional biopsy (right).

Haematoxylin Eosin and Congo red staining of the abdominal fat tissue were suggestive of the presence of amyloid deposition. (Fig 4)

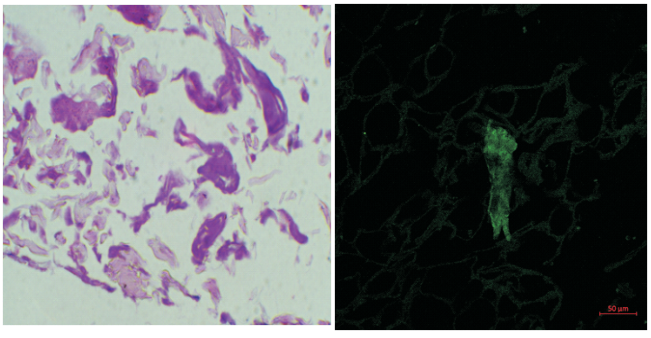

Fig 4. Haematoxylin Eosin staining(left) revealing discreet foci of accumulations showing variable concrescenses/agglomerates of acellular, eosinophilic, amorphous, homogeneous masses dispersed within a loose fibrofatty connective tissue stroma. Congo Red staining (right) revealing apple green birefringence under polarized light suggesting presence of amyloid deposition.

Incisional biopsy from the tongue and buccal mucosa were performed under local anaesthesia to confirm amyloid deposition. (Fig 5)

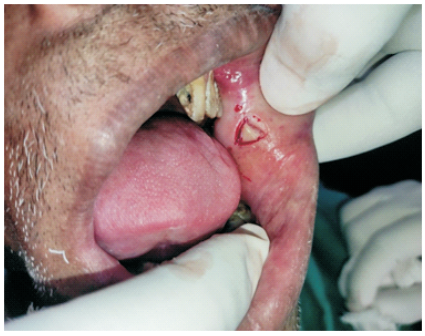

Fig 5. Incisonal biopsy from the left buccal mucosa under local anaesthesia.

Congo red staining of tongue and buccal mucosal biopsy specimens was suggestive of the presence of amyloid deposition. (Fig 6)

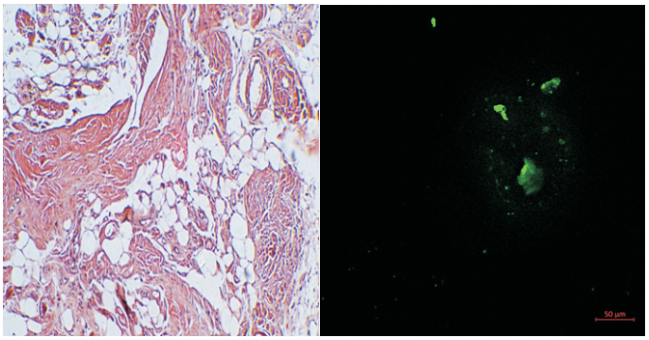

Fig 6. Congo red staining of tongue biopsy under normal halogen bulb illumination (left) showing dark reddish brown accumulation of congophilic amyloid. Congo red staining of tongue biopsy revealing apple green birefringence under polarized light.

Since amyloid deposition was demonstrated in both abdominal fat and oral biopsies a diagnosis of generalized amyloidosis was made and the patient was referred to department of general medicine for differentiation between primary and secondary amyloidosis, and for assessment of systemic involvement. Upon assessment by department of general medicine there was no renal, hepatic, or cardiac involvement. A bone marrow biopsy revealed presence of 12% plasma cells, which suggested plasma cell dyscrasia. A diagnosis of AL amyloidosis was made. Further, molecular biology assessment tests were recommended by department of haematology before institution of appropriate therapy. However, given the long history of present illness in the patient, prolonged hospitalizations, multiple investigations, lack of symptomatic relief, and poor socioeconomic status of the patient, neither the patient nor his family members wanted to go ahead with any further investigations or treatment. The patient and his family members were counseled about the fact that medical treatment for generalized primary amyloidosis and surgical treatment for reduction of tongue size were available. However, due to the reasons given above the patient was disappointed, demoralized, and did not want to proceed with any treatment despite being informed of the fact that not proceeding with treatment could be lethal.

Discussion:

It is on a rare occasion that a clinician encounters a patient presenting with macroglossia, and even rarer that a patient presents with a macroglossia secondary to amyloidosis. Because of the rare nature of such presentations, the varied etiologies related to macroglossia, and the complexity involved in the diagnosis of amyloidosis, it is often too late before a patient with macroglossia secondary to amyloidosis receives a diagnosis. Reports suggest that there is a delay in diagnosis of AL amyloidosis ranging from 180 to 441 days.In general, patients with AL amyloidosis have a short median survival, of less than 4 years, and a high mortality, of around 25–30%, in the first 6 months after diagnosis[9].

Our patient had morphologic evidence of amyloid deposition in the tongue and the abdominal fat pad, along with a small M peak in the gamma region on serum protein electrophoresis.

The median bone marrow plasma cell infiltration in AL amyloidosis is 7–10% but the range is large. In Multiple Myeloma, by definition, the plasma cell infiltration is >10%, but the median infiltration at diagnosis is around 40%[9]. Mere presence of bone marrow clonal plasmacytosis is not sufficient to make a concurrent diagnosis of multiple myeloma, as 18% of AL amyloidosis patients may show >20% clonal plasma cells in bone marrow[10]. Hence, our patient could safely be diagnosed as a patient of AL amyloidosis without concurrent multiple myeloma.

However, even after receiving a diagnosis and options for medical and surgical treatment, our patient refused further management. This is due to the long drawn process and a time period of more than two years between the appearance of symptom and getting a diagnosis. We, hope that such case reports would help clinicians in case they receive a patient with a similar presentation, so that timely diagnosis and management could ease the turmoil faced by such patients.

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