Macroglossia Secondary to Primary Amyloidosis of the Tongue

Hemanth Vamanshankar, Arun B Nair, Marjorie Correa, Ravi C Nayar

ABSTRACT

Introduction: Amyloidosis is a disease entity characterized by the presence of proteinaceous material deposited extracellularly at various locations in the body. The incidence of all forms of amyloidosis is about 8 per million persons per year. It may either be systemic or localized. The systemic variety may be primary, secondary and hereditary or amyloid associated with multiple myeloma. In the head and neck region, the most common sites of involvement in systemic amyloidosis are the tongue (63%) and the larynx (19%). Although lingual involvement is common, macroglossia as a presenting symptom, though pathognomonic is rare (5%).

Discussion: The most common sites of involvement in systemic amyloidosis are the tongue (63%) and the larynx (19%). Although lingual involvement is common, macroglossia as a presenting symptom, though pathognomonic is rare (5%).

Case Report

A 65 years old male, presented to the otolaryngology outpatient department at St John’s Medical College and Hospital, a tertiary care center, Bangalore, South India. He complained of a swelling in the neck, below the right jaw since 7 months. He noticed blebs over the tongue 3 months ago which burst to form ulcers after a week (Fig. 1).

There was a gradually progressive diffuse enlargement of the tongue since 1 month which was associated with speech difficulty. There was history of weight loss since 2 months, and progressive sleep apnea since 1 month. He was diagnosed as having pulmonary tuberculosis 10 years ago, for which he took antitubercular medications for a year.

General physical examination revealed pallor and bilateral pitting type of ankle edema. Head and neck examination confirmed a right submandibular swelling and diffuse thickening of the entire tongue. The submandibular swelling was firm in consistency, separate from the thickened tongue. Skin over the submandibular swelling was normal. A soft, yellowish cystic swelling of 3 × 2 cm was noted on the left lateral border of the tongue.

Laboratory investigations (Table 1) revealed anemia (10.2), with raised total counts (12,000/cu mm) and erythrocyte sedimentation rate (53 mm/hr). Urine microscopy showed proteinuria (2+) with decreased total proteins (4.2) on liver function test. His renal parameters were normal. Sputum acid fast bacilli were negative. Chest X-ray showed multiple well defined calcific nodules seen in both lungs with no evidence of fibrosis or cavity. Computed tomographic scan confirmed the significant symmetrical enlargement of the tongue. There were also lytic lesions in the vertebral bodies (Fig. 2).

The differential diagnoses considered were multiple myeloma, hystiocytosis and hyperparathyroidism. Bence-Jones proteins in urine were negative. Serum protein electrophoresis revealed hypoalbuminemia with decrease in gamma globulins. Levels of T3, T4, TSH in blood were within normal ranges (T3: 0.65, T4: 6.62, TSH: 3.36). Bone scan was also normal. Echocardiogram showed a mild tricuspid regurgitation, pulmonary artery hypertension, sclerosed aortic valve and a left ventricular diastolic dysfunction. Antinuclear antibodies were negative. Hence, a provisional diagnosis of amyloidosis was considered. The
patient underwent a biopsy of the tongue lesion under local anesthesia to confirm the same.

Histopathology of the cystic lesion of the tongue on hematoxylin and eosin (H&E) stain showed a fibromuscular tissue covered by hyperplastic stratified squamous epithelium. There were several thin-walled capillary sized blood vessels noted. Subepithelial stroma showed homogenous eosinophil deposits, consistent with

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**Table 1: Laboratory reports of patient**

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient’s report</th>
<th>Lab reference range</th>
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<tbody>
<tr>
<td>Hemoglobin</td>
<td>10.2</td>
<td>Male: 13-18 gm/dl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female: 12-16 gm/dl</td>
</tr>
<tr>
<td>Total count</td>
<td>12.000</td>
<td>4,000-10,000 cm/mm</td>
</tr>
<tr>
<td>ESR</td>
<td>53</td>
<td>Male: 0-9 mm/hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female: 10-20 mm/hr</td>
</tr>
<tr>
<td>Total protein</td>
<td>4.2</td>
<td>6-8 gm/dl</td>
</tr>
<tr>
<td>Blood urea</td>
<td>26</td>
<td>10-50 mg/dl</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.8</td>
<td>0.6-1.1 mg/dl</td>
</tr>
<tr>
<td>T3</td>
<td>0.65</td>
<td>0.87-1.78 ng/ml</td>
</tr>
<tr>
<td>T4</td>
<td>6.62</td>
<td>6.09-12.23 mcg/dl</td>
</tr>
<tr>
<td>TSH</td>
<td>3.36</td>
<td>0.34-4.1 μ/ml</td>
</tr>
<tr>
<td>Sputum AFB</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Urine microbiology</td>
<td>2+</td>
<td>Nil</td>
</tr>
</tbody>
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Amyloidosis (Fig. 3). The same was confirmed by crystal violet and Congo red staining (Figs 4 and 5). The patient was treated empirically with a corticosteroid (prednisolone) and an alkylating agent (Melphalan). Although no dramatic improvement has been noticed, the patient has been put on a 1 year treatment course with regular follow-up.

**DISCUSSION**

Amyloidosis is a disease process resulting in the deposition and accumulation of fibrillar proteins. Even though Rokitansky first described the process in 1842, Virchow is credited with naming the substance amyloid. Grossly amyloidosis is seen as a structureless translucent material which transmits the color of the underlying tissue. Microscopically, it presents as a hyaline substance which accumulates between parenchymatous cells, staining pink with a H&E stain. Under polarized microscopy, amyloid exhibits an apple green birefringence, which is the diagnostic hallmark. On electron microscope, amyloid appears as a mass of rigid nonbranching fibrils.

The symptomatology reflects organ involvement, and most patients report weakness, fatigue or weight loss. Other common presenting symptoms include ankle edema, dyspnea, paresthesias and light headedness and syncope. The most common physical findings are hepatosplenomegaly, edema, macroglossia, orthostatic hypotension and purpura. A number of associated syndromes are frequently seen, including carpal tunnel syndrome, peripheral neuropathy, nephrotic syndrome, congestive heart failure and sprue. The most significantly involved organ systems are the kidneys and heart; failure of which are the two leading causes of death. The present patient gave a history of weight loss, fatigue and ankle edema since 2 months, which was probably due to hypoproteinemia. Though pathognomonic for amyloidosis, other differentials that must be considered for macroglossia are tuberculosis, lymphangiomia, hypothyroidism, acromegaly, giant cell arteritis, idiopathic muscular hypertrophy and Beckwith-Wiedemann syndrome.

Amyloidosis of the tongue typically results in macroglossia, manifested by increased tongue volume, tongue protrusion beyond the alveolar ridge, speech impairment, drooling and dysphagia. Significant symptoms of sleep apnea and respiratory distress may also be present. Yellow nodules and raised white lesions occurring predominately along the lateral border are also common. There may be hemorrhagic bullae present, which may rupture and ulcerate on mild trauma or with mastication. Enlargement and infiltration of the submandibular glands occurs in 10% of oral cavity cases. Our patient had an increase in tongue volume and speech impairment. There was a cystic swelling in the left lateral border of the tongue, and a right submandibular gland was palpable in our patient. Radiologically, macroglossia is said to be present if the tongue is wider than 50 mm and each genioglossus muscle is wider than 11 mm. Treatment with cyclic oral steroids (prednisolone) and alkylating agents (Melphalan) can decrease the plasma cell burden but complete hematologic remission is rare.

Surgical reduction of the tongue has been suggested in cases of amyloid macroglossia, although surgical intervention is performed only in extreme cases of macroglossia. However, complications like bleeding, difficult primary closure and wound breakdown must be borne in mind. If simply observed, they will have a slowly progressive growth pattern with an associated increase in morbidity. In our case, surgery was not done due to the morbidity associated with the procedure and lack of consensus in literature regarding the benefits of surgery.

**CONCLUSION**

Amyloid involvement of the tongue is almost always secondary to systemic disease. An extensive workup to differentiate systemic and localized amyloidosis is required to treat the underlying inflammatory or infectious disease. Current therapies involving alkylating agents and steroids have poor response rates though some encouraging results have been reported. The effect of treatment is difficult to estimate, and further research needs to be focused on this aspect.

**REFERENCES**


ABOUT THE AUTHORS

Hemanth Vamanshankar (Corresponding Author)
Resident, Department of Otorhinolaryngology, Head and Neck Surgery, St John’s Medical College and Hospital, Bengaluru Karnataka, India, e-mail: vhemanth2000@yahoo.com

Arun B Nair
Registrar, Department of Otorhinolaryngology, Head and Neck Surgery, St John’s Medical College and Hospital, Bengaluru Karnataka, India

Marjorie Correa
Professor, Department of Pathology, St John’s Medical College and Hospital, Bengaluru, Karnataka, India

Ravi C Nayar
Professor, Department of Otorhinolaryngology, Head and Neck Surgery, St John’s Medical College and Hospital, Bengaluru Karnataka, India