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The Clinical Picture

A 66-year-old woman with an enlarged tongue

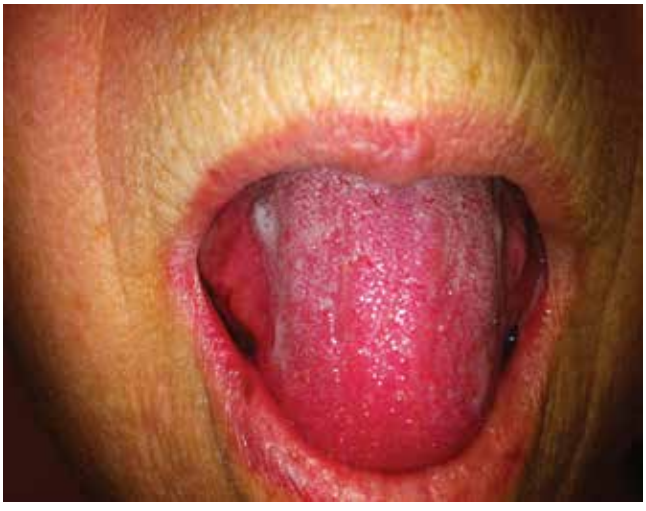

FIGURE 1

A 66-year-old woman was prompted by her dentist to seek medical attention for an unusually enlarged, smooth-appearing tongue (**FIGURE 1**). She also complained of fatigue, dyspnea on exertion, and tingling of her hands.

Basic laboratory tests showed normocytic anemia and renal insufficiency. Her thyrotropin level was within normal limits. Serum protein electrophoresis showed a monoclonal M-spike, which prompted a bone marrow biopsy that was diagnostic of multiple myeloma.

Transthoracic echocardiography revealed diffuse hypokinesis with a restrictive filling pattern, myocardial thickening, and moderate mitral and tricuspid regurgitation, highly suggestive of an infiltrative cardiomyopathy. Biopsy of the right ventricle confirmed cardiac amyloidosis of the amyloid immunoglobulin light chain (AL) subtype.

The patient underwent chemotherapy, followed by autologous stem-cell transplantation. She achieved successful remission, and her cardiomyopathy was compensated.

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AMYLOIDOSIS IS HETEROGENEOUS

Amyloidosis is a heterogeneous syndrome characterized by abnormal folding of proteins that deposit as insoluble fibrils in different tissues, impairing both structure and function. Virchow was the first to describe amyloid (from *amylon*, Greek for starch) as an abnormal material seen in postmortem examination of the liver. On Congo red staining, the extracellular proteins appear as salmon-red conglomerates, which also show apple-green birefringence under polarized light.

Amyloidosis can be localized but more often represents a systemic process, often associated with a plasma cell dyscrasia such as multiple myeloma.

Modern classification is based on the precursor protein,[1] eg:

- Light chains (AL)
- Acute-phase protein (AA)
- Beta-2-microglobulin (Aß2M)
- Transthyretin (ATTR; occurring in senile systemic amyloidosis)
- Other proteins (occurring in various forms of hereditary systemic amyloidosis).

AMYLOIDOSIS AND THE TONGUE

Macroglossia is defined as protrusion of the tongue beyond the alveolar ridge of the teeth at rest. When caused by amyloidosis, it is most often associated with the systemic AL variant and is present in 10% to 23% of patients with this subtype.[2]

On physical examination, tongue enlargement can present with lateral indentations, with a smooth contour or with nodular deposits. Less often, bullous lesions, vesicles, and ulcers can also be seen, particularly on the

lips. Infiltration of salivary glands can result in xerostomia. Functional symptoms, such as hypogeusia, dysarthria, dysphagia, dysphonia, and, in advanced cases, upper-airway dysfunction can result from restricted mobility of the tongue and tethering to deeper structures.

Surgical management may be necessary if severe obstructive symptoms are present, but infiltrative lesions tend to recur.

AMYLOIDOSIS AND THE HEART

Cardiac involvement in amyloidosis is currently the primary determinant of prognosis.[3] It is more often seen in the AL, senile, and hereditary forms. It usually manifests as diastolic heart failure, but angina, orthostatic hypotension, dysrhythmias, and syncope can also occur. Systolic dysfunction is typically a late finding in the course of the disease.

Although an electrocardiographic pattern of low voltage in the precordial and limb leads has been classically associated with cardiac amyloidosis, only 30% of patients with the senile and hereditary forms show this feature.[4] Left ventricular hypertrophy on electrocardiography is thought to be uncommon, but it has been reported in 16% of patients with AL amyloidosis and biopsy-proven cardiac involvement.[5] Cardiac troponin levels can be elevated, as seen in other infiltrative cardiomyopathies.[3] The diagnosis can be established by endomyocardial biopsy or indirectly by cardiac imaging and a positive extracardiac biopsy.

Drug therapy is supportive and mainly involves diuretics, since angiotensin-converting enzyme inhibitors, beta-blockers, and calcium channel blockers may cause hypotension and exacerbate myocardial dysfunction. The specific treatment varies depending on the underlying cause of amyloidosis. ■

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