Congestive Heart Failure in a Male with “Carcinoma Tongue” : A Case of Mistaken Identity

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Abstract
We present a case of primary amyloidosis with macroglossia and restrictive cardiomyopathy, that was mistakenly diagnosed as carcinoma of the tongue. He had characteristic echocardiographic findings, and bone marrow plasmacytosis but with normal serum electrophoresis and no Bence Jones proteins in the urine.

INTRODUCTION
Primary amyloidosis is a disease that masquerades as several conditions and requires a high index or suspicion to clinch the correct diagnosis. We present here a patient who had initially been diagnosed clinically as “carcinoma of the tongue with secondaries in the neck”. The patient had characteristic findings on echocardiography, a positive reaction for Congo Red in the lingual tissue biopsy, and the rarer presentation of bone marrow plasmacytosis without abnormal proteins in serum or urine.

CASE REPORT
A 45 year old male farmer, registered at the Cancer Hospital, Indore, as a case of carcinoma of the tongue with secondaries in the neck was referred to us for a medical check up. He presented with complaints of loss of appetite, loss of weight, easy fatigability and generalized weakness of 5 months duration. He also had a sense of bloating after meals, early satiety, and constipation. Three months prior to admission, he had noticed gradually increasing difficulty in speaking, and a swelling below his chin.

He also complained of progressively increasing shortness of breath on exertion, with distension of abdomen and swelling over both feet. He had been smoking beedies for the past 30 years, but did not chew tobacco and did not take alcohol. There was no history of chest pain in the past or palpitations or syncopal attacks. There was no history to suggest respiratory infection over the preceding years. He was not a known diabetic or hypertensive. There was no history of tuberculosis or jaundice in the past.

Hemoglobin was 14 g/dl. Blood counts were normal. Blood urea was 68.7 mg% and serum creatinine was 1.7 mg%. Urinalysis showed albumin ++, sugar nil, WBCs 4-5/hpf, no RBCs, no casts. The urinary protein excretion was 900 mg/24 hours. Serum bilirubin was 1.32 mg%, SGOT, SGPT and serum alkaline phosphatase were within normal range. Serum proteins were 6 gm% (albumin 3.1 gm%, globulin 2.9 gm%). Stool showed 3-4 RBCs/hpf, with positive occult blood test. ECG showed right axis deviation, poor progression of R waves in chest leads, and small sized complexes in the limb leads. Chest X-Ray revealed a cardiothoracic ratio of 0.54. Ultrasound of abdomen showed normal liver, spleen and kidneys, dilated bowel loops and free fluid in Morrison’s pouch.

The echocardiography revealed marked concentric hypertrophy of the left ventricle with normal cavity size.
(LVId 40 mm, LVIDs 33 mm, interventricular septum 19 mm, LV posterior wall 20 mm). There was speckled echotexture in the hypertrophied left ventricle and also in the right ventricle and the interatrial septum (Fig. 1). Left and right atria showed dilatation and enlargement. There was mild pericardial effusion, with normal appearing pericardium. All cardiac valves were normal. These findings suggested a diagnosis of restrictive cardiomyopathy related to amyloid infiltration.

Meanwhile the lingual tissue biopsy which revealed squamous epithelium with hypertrophy, parakeratosis, and hyperkeratosis, with mild dysplasia but no evidence of malignancy, was reviewed. The sections were stained with Congo Red and PAS which showed a positive reaction (Fig. 2). Also a biopsy was taken from the abdominal fat pad, which showed only mature adipose tissue, and no reaction with Congo Red and PAS.

Serum electrophoresis was done which did not reveal any abnormality. (Alpha 1 Globulin 0.3 gm%; Alpha 2 Globulin 0.6 gm%, Beta Globulin 0.9 gm%; Gamma Globulin 1.1 gm%). Bence Jones Proteins were absent in the urine. Bone marrow was aspirated, which showed large number of plasma cells (30-40%) with significant number of megakaryocytes. Leukocytes and erythroid series were unremarkable. Features were suggestive of plasma cell dyscrasia. Hence the final diagnosis was primary systemic amyloidosis (AL) with marcoGLOSSIA and restrictive cardiomyopathy (amyloid heart) with gastrointestinal and renal involvement.

The patient was discharged on melphalan (5 mg once a day initially, then 2 mg after 2 weeks), and prednisolone (40 mg daily) and is on follow up.

**DISCUSSION**

Primary (AL) amyloidosis (associated with plasma cell dyscrasias) is more common than the secondary forms as described in Western literature. However the great majority of patients with AL amyloidosis do not have the classical multiple myeloma or any other overt B cell neoplasm. Most such patients will have a modest increase in the number of plasma cells in the bone marrow, and which presumably secrete the precursors of the AL protein. These patients may
be referred to as having a "covert" myeloma, where the predominant manifestation is the production of an abnormal protein rather than of tumour masses. This would explain the clinical presentation of our patient. The restrictive cardiomyopathy resulted from infiltration of the myocardium with amyloid. Gastrointestinal involvement other than the macroglossia can be inferred from the complaints of difficulty in swallowing and constipation, the palpable liver, nodularity of the abdomen, and the presence of occult blood in the stool. Renal involvement can be inferred from the presence of albumin in the urine and mildly deranged renal functions, even though the ultrasound of the abdomen does not show any increase in the kidney size. The tongue which was large and nodular and indented was mistaken for malignancy, and the salivary glands were mistaken for lymph nodes. A uniformly enlarged and hard, non-tender tongue, especially with indentations on the lateral and inferior borders due to the teeth should raise the possibility of macrogllossia due to amyloidosis. Such patients frequently have associated enlargement of the submandibular and submental salivary glands as was seen in our patient. In this patient, since we had a tissue diagnosis of amyloidosis from one biopsy site and also the clinical picture fitted in with the diagnosis of primary AL amyloidosis, no further tissue biopsies were carried out.

Amyloidosis results from the deposition of insoluble, fibrous amyloid proteins, mainly in the extracellular spaces of the organs and tissues. Amyloid is not a chemically distinct entity. It is a group of diseases that have in common the deposition of similar appearing proteins. Currently amyloidosis is classified by the composition of the amyloid subunit protein. The common presentations of systemic amyloidosis are shown in the Table 1.

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<th>Primary (AL)</th>
<th>Secondary (AA)</th>
<th>Hereditary</th>
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<td>Monoclonal immunoglobulin in urine or serum plus any of the following: unexplained nephrotic syndrome, hepatomealy, carpal tunnel syndrome, macrogllossia, malabosorption syndrome, unexplained diarrhea or constipation, peripheral neuropathy, or cardiomyopathy.</td>
<td>Chronic infection (osteomyelitis, tuberculosis) or chronic inflammation (rheumatoid arthritis) plus any of the following: proteinuria, hepatomegaly, and unexplained gastrointestinal disease.</td>
<td>Family H/O neuropathy plus any of the following: early sensorimotor dissociation, vitreous opacities, renal disease, autonomic symptoms, cardiovascular or gastrointestinal disease.</td>
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Table 1: Presentations of systemic amyloidosis

Involvement of the heart in amyloidosis is more common in primary (AL) form and rare in secondary. The patient may present with congestive heart failure (restrictive cardiomyopathy, early diastolic failure), cardiomegaly, or any variety of arrhythmias. Echocardiography demonstrates concentric thickening of the LV wall, with hypokinesia and with reduction of the LV cavity size. The diffuse hyperrefractile "granular sparkling" or "speckling" may be seen in LV, RV and its presence in the interaatrial septum is especially suggestive of amyloid heart.3

Primary amyloidosis is a diagnosis that requires a high index of suspicion, the most common symptoms being fatigue and weight loss, which usually prompt a search for an occult malignancy. One must suspect amyloidosis when a patient presents with unexplained nephrotic range proteinuria, heart failure, peripheral neuropathy or hepatomegaly. Clinical findings that are relatively more specific are purpura above the nipple line, which are seen in 15% of the patients. Macroglossia is the most specific sign but seen in only 9%.3

Confirmation of the diagnosis requires Congo red staining of subcutaneous fat pad, rectal biopsy, lingual biopsy, or bone marrow. Especially specific is the yellow green birefringence when observed under a polarizing microscope. The diagnosis should be pursued aggressively if monoclonal protein is found in serum or urine. Bone marrow examination for plasmacytosis will help in the 10% of cases of primary systemic amyloidosis who do not have detectable monoclonal protein in the serum or the urine.4 Our patient was in this group. Alkylation agent based chemotherapy is used most often in the management, such as melphalan and prednisolone. But response can take up to a year and several patients may not survive long enough.5 Both organ and M protein response are monitored. Myeloablative chemotherapy with stem cell reconstitution may be of use in carefully selected patients.5 Average survival of patients with AL amyloidosis is 12-24 months. Echocardiography is performed to determine prognosis. Death is most often due to cardiac causes or renal failure.

REFERENCES