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CASE REPORT

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A Case Report: Macroglossıa as the Inıtıal Fındıng of Systemıc Amyloıdosıs Associated wıth Multiple Myeloma

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Abstract

Amyloidosis is a disease characterized by the accumulation of extracellular amyloid protein in many different tissues and organs, with localized or systemic symptoms. It can be acquired or inherited. Amyloid can accumulate in the liver, spleen, kidney, heart, nerves and blood vessels and cause different clinical syndromes such as cardiomyopathy, hepatomegaly, proteinuria, macroglossia, ecchymoses, neuropathy, renal failure, hypertension, autonomic dysfunctions and corneal abnormalities. In this case report, we present a 73-year-old male patient who presented to our clinic with dysphagia due to macroglossia for 2 years and had no other symptoms.

Keywords: Amyloidosis; Macroglossia; Multiple Myeloma

Introduction

Amyloidosis is a rare and progressive disease characterized by the extracellular accumulation of amyloid protein in various tissues or organs, frequently affecting the kidneys, heart, liver, spleen, nervous system, and gastrointestinal system [1]. Amyloidosis can be hereditary or occur as a complication of a primary disease. Amyloidosis is classified into four types: Primary, Secondary, Familial, and Senile Amyloidosis. The primary type (AL) involves light chains and originates from plasma cell dyscrasias, affecting multiple organs. The secondary type (AA) primarily affects the kidneys and liver and involves protein A. The familial type (ATTR) results from a mutation in the transthyretin (TTR) protein, primarily affecting the liver and nervous system.

Old age type (ATTRwt) amyloidosis is known as the wild-type form of TTR and primarily affects the heart. When it affects a distinct region such as the mucosa or oral cavity, it can be localized, but when it affects tissues like internal organs and connective tissues, it is considered systemic [2].

Accumulation of amyloid proteins in the tongue tissue can manifest as macroglossia, pain, papular nodules on the tongue, and secondary infections [3]. Over time, the patient's speech, swallowing, and breathing may be affected. In later stages, patients typically die due to irreversible loss of heart function caused by the accumulation of amyloid proteins[4].

Diagnosing amyloidosis can be quite challenging, but it becomes definitive when evaluated histopathologically. Apple-green birefringence under Congo red staining is characteristic and distinctive for amyloidosis. Additionally, under hematoxylin and eosin staining, it appears as an amorphous eosinophilic structure [5].

Case Report

A 73-year-old male patient has been referred to our clinic from the hematology department due to tongue enlargement and difficulty breathing persisting for 2 years. The macroglossia in the patient led us to suspect amyloidosis. The patient also had hypertension and COPD (Chronic Obstructive Pulmonary Disease). He has never smoked before, and there is no significant family history of illness. Previously, the patient was examined in the Ear, Nose, and Throat department, and underwent various tests and allergy tests, but no diagnosis was made. During clinical examination, significant tongue enlargement with prominent teeth marks on the tongue edge and multiple deep ulcerative crater lesions ranging from 2 to 4 mm in diameter were observed. A mass lesion was noted on the left lateral side of the tongue. Additionally, periorbital purpura was seen on the left side during external oral examination (Figures 1A, 1B).

A mucosal biopsy specimen measuring 3 x 0.5 x 0.5 cm, with a rough surface and elastic texture, taken from the dorsum of the tongue of the patient at Istanbul Kent University, Department of Oral

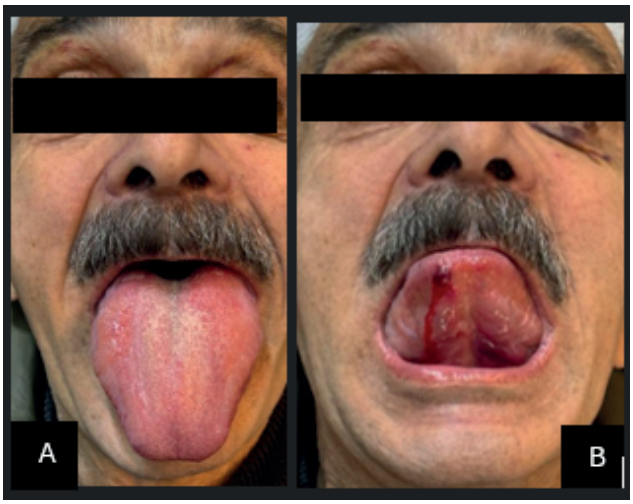

Figure 1: (A) Tongue enlarged to the extent that it does not fit within the oral cavity, with teeth marks on the edges of the tongue, (B) Mass hemorrhagic area on the ventral side of the tongue.

and Maxillofacial Surgery, has been sent to the pathology laboratory (Ref. No: 7324B1437 / 06.02.2024) (Figure 2).

Based on the biopsy results, the patient has been referred to the Oncology Institute with a diagnosis of amyloidosis secondary to Multiple Myeloma. The results of the capillary serum protein electrophoresis showed: Serum Amyloid A Protein (SAA) 25.70 mg/L (Reference: 0.0-7.0), Albumin 62.57% (Reference: 54.7-69.66), Alpha-1 Globulin 6.40% (Reference: 2.63-5.03), Alpha-2 Globulin 11.66% (Reference: 4.87-10.48), IgG 7.02 g/L, IgA 0.61 g/L, IgM 0.53 g/L, and Lambda Free Light Chain 823.0 mg/L (Reference: 5.7-26.3). The patient was diagnosed with secondary amyloidosis associated with Multiple Myeloma (Figure 3).

According to the PET scan results obtained from the patient, a focal hypermetabolic focus measuring 7 x 17 mm was detected in the left lateral base of the tongue. Additionally, hypermetabolic foci with F-FDG uptake were observed in both thyroid lobes, the lower lobe of the right lung, and the pelvis.

Melphalan 50 mg IV has been started in chemotherapy.

During this time, the patient developed Congestive Heart Failure due to systemic amyloidosis and was admitted to the Intensive Care Unit. An echocardiogram performed in the ICU showed left ventricular hypertrophy, mild pericardial effusion, and an ejection fraction (EF) of 65%, indicating echocardiographic findings associated with cardiac involvement of amyloidosis.

The patient is still being kept under observation in the intensive care unit, conscious and alert.

Discussion

Evaluating the epidemiology of amyloidosis is quite challenging. According to the National Institutes of Health (NIH), in the United States, approximately 78% of diagnosed amyloidosis cases each year are attributed to AL amyloidosis, 10-20% to ATTR amyloidosis, and 6% to AA amyloidosis [2].

Amyloidosis is a disease with both localized and systemic involvement. Symptoms vary depending on the affected organ and typically include edema, fatigue, weight loss, macroglossia,

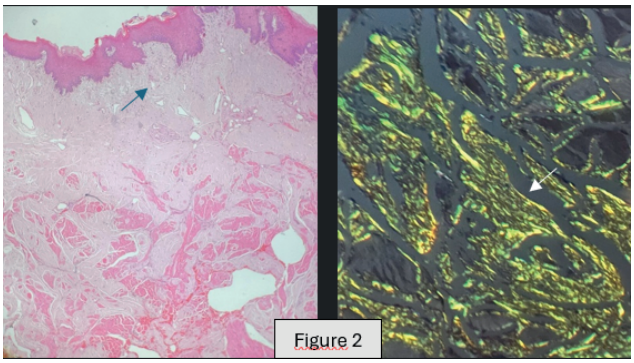

Figure 2: The biopsy sample taken showed areas of apple-green birefringence, diagnostic for amyloidosis, under Congo red stain. The histological appearance of amyloid shows the accumulation of eosinophilic, acellular, amorphous material throughout the submucosa, including between muscle fibers.

TETKİK ADI	SONUÇ	BİRİM	REFERANS
Amiloid A Proteini (SAA)	25.70	mg/L	0.0-0.7
Albumin	62.57	%	54.7-69.66
Alfa-1 Globulin	6.40	%	2.63-5.03
Alfa-2 Globulin	11.66	%	4.87-10.48
IgG	7.02	g/L	6.5-16.0
IgA	0.61	g/L	0.45-3.8
IgM	0.53	g/L	0.5-3.0
Lambda Serbest Hafif Zincir	***823***	***mg/L***	***5.7-26.3***
Kappa/Lambda Serbest (Serum)	***0.02***	***mg/dL***	***0.26-1.65***

Figure 3: The patient's preoperative hematological laboratory findings.

nephropathy, cardiomegaly, or interstitial pulmonary edema [2]. The patient in this publication presented initially with macroglossia, which led to challenges in diagnosis by other specialties.

Macroglossia is defined as the painless enlargement of the tongue [6]. Macroglossia can be an early diagnosis for amyloidosis (25%) and is the only region observed in 9% of all amyloidosis cases [7]. In this patient, macroglossia served as an early diagnosis for amyloidosis. Among other oral manifestations of oral amyloidosis are yellow-white nodules, purple bulla-like masses, or white patch-like lesions [8]. None of these findings were observed in the patient.

Macroglossia is seen not only in amyloidosis but also in Down Syndrome and acromegaly. In this case presentation, there was no intellectual disability or Down Syndrome present. Another differential diagnosis, acromegaly, is a rare condition characterized by physical deformities due to excessive production of growth hormone resulting in somatic overgrowth. Common clinical features include arthralgia, soft tissue edema, hyperglycemia, hypertension, and hyperhidrosis [9]. In the craniofacial region, patients with acromegaly may present with prognathism, malocclusion, and macroglossia [9]. None of these findings were present in the patient.

Amyloid deposition in the body can lead to hepatomegaly (50%), Carpal Tunnel Syndrome (25%), splenomegaly (10%), peripheral

neuropathy, and renal amyloidosis. Cardiac involvement can lead to Congestive Heart Failure, contributing to 40% of deaths [10]. In this publication, the patient also presents with Carpal Tunnel Syndrome and Congestive Heart Failure.

Amyloidosis can be caused by more than 25 types of proteins [11]. In secondary (AA) amyloidosis, the accumulated protein is serum amyloid (SSA), an acute phase reactant. AA amyloidosis typically arises as a secondary complication of another disorder related to chronic inflammations, infections, genetic disorders, hematological disorders, or neoplasms. Hematological disorders shown to be associated with AA amyloidosis include Waldenström's macroglobulinemia, Hodgkin lymphoma, Non-Hodgkin lymphoma, as well as multiple myeloma and monoclonal gammopathy, which are recognized in the literature to have a connection with AA amyloidosis [12]. In this case report, SSA levels were elevated (25.70 mg/L), and a diagnosis of multiple myeloma was made.

Multiple Myeloma (MM) is characterized by the excessive production of monoclonal immunoglobulins by plasma or B cells in the bone marrow [12]. Elevated levels of interleukin-6 (IL-6) have been found in one-third of multiple myeloma patients and are associated with poor prognosis of the disease. According to Terre et al., debates continue regarding the relationship between IL-6 and inflammation leading to AA amyloid accumulation [13].

Conclusion

Amyloidosis is a challenging diagnosis that can only be confirmed through histopathological evaluation. Macroglossia is an early diagnostic sign of amyloidosis and is seen in 9% of all cases. We presented a case where the initial symptom of macroglossia led us to diagnose amyloidosis with organ involvement associated with multiple myeloma. This publication is particularly significant in our profession as the diagnosis was made by a dentist. Therefore, careful evaluation of medical history and clinical findings can lead to early diagnoses that may save a patient's life.

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