Excessive Tongue Amyloidosis as the Diagnostic Sign of Multiple Myeloma: a Case Report

SUMMARY

Background: Deposition of amyloid in oral mucosa may be related to systemic disorders, including immune-related diseases and malignancies.

Clinical Presentation: We describe a case of 76-year-old patient with excessive, painless, multi-nodular tongue enlargement, and petechiae on the vermilion border and perioral skin that appeared 2 months ago. The biopsy detected subepithelial, Congo’s Red positive amyloid depositions. Consequent laboratory investigation and bone marrow biopsy confirmed the diagnosis of multiple myeloma stage 2 (International Prognostic Index - IPI).

Conclusion: Multi-nodular excessive tongue enlargement could be of high significance as initial sign of undiagnosed, underlying systemic disease including severe malignancy like multiple myeloma.

Keywords: Oral Amyloidosis; Macroglossia; Multiple Myeloma

Introduction

The term amyloidosis represents extracellular deposits of amyloid, a group of unrelated proteins present as a homogenous eosinophilic material. The current classification of amyloidosis is based on the nature of precursor plasma proteins that form these fibril deposits. Amyloid depositions may occur in a single (localized) or in many organs (systematic) and amyloidosis is also divided into primary or secondary based on its relation with other concurrent systemic diseases, including malignancies.

Manifestations of amyloidosis in the head and neck area may be usually present in its secondary form, affecting orbit, sinuses, salivary glands, pharynx/larynx and oral cavity in 10-40% of the cases. Potential sites of oral lesions are buccal, palatal and gingival mucosa and tongue, manifesting rarely as excessive macroglossia. Oral lesions can often represent an early manifestation, especially in cases of amyloid light chain depositions (AL amyloidosis) and provide the first sign of multiple myeloma (MM) or other monoclonal gammopathies.

Microscopically, amyloid depositions are detected through specific staining with Congo Red, and the apple-green birefringence appearance under polarized light.

This report describes a case of an elder patient with excessive tongue enlargement (macroglossia) as the initial sign of AL amyloidosis related to underlying multiple myeloma.

Case Report

A 76-year-old patient was referred complaining for a 2-month painless, multi-nodular enlargement of the tongue (Fig. 1), leading to discomfort, dysphagia and speech impairment. Clinically, the nodules were solid in palpation, with normal or bluish colour, and normal covering mucosa. Also, petechiae on the vermilion border and the skin around both lips were observed. The patient’s information for his medical history was unclear.
swelling of the lower extremities and a solid mass at the right shoulder (scapula) were observed, too. Also, the ultrasound of the heart showed wall hypertrophy with sigmoid inter-ventricular septum. Finally the patient died 5 years after the diagnosis and treatment.

Figure 1. Excessive nodular enlargement of the tongue at the time of diagnosis

Under local anesthesia a partial biopsy was taken from a nodular mass of the lateral border of the tongue; histological examination revealed a subepithelial, multinodular amorphous, fibrillar accumulation (Fig. 2a), positively stained for Congo-Red, having a reddish colour under the light microscopy (Fig. 2b) and apple green birefringence under polarized light.

Figure 2. Histological finding. a. Subepithelial, multinodular amorphous fibrillar accumulation (H&E x 20); b. Positive staining for Congo-Red. The multinodular amorphous fibrillar accumulation with a reddish colour (x10)

The laboratory investigation revealed increased free light chain Kappa in serum (5360mg/l) and urine (2170mg/l), κ/λ ratio 324, anaemia (Hb= 9.7 g/dl), urine Bence- Jones protein and chronic renal failure (Creatinine 2 mg/dl). In addition, bone marrow biopsy showed plasmacytic infiltration (22%), but the imaging analysis failed to detect any clear bone lesion. According to the findings, the diagnosis of Multiple Myeloma stage 2 by the International Prognostic Index (IPI) was settled and combined treatment consisting of Bortezomid, Melphalan and Dexamethazone was administrated with good tolerance from the patient and efficacy for the disease based on laboratory tests. However, during the follow-up, the tongue enlargement excessively increased (Fig. 3), causing obstruction. Carpal tunnel syndrome, systolic hypertension with wide neck pulsation (Brachio-цеphalic) and a soft mass at the right arm (epicondylus) were observed, too. Also, the ultrasonic of the heart showed wall hypertrophy with sigmoid inter-ventricular septum. Finally the patient died 5 years after the diagnosis and treatment.

Figure 3. Tongue enlargement 55 months later

Discussion

Systemic amyloidosis can be associated with immunocytes’ dyscrasia, such as multiple myeloma, monoclonal gammopathy, or macroglobulinemia, or presents as a complication of an underlying chronic inflammatory or tissue destructive process such as Crohn’s disease, tuberculosis, rheumatoid arthritis, ankylosing spondylitis and chronic osteomyelitis1. Etiopathogenesis of amyloidosis is not clear. The proposed schema of the pathogenesis includes production of amyloid fibrils in the extracellular matrix, causing tissue damage or impairment. It is widely accepted that the major constituent of amyloid fibres in patients with multiple myeloma consists of light chain fragments termed Bence-Jones proteins, and the light-chain variable region of the immunoglobulin represents the main component of AL-amyloid deposits. It is thought that light chain proteins may be secreted by macrophages8. The class of light chain involved in amyloidosis in MM is most often λ versus κ in a ratio 3:19, which is in contrast to our case with κ chains.

Oral manifestations can often represent the initial sign, especially in the case of amyloid light chain depositions (AL amyloidosis), and provide a sign of multiple myeloma or other monoclonal gammopathies5,6. Interestingly, oral amyloidosis has been referred to be related with chronic periodontitis. Periodontitis can increase the levels of APRs and potentiate the development of amyloidosis by increasing the levels of...
systemic inflammatory mediators. Additionally, deposition of amyloid in periodontal tissues causes accelerated periodontal destruction and bone loss10.

Our patient suffered from oral amyloidosis associated with multiple myeloma and he died 60 months after diagnosis and treatment. 7 to 20 percent of patients with multiple myeloma manifest amyloidosis. When diagnosis of amyloidosis is established in patients with multiple myeloma it forecasts a poor prognosis due to renal impairment caused by the excretion of excessive light chains. The prognosis for patients with AL amyloidosis depends on the degree of the organ involvement. Also the median survival in λ-light chain disease is reported to be significantly shorter than κ-light chain diseases. Generally, the prognosis of a patient is poor in cases of late diagnosis and if left untreated, with a median survival of 1 to 2 years11,12.

Conclusion

Although oral amyloidosis rarely involves oral mucosa or may be present as a localized lesion, its detection in oral mucosa could be of high importance as a clinical sign suspicious for amyloid depositions accompanying systemic disorders, ranging from immune-related diseases, inflections or severe malignancies (such as multiple myeloma). Noteworthy, in multiple myeloma cases amyloidosis is also related to prognosis and hence affects the therapeutic procedure of the disease.

References


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