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Case Report

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Ulcerated Tongue Borders as a Sign of Amyloidosis in a Patient with Multiple Myeloma

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ABSTRACT
Amyloidosis is characterized by extracellular deposition of amyloid material in various tissues and organs. Deposition of amyloid in the tongue is rare but often occurs in multiple myeloma. Here we present the case of a 44-year-old woman under treatment for multiple myeloma who complained of lateral tongue pain. Intraoral examination revealed an ill-defined, firm, whitish swelling with ulcerated surface on the bilateral borders of the tongue. Histopathological analysis revealed a lympho-mononuclear infiltration in the lamina propria with the presence of acellular and amorphous material positive for Congo red staining. Further examination revealed amyloidosis in a cervical mass associated with neural compression. Thorough examination of the oral cavity in patients with multiple myeloma is critical for early detection of amyloidosis. Biopsy is mandatory to confirm the diagnosis, thereby facilitating intervention and management if necessary.

Keywords: Amyloidosis; Multiple myeloma; Tongue; Ulcers; Macroglossia

INTRODUCTION

Amyloidosis is a pathological process characterized by the extracellular deposition of insoluble fibrillar protein material, known as amyloid, which may affect various tissues and organs and may be primary (AL amyloidosis), as in cases of multiple myeloma (MM), or secondary (AA amyloidosis) to chronic inflammatory and infectious diseases. This condition is often systemic, with multiorgan involvement, which has the worst prognosis[1-4], while its localized form is rare[1,2].

Oral amyloidosis is a rare manifestation of this condition[2], and it mainly affects anatomical region is the tongue[2,3]. Oral lesions are often the first sign of localized amyloidosis rather than the systemic form[5]. The main clinical characteristic of this manifestation is macroglossia and dysphagia[3-5], while nodular or ulcerative lesions are rare[1,5]. Here, we report a case of systemic amyloidosis in a patient with multiple myeloma, presenting as ulcerative lesions on the lateral borders of the tongue.

Case presentation

A 44-year-old woman, diagnosed with IgA lambda multiple myeloma in May 2024, initially presented with anemia and altered renal function, evidenced by elevated creatinine levels. According to the International Staging System (ISS), she was classified as stage III, corresponding to a high-risk group. The patient presented to the hospital's department of dentistry with complaints of lateral tongue pain.

These symptoms appeared after hospitalization and intubation in the Intensive Care Unit due to pneumonia. She had been receiving daratumumab combined with bortezomib, lenalidomide, and dexamethasone (D-VRd regimen) since July 2024, and the oral lesions were identified after the first chemotherapy cycle.

Her medical history revealed bilateral sacroiliitis, attributed to mechanical inflammation, and generalized muscle weakness, which was related to a pathological vertebral fracture with medullary compression. She was taking pregabalin, duloxetine, losartan, and muscle relaxants. Laboratory findings included anemia (8.8 g/dL), leukocytosis (18,900/mm³), and thrombocytosis (520,000/mm³). She was prescribed with pregabalin (150 mg each 12 hours), methadone (2,5 mg each 8 hours), metamizole (1g each 8 hours), baclofen (10mg each 12 hours), turmeric and vitamin D.

Intraoral examination revealed bilateral, poorly defined, firm, white-colored swellings with ulcerated surfaces on the lateral borders of the tongue, measuring approximately 3 centimeters on the right border and 1.5 centimeters on the left border (Figure 1A-C). Among the differential diagnosis was included traumatic ulceration due to intubation, amyloidosis, and sarcoidosis.

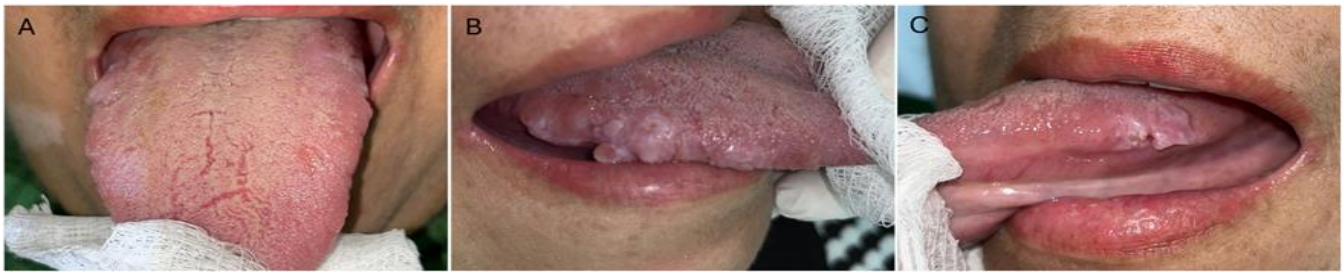

Figure 1. Clinical presentation of tongue amyloidosis: (A-C) Poorly defined, firm, white swelling with an ulcerated and granulomatous surface on the bilateral borders of the tongue

Histopathological analysis of incisional biopsy revealed hyperplasic stratified squamous epithelium, without atypical characteristics, with the lamina propria exhibiting lymphomononuclear infiltration and acellular, amorphous material in the subepithelial region and recent peripheral hemorrhagic focus. Congo red staining with refringence at polarized light was positive (Figure 2A-C).

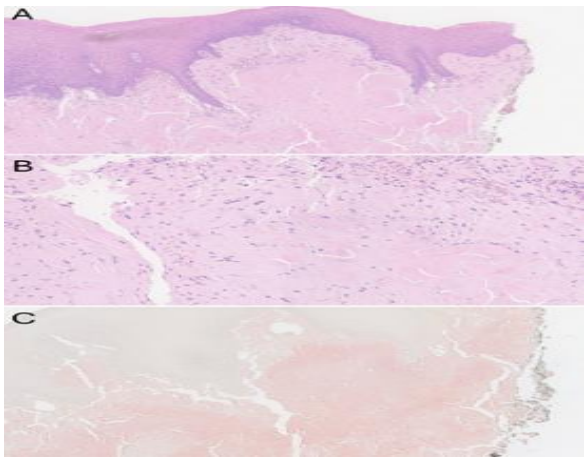

Figure 2. Histopathological features of tongue amyloidosis (A) Hyperplastic squamous epithelium with no atypia; accumulation of acellular, amorphous material in the subepithelial region, (B) Amorphous material deposited in the subepithelial area, with lymphomononuclear infiltration and foci of recent hemorrhage interspersed, (C) Positive Congo red staining for amyloid material (lower half and right side of the image)

Further examination revealed amyloidosis in a cervical mass associated with neural compression, and the diagnosis of systemic AL amyloidosis was established. The patient continued chemotherapy with the D-VRd regimen and achieved a very good partial response, being prepared for autologous stem cell transplantation. However, she died subsequently due to complications following femur fracture correction surgery.

DISCUSSION

The pathogenesis of amyloidosis in MM is driven by the overproduction of monoclonal light chains, typically of the lambda type, by malignant plasma cells. These light chains misfold and aggregate into insoluble amyloid fibrils, which are deposited extracellularly in various tissues. While amyloid deposition commonly affects highly vascularized organs such as the kidneys, heart, and liver, localized amyloidosis confines deposition to a single organ, as seen in rarer presentations. The mechanisms that determine whether amyloidosis presents as localized or systemic are not fully understood but may involve tissue-specific amyloid precursor production and local clearance capacity[1,3,5]. Serum laboratory examination may reveal anemia, a systemic presentation that also appears in this clinical case[1,6-8].

Oral amyloidosis is a rare condition[2,9-11], with 158 cases reported in the literature up to 2023[2]. It is more commonly the first sign of disease in patients with localized amyloidosis[3], unlike our patient. The condition is 22% more prevalent in women than in men, with a mean patient age of 61.1 years. Although our patient is younger than this average, amyloidosis can occur at any age, ranging from 7 to 90 years. Notably, the mean age at diagnosis is slightly higher in women (62.5 years) than in men (59.4 years)[2].

Although it can manifest in any region of the oral mucosa, a remarkable predilection for the tongue is observed[2,3,7,12], also reinforced by our report. Clinical signs of oral amyloidosis may include macroglossia,[3-5,7-10,12-16] ulcerative lesions[1,5,7,9,13,15,17], and nodular lesions that appear whitish, purplish, or yellowish[5,7,10,11,13,17]. Some patients may also report dysphagia[3,5,8-10,12,14-16], hoarseness[5,12], airway obstruction[5], tongue movement restriction[4,9,15], scalloping[7,9,12,15] and necrotic areas of tongue lateral borders[7,13], which is a rare presentation that also appeared in this case report and led it to diagnosis[7,13]. The oral lesion may assume a large range of sizes, between 1.8mm to 50 mm, with the mean size of 17.5mm[2].

Thorough examination of the oral cavity in patients with multiple myeloma is critical for early detection of amyloidosis.[2] Biopsy remains a key diagnostic tool to confirm this condition, thereby facilitating intervention and management if necessary[1-3,7,13,14]. Alternatively, the diagnosis can be established by removing a minor salivary gland, a method known for its high sensitivity[7]. Histologically, amyloidosis is characterized by interstitial deposits of amorphous, acellular, eosinophilic material in the lamina propria that stain positively with Congo red[5,7-18], with apple-green birefringence under polarized light[7-12,14-16,18]. Perivascular amyloid deposition is frequently seen[12,15,16]. The histopathological analysis of this case was correspondent to the characteristics demonstrated by the literature.

There are plenty types of treatment for this lesion, depending on the type of amyloidosis and the occurrence of associated diseases[2]. Most commonly elected treatment is the conservative long term follow-up[2,3,11], symptomatic treatment[5] or the lesion surgical removal[2,11,13,14,18]. For cases of secondary amyloidosis, the treatment of the primary disease seems to be the best alternative to treat the oral condition[3,9]. In cases of amyloidosis associated with MM, the lesions tend to follow the remission of the disease with chemotherapy and bone marrow transplantation[2,9]. Although its recurrence is uncertain, most studies indicate a high recurrence rate[3,7,12,18].

Systemic cases, like the one reported in this article, present worse prognosis[1–5,7,13], representing 88.9% of those patients who died[2], which highlights the importance of a fast and accurate diagnosis.[3,8] Also, these cases may demand being referred to a hematologic[3,5,12,13] or rheumatology services[15] to further investigations and treatments[3,5,12,13,15].

Such oral manifestation cases, especially the primary manifestation ones, as presented in the case report, reinforces the importance of dentists in the

composition of a multiprofessional team, so they might participate in the diagnoses process of systemic conditions first presented on the stomatognathic system, leading to an early diagnosis and treatment, guaranteeing a better prognosis to those patients[7,9,10,16].

CONCLUSION

This case report describes a manifestation of oral amyloidosis, presenting as ulcerative lesions on the lateral tongue, which was the primary symptom of systemic amyloidosis. It helps elucidate the importance of a meticulous oral diagnosis, which should include all its anatomical locations, and look forward to any alteration in tissues color, volume, sensitivity and integrity, that guarantees both early diagnosis and treatment, and, consequently, better prognosis to the patients.

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Consent to participate: Informed consent was obtained from the patient.

Consent to publish: The participant has consented to the submission of the case report to the journal.

REFERENCES

1. Maturana-Ramírez A, Ortega AV, Labbé FC, et al. Macroglossia, the first manifestation of systemic amyloidosis associated with multiple myeloma: Case report. J Stomatol Oral Maxillofac Surg. 2018; 119(6): 514-517.

2. Pontes FS, Ferreira GB, Fonseca FP, et al. Oral amyloidosis: an update. Med Oral Patol Oral Cir Bucal. 2023;28(4): e341-e346.

3. Matsuo FS, de Paulo LFB, Servato JPS, et al. Involvement of oral tissues by AL amyloidosis: a literature review and report of eight new cases. Clin Oral Investig. 2016; 20(8): 1913-1920.

4. Dawoud BE, Taylor J, Ariyaratnam S, et al. Amyloidosis presenting as macroglossia and restricted tongue movement. Dent Update. 2016; 43(7): 641–2, 645-7.

5. Dissanayaka DWVN, Bandara HMMR, Sabesan T, et al. Oral manifestations of systemic amyloidosis, an aid to diagnosis of multiple myeloma - report of two cases. Braz J Otorhinolaryngol. 2022; 88(1): 146-149.

6. Leiba M, Jarjoura S, Abboud W, et al. Role of oral examination in newly diagnosed multiple myeloma patients: A safe and simple way to detect light chain amyloidosis. Oral Dis. 2018; 24(7): 1343-1348.

7. Chebil RB, Nour M, Eya M, et al. Oral manifestations of undiscovered systemic amyloidosis: a series of seven cases. Pan Afr Med J.2024; 49:89.

8. Suriyakala M, Sreela LSN, Mathew P, et al. Macroglossia Associated With Primary Systemic Amyloidosis-Case Report With Unusual Clinical Presentation. J Ayub Med Coll Abbottabad. 2022; 34(1): 197-199.

9. Tao Y, Qiu X, Ye F, et al. Amyloidosis of the tongue: a rare case report. Braz J Otorhinolaryngol. 2023; 89(4): 101286.

10. Kaushik R, Pushpanshu K, Punyani SR. Orofacial amyloidosis—unusual presentation of a rare condition: A case report. Spec Care Dentist. 2016; 36(2): 104-107.

11. Bezerra HKF, de França TRT, Prado JD, et al. Oral localized amyloidosis. Head Neck Pathol. 2022; 16(3): 818-822.

12. Penner CR, Műller S. Head and neck amyloidosis: a clinicopathologic study of 15 cases. Oral Oncol. 2006; 42(4): 421-9.

13. Kanemoto H, Obata K, Kadoya K, et al. A Rare Case of Multiple Myeloma Identified Following the Diagnosis of Amyloidosis of the Tongue. Case Rep Dent. 2024; 2024: 2024:8836103.

14. Gómez-Piña JJ, Quiroz DM, Sierra-Hernández A, et al. Lengua gigante condicionante de disfagia en paciente con amiloidosis de cadenas ligeras. Rev Med Inst Mex Seguro Soc. 2023; 61(6): 863-867.

15. Mawardi HH, Akeel SK, Ali SA, et al. A 65-Year-Old Woman with an Enlarged Tongue Due to Amyloidosis. Am J Med Case Rep. 2022; 23: e936192.

16. da Costa KVT, Ribeiro CMB, Ferreira DC, et al. Dysphagia due to macroglossia in a patient with amyloidosis associated with multiple myeloma: A case report. Spec Care Dentist. 2018; 38(4): 255-258.

17. Tavares TS, da Costa AAS, Araújo ALD, et al. Oral manifestations of amyloidosis and the diagnostic

applicability of oral tissue biopsy. J Oral Pathol Med. 2024; 53(1): 61-69.
18. Razmara F, Derakhshan S, Mahdavi N, et al. Solitary amyloid tumor of the palate: A case report and literature review. Rare Tumors. 2023; 15: 20363613231166540.