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# *Lingual amyloidosis associated to multiple myeloma: case report*

# *Amiloidose lingual associada a mieloma múltiplo: relato de caso*

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## ABSTRACT

Oral amyloidosis is a disease characterized by extracellular and irreversible deposition of amorphous and fibrillar proteins in the oral cavity, being strongly associated with Multiple Myeloma. The objective of this study is to report a case of a 62-year-old woman diagnosed with Multiple Myeloma who, approximately 2 years after starting treatment for the underlying disease, presented a lesion on the lateral border of the tongue with exophytic growth, pinkish color, vascularized, painless, measuring 3cm in its largest diameter. After histopathological analysis through incisional biopsy, a final diagnosis of amyloidosis was obtained. As a local treatment, we opted for complete excision of the lesion. The patient evolved to death due to Multiple Myeloma influenced by the diagnosis of systemic amyloidosis. Oral amyloidosis is usually associated with the systemic presentation of the disease, making it necessary to conduct a thorough investigation of other organs. Its diagnosis is important since the prognosis is directly related and can negatively influence survival rates and treatment of the underlying disease.

**Indexing terms**: Amyloidosis. Multiple myeloma. Oral diagnosis.

## RESUMO

*A amiloidose oral é uma doença caracterizada pela deposição extracelular e irreversível de proteínas amorfas e fibrilares na cavidade bucal, sendo fortemente associada com Mieloma Múltiplo. O objetivo deste trabalho é relatar o caso de uma mulher com 62 anos de idade diagnosticada com Mieloma Múltiplo que, aproximadamente 2 anos após o início do tratamento para a doença de base, apresentou lesão em borda lateral de língua com crescimento exofítico, de coloração rósea, vascularizada, indolor, medindo 3 cm em seu maior diâmetro. Após análise histopatológica através de biópsia incisional, obteve-se diagnóstico final de amiloidose. Como tratamento local, optou-se pela exérese completa da lesão. A paciente evoluiu para óbito por consequência do Mieloma Múltiplo com*

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*complicações associadas à amiloidose sistêmica. A amiloidose oral geralmente está associada com a apresentação sistêmica da doença, tornando necessária uma investigação aprofundada nos demais órgãos. Seu diagnóstico é importante uma vez que pode influenciar diretamente no prognóstico e, consequentemente, negativamente nas taxas de sobrevida e no tratamento da doença de base.*

***Termos de indexação***: *Amiloidose. Mieloma múltiplo, Diagnóstico bucal.*

## INTRODUCTION

Multiple Myeloma (MM) is a malignant disease characterized by the proliferation of plasma clonal cells in the bone marrow and is usually accompanied by the secretion of monoclonal immunoglobulins detectable in serum or urine [1].

The condition accounts for 1.6% of all cancer cases and approximately 10% of hematological cancers in the United States [2]. In Brazil, it is estimated that more than 30,000 patients were under treatment [3]. Patients over 65 years-old represent 85% of diagnosed cases and the risk is twice as high in Afro-Americans when compared to Caucasians [4]. Patients may experience bone pain, in addition to nonspecific symptoms such as nausea, vomiting, weakness, recurrent infections, and weight loss [2]. Also, some patients may be asymptomatic, being diagnosed through laboratory findings such as anemia, kidney disease, and high levels of proteins [2].

About 12% to 15% of MM patients develop amyloidosis during the course of the disease, although up to 30% have subclinical amyloid deposits [5]. Amyloidosis manifests itself as extracellular and irreversible deposition of amorphous and fibrillar proteins, known as amyloid, in different organs and tissues [6]. It can be classified as localized and systemic, primary, and secondary, inherited or acquired, resulting in different prognoses [7].

Localized amyloidosis presents in only one organ, with a good prognosis. Systemic amyloidosis (SA) is the most common form of the disease and is classified into primary, secondary, and hereditary. Primary AS is related to the deposition of light chain immunoglobulin, often associated with lymphoid or plasma cell neoplasms, such as MM. The secondary form is associated with chronic inflammatory diseases, such as tuberculosis, and rheumatoid arthritis. And the hereditary presentation is characterized by an autosomal dominant inheritance, representing less than 2% of all cases [6,8].

Oral amyloidosis (OA) is mainly secondary to SA. Clinically, the oral manifestation can present itself in various forms, such as macules, papules, and nodules, as well as macroglossia, increased submandibular volume, and xerostomia [6].

There is no consensus on the most appropriate treatment for OA manifestations, however, the excision of the lesion can be an alternative, taking into account aspects such as the extent of the lesion and the presence of discomfort to perform routine activities. [5]. The surgical approach presents a probability of recurrences, therefore, regular follow-up is indicated [5].

## CASE REPORT

A 62-year-old female patient was referred to the Hematology team after being diagnosed with anemia, acute renal failure, severe weight loss, and complaints of low back pain. Through bone marrow biopsy, the diagnosis of MM IgA-secretory was obtained.

After the diagnosis, the patient underwent chemotherapy treatment in addition to regular dialysis, 3 times a week. Initially, cyclophosphamide, thalidomide, and dexamethasone were prescribed, which subsequently had their dose reduced by 50% due to chronic renal failure. With a partial response to treatment, a new chemotherapy protocol composed of melphalan, bortezomib, and prednisone was chosen. The patient was considered ineligible for Hematopoietic Stem Cell Transplantation due to poor performance as well as difficulty in adhering to treatment.

During outpatient follow-up, recurrence of the underlying disease, worsening of chronic kidney disease, and cytopenia were identified, requiring hospitalization.

During the hospitalization period, the patient was evaluated by the Dentistry team who identified an exophytic lesion on the left side of the tongue, measuring approximately 3 cm in its largest diameter, with irregular edges, vascularized, and with a pink color (figure 1).

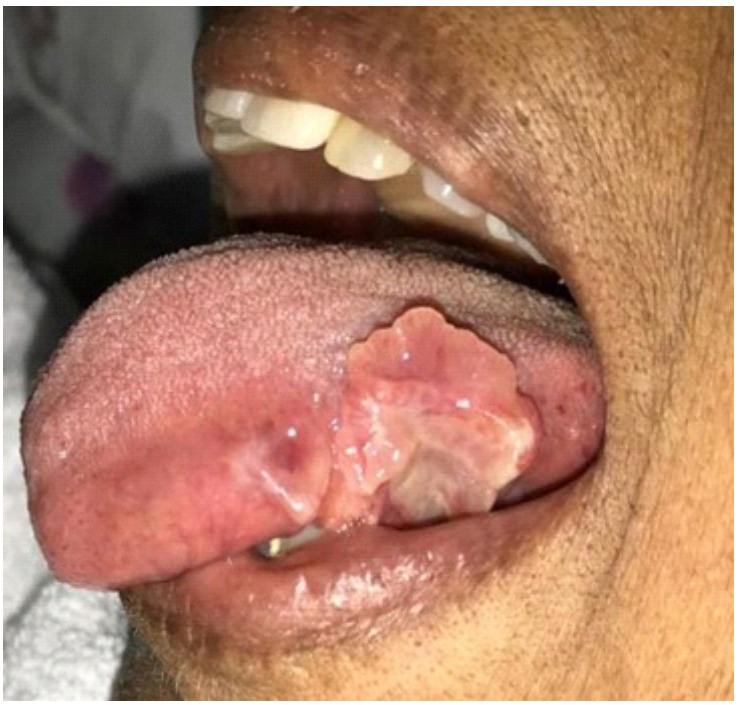

**Figure 1** – Clinical manifestation of the oral lesion.

The oral lesion presented by the patient: pinkish nodule, with irregular edges, painless, vascularized, presenting about 3 cm in its largest diameter.

Although painless, the injury caused discomfort during feeding. Taking into account the clinical aspect of the lesion and the patient's history, the main diagnostic hypotheses raised were, in addition to oral amyloidosis, non-neoplastic proliferative processes, such as pyogenic granuloma. For diagnostic purposes, an incisional biopsy was performed. In addition to the oral manifestation, an ulcerated lesion in the duodenum was identified by digestive endoscopy, which was also biopsied.

The collected fragments were sent for histological analysis with Violet Crystal staining. The histopathological report described the deposition of amyloid material for both lesions, confirming the diagnosis of SA, in the mouth and intestine. As a local treatment for oral manifestation, we opted for total excision of the lesion (figure 2), confirming the diagnosis of OA. The color used for histopathological analysis was Congo Red, showing amyloid deposits (figure 3).

Still in hospital, the patient was emaciated, asthenic, dependent on self-care, limited to a wheelchair, with abdominal pain and difficulty tolerating oral medications. Also, she underwent a surgical procedure and antibiotic therapy for septic arthritis in her right knee.

Because of the general health situation, presence of active disease and together with family members, exclusive palliative care was chosen. The patient died a few months later.

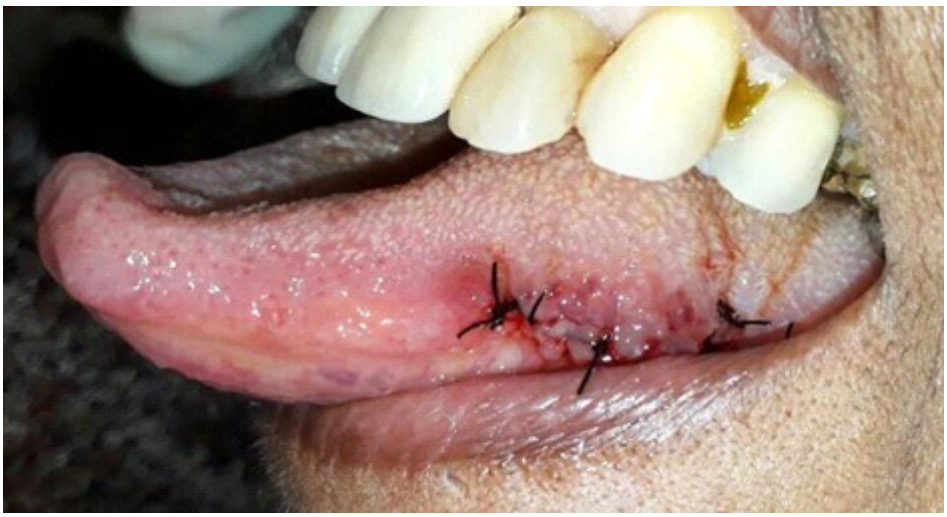

**Figure 2** – Immediate postoperative after total excision of the oral lesion.

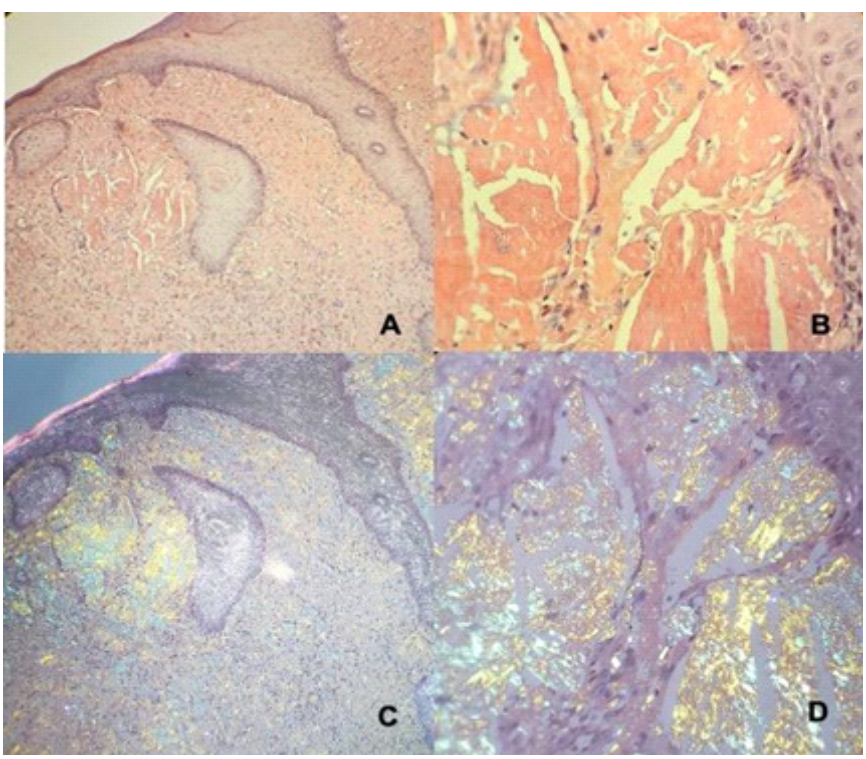


**Figure 3** – The histopathological aspect of the lesion.

## DISCUSSION

Amyloidosis is a rare metabolic disorder and its systemic manifestation worsens the prognosis. In most cases with oral involvement, there is an association with SA [8]. Although, Angiero et al. [9] have not found any systemic involvement or associated disease in three localized amyloidosis-related cases. Other authors, such as Gouvêa et al. [8] and Matsuo et al. [6] have found an equivalent distribution of 50% between localized and systemic.

SA might be secondary to other diseases, such as MM. MM is the most frequent disease associated with OA [7,8]. In these cases, the most commonly amyloid protein is the light chain AL protein, however other types might be diagnosed in these patients [7,8]. Penner et al. [10] have reported that about 15% of patients with MM develop amyloidosis. Leiba et al. [5] have evaluated 212 patients diagnosed with MM and of these, 6% were diagnosed with light chain amyloidosis, and 54% showed lesions in the oral cavity with amyloid deposits. No studies were identified where the manifestation of OA led to a diagnosis for the underlying disease, in this case, MM.

In the oral cavity, the tongue is the most common amyloid deposition site [6]. A literature review conducted by Matsuo et al. [6] has found an incidence ranging from 53.3% to 90.9% of amyloid deposits on the tongue. Other locations in the oral cavity where amyloid deposition can be found are buccal mucosa, lips, gingiva, palate and floor of the mouth.

A wide range of clinical features may occur, atypical presentations are reported such as bullous lesions and multiple, extensive and disseminated ulcerations [11]. Nodular lesions are more often and range from a mucosa similar colour, as seen in this case, to red, purplish and the most common yellow-white.

Deng et al. [12] have reported that 25% of patients with SA affecting oral tissues present macroglossia. In these cases, the tongue presents with an increase in volume, with a hard texture on palpation and impaired mobility, affecting food intake and speech. Although the diagnosis of amyloidosis is not the first to be considered in cases of macroglossia, it should not be neglected [7].

In general, the diagnosis is made through histopathological analysis with Congo Red staining, where amyloid deposits with apple-green birefringence are identified in polarized light microscopy, being the technique used in this case report. Metachromatic staining by crystal-violet can also be used, being also considered a good histochemical method for identifying amyloid deposits under an optical microscope [13].

There is no consensus regarding the management of lingual amyloidosis. An effective intervention is not yet available to treat most types of OA. Surgical excision should be considered, however, there is a high rate of recurrences [6]. Thus, regular monitoring is recommended [6]. The prognosis is uncertain, due to the rarity of the condition and its different classifications, however, in cases of systemic amyloidosis associated with untreated AL protein, the survival time is approximately 2 years [6].

## CONCLUSION

Although rare, amyloidosis is commonly reported in patients diagnosed with MM. Thus, these patients need to be monitored for amyloid depositions. Also, the oral manifestation of the disease is usually associated with the systemic presentation, therefore an investigation of the other organs is necessary. Its diagnosis is important because the prognosis is directly related, and can negatively influence survival rates and treatment of the underlying disease.

### Collaborators

GA LEAL and BS BALLARDIN conceptualization, methodology, data curation, writing - original draft preparation. MTM RISSETE, conceptualization, writing - review & editing. JM AMENÁBAR, supervision, conceptualization, methodology, data curation, writing-review & editing. JL SCHUSSEL, supervision, conceptualization, methodology, data curation, writing-review & editing.

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