

Diagnosis of Systemic Amyloidosis with the aid of tongue and minor salivary gland biopsy

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ABSTRACT

Amyloidosis is a rare group of metabolic disorders whose diagnosis is based on clinical criteria and confirmed by biopsy of the affected organ, but it is not always possible to perform it due to the invasiveness of the procedure. Oral tissues have been an alternative and non-invasive source of detection of amyloid deposition.

Objective: To describe a case of systemic amyloidosis in a 79-year-old female patient, diagnosed with the aid of tongue and minor salivary gland biopsy.

Conclusion: The detection of oral alterations contributed to the early clinical diagnosis of systemic amyloidosis.

Key words: amyloidosis; macroglossia; minor salivary gland; biopsy.

INTRODUCTION

Amyloidosis is a rare group of metabolic disorders, caused by the extracellular deposition of fibrillar proteins in important organs. According to the place of deposition and extent, it can be classified as systemic or localized. There is also a classification based on the biochemical nature of its protein subunits, subdivided into: 1) Amyloidosis derived from light chain immunoglobulins (AL); 2) Protein A (AA) amyloidosis and 3) Familial prealbumin (currently called transthyretin) amyloidosis (FA) ^(1,2).

Despite the few epidemiological data, the AL subtype, the most common, has an incidence of 8 to 12 cases per million people per year, with a slight predilection for males and a mean age between 64 and 76 years ⁽³⁻⁵⁾. In general, systemic amyloidosis is considered an underdiagnosed disease, whose diagnosis is made late, which results in a high burden of symptoms for the patient, such as difficulty in swallowing, and consequently in eating and speaking. This fact causes damage to quality of life and reduced survival. Thus, it is important to apply early and alternative methods for the patient with this diagnostic suspicion ^(3,4,6). The diagnosis is made based on clinical criteria and confirmed through biopsy of the affected organ, with the presence of amyloid protein in the histological tissue. It is not always possible to perform a biopsy

on the target organ due to invasiveness and increased morbidity. Biopsy at a surrogate site that offers reasonable diagnostic sensitivity is therefore recommended. In this context, oral tissues, such as the tongue and minor salivary glands of the labial mucosa, have been advocated as an alternative and non-invasive source for detecting amyloid deposition ^(7,8). Thus, the objective of this study is to describe a case of systemic amyloidosis diagnosed with the contribution of biopsy in the region of the tongue and minor salivary gland.

CASE REPORT

Patient M.L.A.N, female, feoderm, 79 years old, was referred to the University Hospital for etiological investigation of severe oropharyngeal dysphagia with a 3-year evolution. The patient had a medical history of systemic arterial hypertension, left ventricular diastolic dysfunction, hypothyroidism, and surgically treated bilateral carpal tunnel syndrome. In the dental evaluation, during the intraoral examination, macroglossia (Figure 1), crenate tongue (Figure 2) and lingual varicosities (Figure 3) were observed, in addition to buccal anterior-inferior teeth and accumulation of saliva in the oral cavity, due to significant odynophagia. Thus, given the clinical picture presented, the diagnostic hypothesis



FIGURE 1 – Aspect of the tongue with macroglossia.



FIGURE 2 – Aspect of the crenate tongue.



FIGURE 3 – Presence of varicosities in the belly of the tongue.

was amyloidosis. During the period of hospitalization, due to the degree of evolution of dysphagia, confirmed by videoendoscopy of swallowing, the patient underwent a gastrostomy to ensure adequate nutritional support. In discussion with a multidisciplinary team, it was decided to perform an incisional biopsy in alternative sites, in the region of the dorsum of the

tongue (Figure 4), affected by macroglossia; and on the intraoral mucosa of the lower lip (minor salivary gland) (Figure 5). The anatomopathological examination in Hematoxylin-Eosin (HE) (Figures 6 and 7) of both specimens revealed the extracellular deposition of amorphous, eosinophilic and hyaline material in the submucosal connective tissue. To confirm the presence of amyloid, special staining with Congo red was performed, which showed a peach red color under light microscopy (Figure 8) and apple-green birefringence under polarized light (Figure 9), which is compatible with amyloidosis. Additionally, the patient underwent abdominal fat biopsy for diagnostic control which also showed amyloid tissue. The differential diagnosis for multiple myeloma was performed through myelogram and immunophenotyping, being discarded and the definitive diagnosis was systemic amyloidosis. After hospital discharge, the patient continued with medical treatment with a hematologist and outpatient speech therapy.



FIGURE 4 – Transoperative. A - Incisional biopsy on the dorsum of the tongue, affected by macroglossia. B – Macroscopic appearance of the surgical specimen.



FIGURE 5 – Transoperative. A - Incisional biopsy of the intraoral mucosa of the lower lip (minor salivary gland). B – Macroscopic appearance of the surgical specimen - minor salivary glands.

DISCUSSION

Among the various diseases that affect the stomatognathic system, there are oral lesions that are related to the onset or evolution of systemic diseases. Of these, the main ones with oral findings include autoimmune, hematological, endocrine and neoplastic processes^(9,10). Saccucci et al (2018)⁽⁹⁾, in a review of the literature, described the oral signs and symptoms that are primarily in autoimmune diseases⁽⁹⁾. Sjögren's syndrome, for example, is an

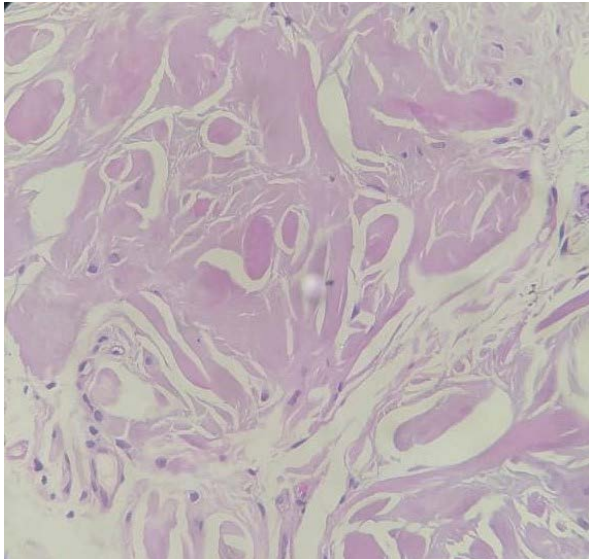


FIGURE 6 – Dorsal tongue, with extracellular deposition of amorphous, eosinophilic and hyaline material in the submucosal connective tissue (HE - 40x).

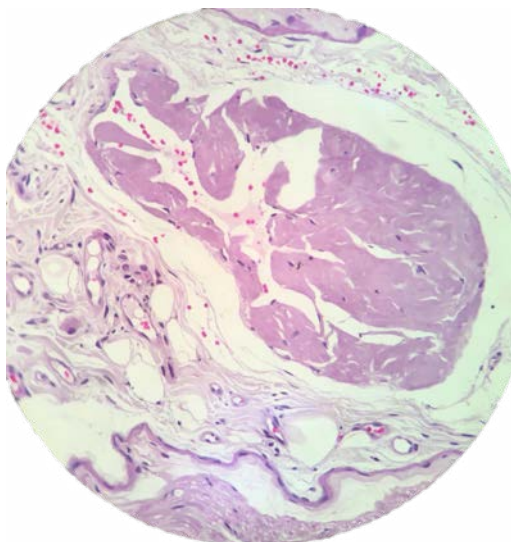


FIGURE 7 – Minor salivary gland, with extracellular deposition of amorphous, eosinophilic and hyaline material in the submucosal connective tissue (HE - 40x).

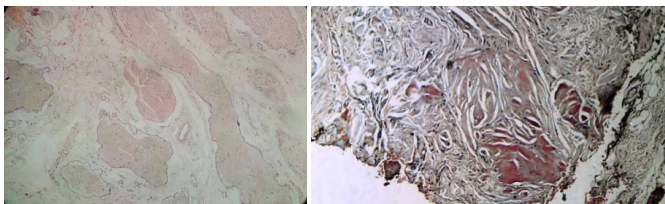


FIGURE 8 – Special staining with Congo red. A - Minor salivary gland showing peach red color under light microscopy, compatible with amyloidosis. B – Tongue dorsum.

autoimmune disease that affects the salivary and lacrimal glands, whose main manifestations are related to the oral cavity, such as xerostomia and hyposalivation. Another important example is pemphigus vulgaris, which in more than 50% of the cases, the first

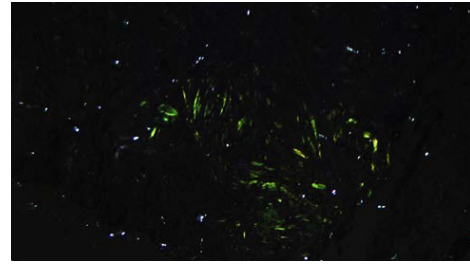


FIGURE 9 – Congo Red staining subjected to polarized light, region of the dorsum of the tongue showing apple-green birefringence, being compatible with amyloidosis.

signs of the disease appear in the oral mucosa and, almost always, the cutaneous lesions are subsequent to the oral manifestations⁽⁹⁾. By performing a complete anamnesis and a detailed physical examination, dentists can help in the investigation, detection and in the determination of the etiology of such alterations, as well as of systemic amyloidosis^(2,10,11).

Several authors corroborate that the diagnosis of amyloidosis is based on the proof of its presence in the tissue, the gold standard being the biopsy of the affected organ followed by histopathological analysis^(4,6,7). However, it is not always possible to perform a biopsy on the target organ, due to the risk of complications of the procedure (according to the organ), the professional's technical knowledge and the discomfort to the patient⁽⁸⁾. Therefore, it is necessary to resort to substitute tissues, such as abdominal fat, and more accessible ones, such as oral tissue biopsy, which have been advocated as an important auxiliary method^(12,13). In this context, aspiration of subcutaneous abdominal fat is the most widely used method for this purpose, with sensitivity ranging from 54% to 82% and specificity of 100%⁽¹⁴⁾. However, this is a more invasive procedure with greater morbidity, causing greater discomfort to the patient⁽¹²⁾. In the present case, after the detection of amyloid protein in the oral cavity, both in the tongue and in the minor salivary gland, it was decided to perform the diagnostic test in abdominal fat and thus the systemic involvement was confirmed.

In 1989, Delgado and Mosqueda had already described that all samples of minor salivary glands from the labial mucosa had some form of amyloid deposition⁽¹⁵⁾. Stoopler et al. (2003), in a retrospective study, demonstrated that the oral mucosa biopsy has a high diagnostic value, with the tongue being the most common site of amyloid deposition in the oral cavity, followed by the palate, gingiva and floor of the mouth⁽¹²⁾. More recent studies by Suzuki et al (2016) concluded that minor salivary gland biopsy may be the first choice for diagnosing AL amyloidosis due to its safety and high sensitivity of approximately 80% to detect amyloid deposition⁽¹⁶⁾. Similar results were found in a prospective study by Lecadet et al (2018)⁽¹⁷⁾. They concluded that minor salivary gland biopsy is

more effective for detecting amyloidosis when compared to normal skin biopsy, with sensitivities of 68.4% and 28.6%, respectively⁽¹⁷⁾. Thus, it is recognized that the oral mucosa is an important alternative area for the diagnosis of amyloidosis, as it is easily accessible by surgery, with high cell turnover and rapid healing, which contributes to greater patient comfort. In the case reported, the presence of amyloid was identified both on the dorsum of the tongue and in the minor salivary gland of the lower labial mucosa.

Macroglossia is the most frequent oral manifestation of AL amyloidosis and is present in 10 to 20% of patients. Often, it can be found as the only manifest sign of the disease, being, therefore, an important alteration to be identified for an early diagnosis⁽¹⁸⁻²¹⁾. Tongue biopsy, performed in the present case, is advocated as an alternative diagnostic method, with or without macroglossia, as it is one of the intraoral sites most affected by amyloid deposition. In addition, if it is extensive, it can cause the patient to have difficulties in speaking, chewing and swallowing⁽¹²⁾. In the case presented, it is not known whether macroglossia was the first manifestation of systemic amyloidosis, as the patient had already had severe dysphagia for 03 years, in addition to cardiac involvement and bilateral carpal tunnel syndrome.

It is important that the dentist, when identifying a case of macroglossia, be aware of the possible causes, considering amyloidosis as a diagnostic hypothesis⁽²²⁾. In this way, it can provide early diagnosis and, consequently, a better prognosis of cases, with consequent improvement in quality of life and increased survival of patients. In the present case, the intraoral physical examination of the patient, performed by the dental team, was essential for the detection of macroglossia and the decision to perform an incisional biopsy in the tongue and minor salivary gland. This fact avoided performing more invasive

surgical methods in other regions affected by amyloidosis, such as esophageal and heart biopsy, which would bring greater morbidity and risks to the patient.

CONCLUSION

In this context, the importance of the performance of the dentist, inserted in the hospital multidisciplinary team, for the detection of oral alterations that can contribute to the early clinical diagnosis of systemic amyloidosis and, thus, increase the efficiency and effectiveness of strategies of patient treatments.

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STATEMENTS

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