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Oral localized amyloidosis

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Abstract
This report describes two cases of oral localized amyloidosis (LA). In case 1, a 52-year-old man appeared with painful slightly, yellowish multiple nodules located on the dorsum of the tongue, of unknown duration. Incisional biopsy was performed, and the histopathologic analysis revealed a homogeneous, eosinophilic, and extracellular material. Congo red stain showed salmon pink coloration at light microscopy and apple-green birefringence at polarized light. In case 2, a 74-year-old man presented asymptomatic nodular lesions on the labial commissures with duration of several months. An excisional biopsy was performed in both lesions, and microscopically the specimen demonstrated the same histopathologic features of the case 1. Furthermore, amyloidosis with systemic involvement was excluded after investigations for both patients. Thus, the final diagnosis for both cases was LA. The patient 1 refused the surgical excision of the residual lesion, and in both cases, no signs of clinical and systemic progression were observed after 24 and 84 months of follow up. Although it is rare, LA should be considered in the differential diagnosis of multiple or single yellowish nodules on the oral cavity.

Keywords Amyloidosis · Mouth · Tongue

HISTORY AND CLINICAL FINDINGS

Case 1

A 52-year-old man presented with a chief complaint of multiple nodules on the tongue of unknown duration. Medical history was not contributory. Intraoral examination revealed painful slightly, well-circumscribed, yellowish multiple nodules located on the dorsal tongue (Fig. 1), with a firm consistency. Choristoma, ectopic lymphoid tissue and amyloidosis were the main clinical diagnoses. Under local anesthesia, an incisional biopsy was performed.

Case 2

A 74-year-old man was referred for evaluation of lesions on the labial commissures with duration of several months. The patient was asymptomatic. His past personal and family histories were not contributory. These lesions improved with antifungal treatment but did not disappear. Oral examination revealed nodules with smooth surface and firm consistency, located on the right and left labial commissures (Fig. 1). The main hypothesis of diagnosis was a reactive/inflammatory lesion. Under local anesthesia, an excisional biopsy was performed in both nodules.

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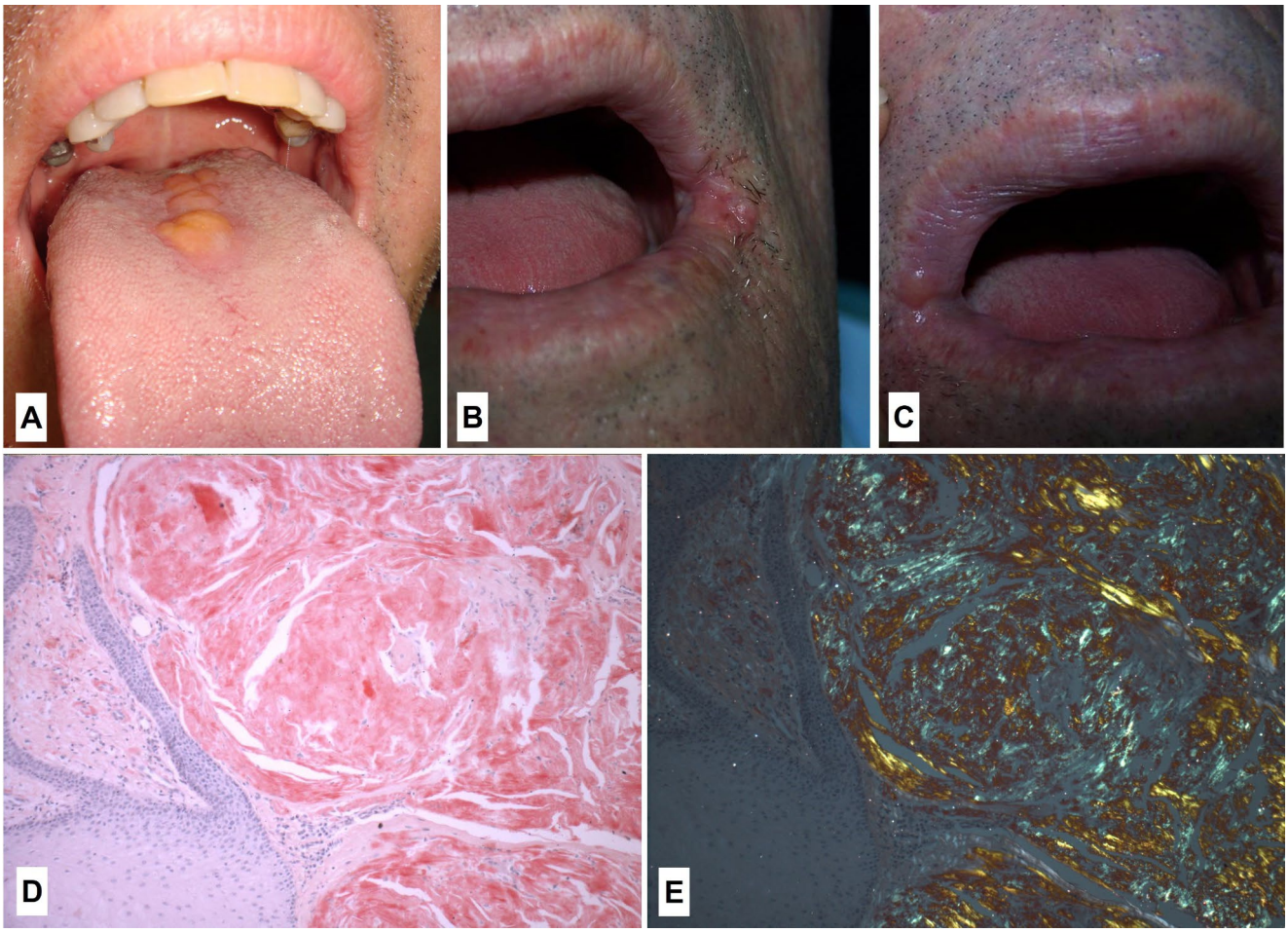

Fig. 1 – **A**: Well-circumscribed and yellowish multiple nodules located on the dorsal tongue. **B-C**: Oral examination revealed nodules with smooth surface and firm consistency located on the left (B) and right (C) labial commissures. **D**: Abundant amount of eosinophilic, amorphous, and extracellular material adjacent to a hyperplastic epithelium, showing salmon pink coloration (Congo red stain, original magnification, x100). **E**: Amorphous and extracellular material exhibiting apple-green birefringence at polarized light (Congo red stain at polarized light, original magnification, x100)

DIAGNOSIS AND TREATMENT

Microscopically, in both cases, it was observed abundant amount of eosinophilic, amorphous, and extracellular material in the subepithelial region. The epithelium was hyperplastic (Fig. 1). Congo red stain showed salmon pink coloration at light microscopy and apple-green birefringence at polarized light (Fig. 1). According to microscopical features, the diagnosis of amyloidosis was established. In both cases, hemogram, VSG, biochemistry, serum and urine protein electrophoresis, liver function tests and bone marrow aspiration were normal. Thus, the final diagnosis was LA.

In case 1, it was proposed the surgical excision of the residual lesion, but the patient refused the treatment. The patient is under follow-up and the lesion remains unaltered after 24 months of diagnosis. No signs of systemic amyloidosis were also observed. In case 2, after an 84-month follow up, no signs of recurrences or clinical and systemic changes have been observed.

DISCUSSION

Amyloidosis represents a heterogeneous group of disorders characterized by abnormal extracellular deposition of various insoluble fibrillar proteinaceous materials [1, 2]. There are three forms of amyloidosis defined by the presence or absence of systemic disease: primary systemic amyloidosis (PSA), secondary systemic amyloidosis (SSA), and localized amyloidosis (LA) [3].

PSA is a condition with unknown underlying cause, different from the SSA, which occurs associated with other known diseases, such as tuberculosis, rheumatoid arthritis, and mainly multiple myeloma [4]. LA consists in a nodular mass of amyloid deposit without association with

a systemic disease [5–7]. Head and neck region is affected about 12–90% of the cases, typically with involvement of the larynx and tongue [8]. However, involvement of the tongue is almost always resulting of a systemic disease [9].

Oral amyloidosis tends to involve the tongue, buccal mucosa, and gingivae [7, 10]. Head and neck LA is a rare and benign disease [5, 8]. The most reported features of oral LA are multiple soft nodules accompanied by yellowish, red, blue, or purple color changes of the mucous membrane [5, 6, 11]. To the best of our knowledge, only 53 well-documented cases of LA in the oral cavity have been previously described in the English-language literature [1, 6, 7, 10, 11–38]. Thus, this article describes the clinicopathological features of two rare cases of oral LA and review of the literature. Considering all oral LA, the case 2 seems to be the 4th LA case on the labial commissures published in the English-language literature [1, 6, 7, 10, 11–38].

Amyloidosis most commonly affects individuals between 50 and 70 years of age, with a male-female predominance of 3:1 to 3:2 [17]. The mean age of the patients with oral LA is 57.5 years (range 10–90 years), with a female predilection. Among 55 cases of oral LA, including the current cases, 28 (51%) were localized in the tongue, 10 (18.2%) in the palate, 4 (7.3%) in the labial commissure, 1 (1.8%) in the maxilla, 1 (1.8%) in the floor of the mouth, 2 (3.6%) in maxillary alveolar ridge, 3 (5.5%) in the gingiva, 2 (3.6%) in the lower lip. In addition, 1 (1.8%) case involved the tongue, lower lip, and buccal mucosa, 1 (1.8%) the buccal mucosa and tongue, and 2 (3.6%) were in unspecified sites of the oral cavity [1, 6, 7, 10, 11–38].

Oral LA does not usually progress to systemic disease [10]. Although involvement of the tongue may be linked to systemic disease, the case 1 does not have systemic involvement. To date, the patients have not developed clinical or laboratory evidence of systemic amyloidosis or multiple myeloma for 24 and 84 months of follow-up.

The most common head and neck presentations are hoarseness, nasal congestion, odynophagia, articulation problems, mandibular deformities, dysphagia, airway obstruction, speech disorders and hypogeusia [26]. Manifestations of oral amyloid deposits may include macroglossia, xerostomia, and gingival involvement with swelling and hemorrhage [27]. Amyloidosis in the tongue typically results in macroglossia, manifested by increased tongue volume, tongue protrusion beyond the alveolar ridge, speech impairment, and dysphagia [26]. Yellow nodules or raised white lesions occurring predominately along the lateral border are also common. Clinically, the mucosal surface is usually intact, and the underlying lesion may be nodular or flat, with a yellow, pink, or bluish hue [26, 39]. In the case 1, it appeared as a painful, yellowish well-circumscribed multiple nodules located on the dorsum of the tongue and the lesions presented a firm consistency. In case 2, LA appeared as asymptomatic nodular lesions on the labial commissures.

Histologically, amyloid is an eosinophilic amorphous extracellular protein deposit. The diagnosis is based on amyloid binding of Congo red stain, yielding apple-green birefringence under polarized microscopy [33].

The investigation of organ involvement, underlying diseases, and amyloid protein subtypes is important for differentiating between systemic and localized amyloidosis. Underlying diseases are investigated by screening for abnormal proteins in serum and urine, and a bone marrow biopsy to analyze plasma cells. Immunohistochemical staining using anti-λ or κ immunoglobulin light chain antibodies, anti-SSA antibodies, anti-TTR antibodies, and mass spectrometry may be useful to identify amyloid protein subtypes [40]. In the current cases, no signs of systemic diseases were evidenced. Additionally, the microscopic analysis confirmed the amyloid deposition and after long-term follow-up, no evidence of systemic diseases was observed. These findings confirmed the diagnosis of LA.

There is still no consensus regarding the management of oral LA, although numerous therapies have been proposed, including surgical excision and pharmacological treatment. However, lesions often persist or recur. The prognosis is uncertain, owing to the rarity of the condition, requiring regular follow-up and monitoring [31]. In the present cases, no further treatment was performed, and the lesions remained stable after 24 and 84 months of follow-up.

In summary, oral LA is rare. Despite of this, LA should be considered in the differential diagnosis of multiple or single yellowish nodules on the oral cavity.

Authors' contributions Conceptualization: Danyel Elias da Cruz Perez; José Divaldo Prado; Rafael Segura Saint-Gerons. **Supervision**: Danyel Elias da Cruz Perez; José Divaldo Prado. **Visualization**: Elaine Judite de Amorim Carvalho. **Writing – original draft**: Hélen Kaline Farias Bezerra; Talita Ribeiro Tenório de França. **Writing – review & editing**: Danyel Elias da Cruz Perez; Elaine Judite de Amorim Carvalho; Rafael Segura Saint-Gerons.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical Approval The study was performed following the 1964 Helsinki Declaration standards.

Consent to participate Not applicable.

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