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RELATO DE CASO

Dialysis-related amyloidosis of the tongue

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Abstract:

Background: As the aging process of the world population evolves, a progressive increase in the number of patients with kidney failure and consequently under long-term hemodialysis is expected. Dialysis-related amyloidosis, a disease characterized by deposits of β2-microglobulin, affects mainly the osteoarticular system, while involvement of the oral tissues is rare. **Objective:** We present an unusual case of lingual amyloidosis associated with hemodialysis in a 67-year-old male under dialysis for 24 years. **Conclusion:** It is important to understand the oral manifestations of systemic diseases for appropriate diagnosis and treatment of the affected patients.

Keywords: Amyloidosis; Renal Failure; Dialysis; Tongue.

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BACKGROUND

Amyloidosis is a rare condition caused by deposition of misfolded proteins as aggregates in the extracellular tissues, leading to impairment of organ function. These proteins are able to assume an insoluble β-pleated sheet structure[1]. The disease can be divided into systemic and localized forms. The systemic forms are a group of biochemically distinct conditions that can affect various organs or tissues[2].

They can be divided into: primary or immunoglobulin light-chain amyloidosis (occurs at any lymphoid clonal disease, such as non-Hodgkin lymphomas, or hematopoietic cell dyscrasias, such as multiple myeloma); secondary or amyloidosis by serum amyloid A (occurs in association with inflammatory diseases or chronic infections and occasionally with neoplasms); hereditary amyloidosis (transmitted by dominant inheritance in combination with a mutation that enhances the inappropriate unfolding of proteins, usually associated with the accumulation of transthyretin); and dialysis-related or β-2 microglobulin amyloidosis (affecting patients under dialysis for long periods or renal failure due to β-2 microglobulin accumulation)[3,4].

Dialysis-related amyloidosis (DRA) predominantly involves the osteoarticular system and can induce several disorders such as carpal tunnel syndrome, spondyloarthropathy and cystic destructive bone lesions. It is less frequently reported in extra-articular tissues, such as the heart, especially when the disease is diagnosed at an advanced stage. As the number of patients under long-term hemodialysis is increasing, it is expected that DRA progressively tends to appear in extra-articular systems[5].

Tongue DRA is rare and it has been considered a late complication of the disease, usually affecting patients under dialysis for more than 20 years. Lingual involvement is usually characterized by the presence of firm white-yellowish nodules of various sizes that can lead to dysfunction on taste, mobility and speech[6].

It is noteworthy that the diagnosis of tongue DRA is difficult because the clinical signs are sometimes nonspecific. Other diseases, such as fibromas, neuromas and granular cell tumors, as well as involvement of tongue by systemic diseases, such as hypothyroidism, should always be ruled out and biopsies are usually indicated to confirm diagnosis[7,8].

There is no specific therapy for DRA of the tongue except surgical intervention, if necessary[9]. Yusa et al.[10] reported the excision of the nodular lesions of DRA of the tongue by CO_2, laser evaporation under local anesthesia, considering it a useful method for selective removal of lingual amyloid. Increasing the duration and frequency of dialysis, hemodiafiltration, or renal transplantation may also enhance the removal of β-2 microglobulin and, consequently, reduce DRA progression[9].

The aim of the present study is to report an unusual case of DRA of the tongue in an adult male under dialysis for 24 years.

CASE REPORT

A 67-year old male was referred evaluation of tongue lesions leading to speech impairment lasting one year. Medical history revealed that the patient was under hemodialysis for 24 years due to nephritis associated with renal failure. Moreover he had hypertension and hepatitis C infection and was prescribed enalapril, calcium bicarbonate, folic acid, B complex vitamins, calcitriol and omeprazole.

Oral examination showed a swelling of the tongue and the presence of multiple well-defined firm yellow-whitish sessile papules and nodules, some with granular surface (Figura 1A e 1B). Clinical provisional diagnosis included Crohn disease and pyostomatitis vegetans and an incisional biopsy under local anesthesia was performed.

The specimen was submitted to routine laboratorial procedures and histological analysis of the HE-stained sections showed a fragment of the oral mucosa lined by a stratified squamous epithelium. The adjacent fibrous connective tissue showed the presence of deposits of a diffuse eosinophilic homogeneous amorphous material (Figura 2A, 2B, 2C, 2D). Congo red staining showed that the material was birefringent and compatible with amyloid. Final diagnosis was DRA and the patient was referred for further medical evaluation. No other signs and signals such as carpal tunnel syndrome, spondyloarthropathy and cystic destructive bone lesions could be found. Six months after diagnosis of DRA of the tongue the patient died by infection in the catheter.

DISCUSSION

DRA predominantly involves the osteoarticular system and commonly manifests as erosive and destructive osteoarthropathies, destructive spondyloarthropathy and carpal tunnel syndrome[9]. The present patient presented no bone and/or joint involvement, contrarily to what has been expected to DRA. When present, oral DRA is usually diagnosed in patients under long-term (more than a decade) dialysis[6,11,12], such as in the present case.

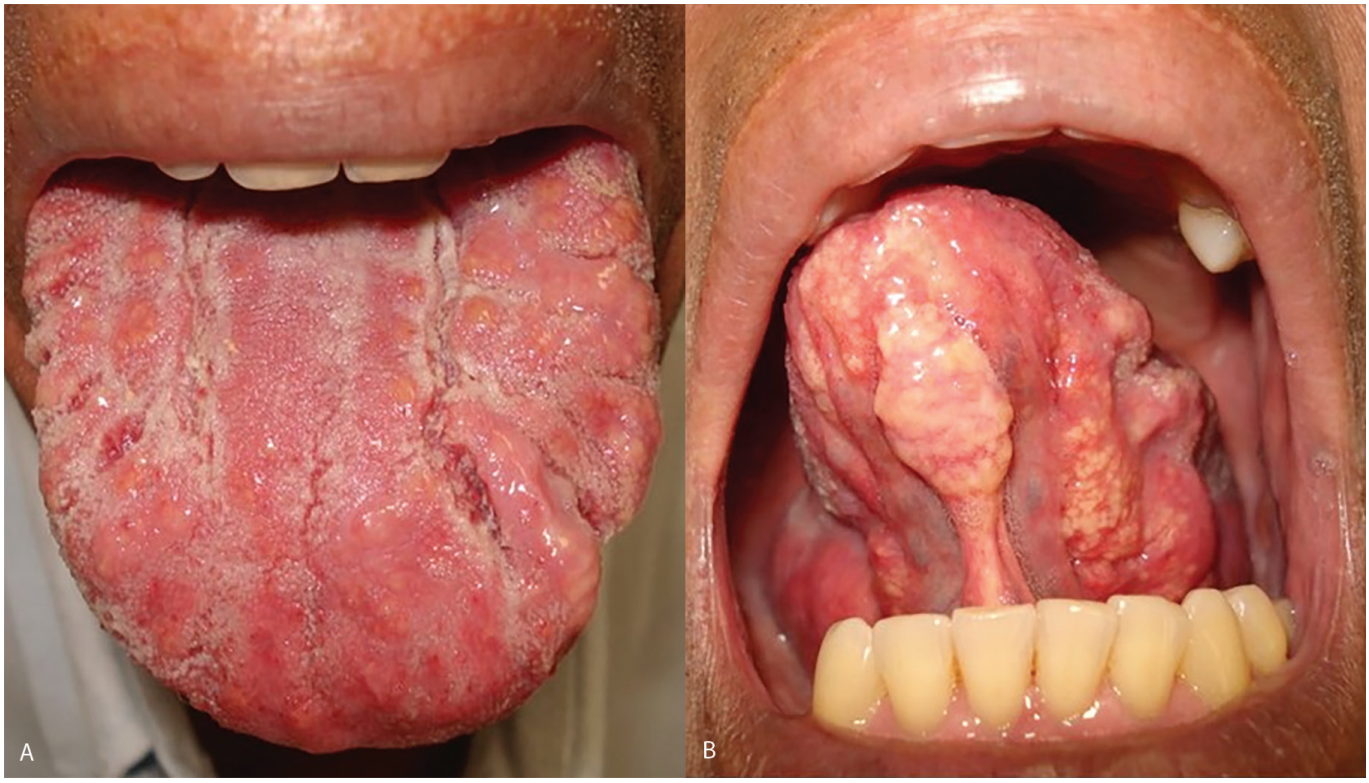

Figure 1. Clinical aspect of the tongue showing multiple white-yellowish papules and nodules (A) associated with fissured tongue (B).

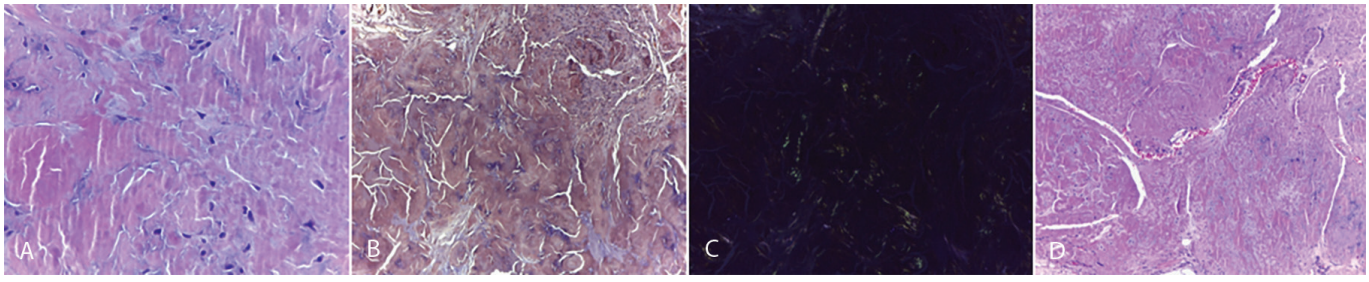

Figure 2. Histological aspects of Dialysis-related amiloidosis showing the deposition of extracellular amorphous material (A, HE 100x; B, HE 400x) that proved to be positive to Congo red (C, 400x) and birrefringent under polarized light (D, 400x).

Oral involvement in DRA is rare and few cases have been reported. The entity is usually diagnosed in males (male to female ratio of 7:1) in their fifth to seventh decades of life6, in accordance with the present report. The tongue is the most common involved site and lingual involvement can result in the clinical impression of macroglossia[13], as in the present case.

Clinical presentation usually includes the presence of multiple variable sized yellow-whitish firm nodules and papules[6,14], sometimes associated with burning, numbness, pain and muscle weakness[15,16]. Matsuo et al.6 classified the tongue involvement in DRA according to the location of the nodules: lateral type (involvement of the lateral border of the tongue) and diffuse (diffuse involvement of the tongue, usually associated with taste alterations and mobility and speech difficulties). The present case was classified as a diffuse type of involvement associated with speech impairment.

When there is clinical suspicion of oral amyloidosis, biopsy and histological analysis of the affected tissue should be performed8. Histological findings include the presence of an amorphous homogeneous eosinophilic material diffusely infiltrating the connective tissue. Congo red stain is useful in highlighting the amyloid nature of the deposits.

Diagnosis of DRA is reached after histological analysis and association with clinical and medical history. Differential diagnosis of tongue DRA should include

other entities and conditions such as tuberculosis, lymphangioma, hypothyroidism, acromegaly, lingual infarction caused by giant-cell arteritis, idiopathic muscular hypertrophy, Beckwith-Wiedemann syndrome, fibromas, lipomas, granular cell tumors, sarcomas and salivary gland tumors[7].

Advanced DRA of the tongue leads to lingual dysfunction, such as abnormal taste and altered mobility. With severe and prolonged lingual dysfunction, malnutrition and other associated comorbidities can occur. Altering the duration, frequency and type of dialysis treatment with biocompatible high flux dialysers can be potentially helpful strategies to prevent DRA-related morbidity[16]. Surgical intervention, when possible, is considered an option9. Unfortunately our patient died before any intervention could be performed.

The present report showed the importance of oral signs and symptoms in the diagnosis of systemic diseases, such as DRA.

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