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Case Report

Uremic stomatitis in three patients and review of the literature

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Abstract

Uremic stomatitis is a rare disease that affects the oral mucosa, caused by acute or chronic advanced kidney failure. Of poorly known etiopathogenesis, the condition has been associated with high levels of salivary ammonia. Four clinical manifestations have been described: ulcerative, non-ulcerous pseudo membranous, hyperkeratotic, and hemorrhagic uremic stomatitis. Since uremic stomatitis has been associated with sharp rise in urea levels in blood, it may be used as a clinical indicator of advanced kidney failure. Though rare, uremic stomatitis should be included in the differential diagnosis of various oral mucosa lesions in patients with a record of chronic kidney failure. This report described three uremic stomatitis cases in elderly patients with chronic kidney failure.

ABBREVIATIONS

US: Uremic Stomatitis; CKF: Chronic Kidney Failure; HE: Hematoxylin-Eosin

INTRODUCTION

Uremic stomatitis (US) is a rare disease caused by acute or chronic advanced kidney failure that affects the oral mucosa. Etiopathogenesis of US is poorly understood, though the condition has been associated with high salivary ammonia levels in kidney failure patients. It has been hypothesized that high levels of salivary urea are hydrolyzed to ammonia by urease, an enzyme active in the oral mucosa. Urease is detected mainly in dental calculus and bacterial biofilms, which explains the emergence of lesions on the regions of the mucosa that interact with teeth [1-3]. High salivary ammonia levels have also been considered responsible for the chemical rash and the development of lesions on the oral mucosa [1,3,4].

The prevalence of US is quite low, and the disease does not manifest in all kidney failure patients [5]. The condition has been associated with urea levels in blood are higher than 300 mg/mL [6,7], and therefore may be seen as a candidate clinical indicator of advanced kidney disease [8-10]. But several other factors have been implicated in the emergence of US, such as poor oral hygiene, inflammatory diseases of gingivae, caries, and smoking habit [3,5]. Interestingly, one study has discussed the possible relationship between US and hemorrhagic diathesis, a condition associated with uremia, which in turn has been held implicated in poor tissue viability, which favors the development of ulcerative lesions on the oral mucosa [4].

Clinically, US may take a few different manifestations. The condition is often characterized by the presence of painful erosive or ulcerative lesions frequently covered with a yellow-to-whitish pseudomembrane. These lesions are usually diagnosed on the jugal mucosa, gingivae, lips, palate, lip commissure, mouth floor, or tongue [1,3,8,11,12]. Four clinical manifestations of US have been described, namely ulcerative, non-ulcerous pseudomembranous, hyperkeratotic, and hemorrhagic US [2,4,8-10]. These forms of the disease may mimic other lesions of the oral mucosa, whether of infectious or autoimmune character. Some more specific oral lesions that have been included in the differential diagnosis of US include pilous leukoplakia [4,12], lichen planus [7,12], and hyperplasic candidiasis [7,12].

Importantly, US may be associated with xerostomia, dysgeusia [1,4,10,12] and burning sensation, uremic breath and malodorous of ammonia [7,13]. The discomfort caused by these lesions may interfere with feeding, to the point making it difficult to ingesteven liquid foods [1].

This report describes tree US cases in elderly patients with chronic kidney failure (CKF).

CASE PRESENTATIONS

Case 1

A 78-year-old Caucasian woman looked for assistance in the Stomatology Unit, Hospital de Clínicas de Porto Alegre (SU-HCPA), Porto Alegre, RS, Brazil with a complaint of painful lesion on the oral mucosa. Medical record included hyperthyroidism, systemic arterial hypertension, and hydronephrosis. Radical right nephrectomy had been performed 20 years before, due to oncocytoma. Three years before the first visit the patient was diagnosed with late-stage CKF and was receiving hemodialysis.

Serum tests revealed high urea (67 mg/mL) and creatinine (4.09 mg/dL) levels. Painful, extensive hemorrhagic ulceration partly covered with a crust affecting the vermillion of the lower lip and the right lip commissure was detected during extra-oral examination (Figure 1). No intra-oral lesions were observed. The diagnostic hypothesis was US based on the physical examination and results of serum tests of uremia and creatinine levels. Symptomatic treatment was prescribed including a chlorhexidine 0.12% mouthwash and medical management of kidney failure. Remission of all lesions was observed when kidney function was reestablished.

Case 2

An 82-year-old Caucasian woman diagnosed with CKF three years before was referred to the SU-HCPA with a record of congestive heart failure, embolism, and thrombosis of lower limbs. Urea (61 mg/mL) creatinine (4.02 mg/dL) levels were high. Extra-oral examination revealed ulcerations on lip commissures. Intra-oral inspection showed white plaques adhered on the lower lip mucosa, tongue dorsum, and bilateral jugal mucosa (Figure 2). Initial diagnosis hypothesis included autoimmune or infectious disease, and incisional biopsy of the lesion on the lower lip mucosa was carried out. Anatomopathological findings indicated ulceration with unspecific inflammatory process (Figure 3). Clinical findings, serum tests, and histopathological examination pointed to US as final diagnosis. Symptomatic treatment included a chlorhexidine 0.12% mouthwash and medical follow-up to stabilize kidney failure. Lesions disappeared completely when kidney function was stabilized.

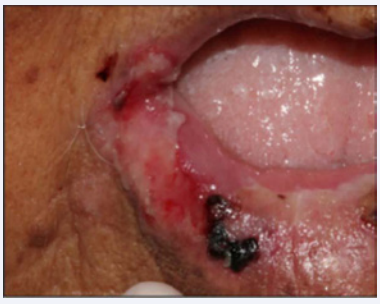

Figure 1 Irregularly outlined ulcerative lesion partly covered with pseudomembrane, affecting lower lip vermilion and right lip commissure, with hemorrhagic crust.

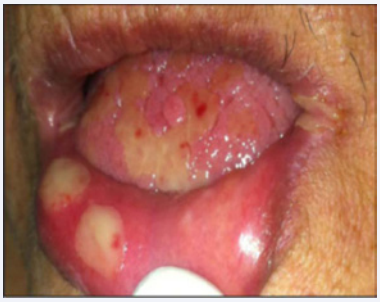

Figure 2 Yellowish adherent plaques affecting the lower lip mucosa, lip commissures, and tongue dorsum.

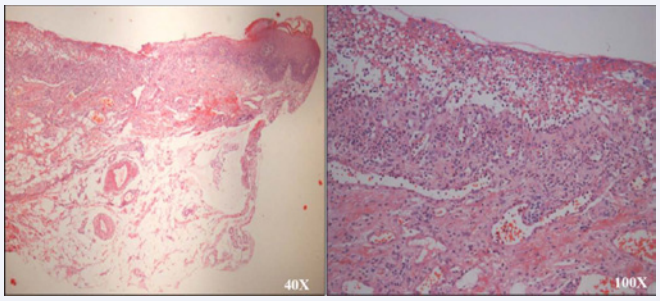

Figure 3 Microphotograph of lower lip lesion in Case 2. Presence of ulcer with fibrinoleukocyte exudate and inflammatory process. HE, 40x and 100x magnification.

Case 3

An 88-year-old Caucasian man with a record of ischemic heart disease and systemic arterial hypertension was admitted to hospital due to an abdominal abscess. During treatment as in-patient he complained of painful lesions on the oral mucosa, when an examination by the staff of SU-HCPA was requested. The patient had CKF, and tests revealed high serum levels of urea (99 mg/dL) and essentially normal creatinine concentration (1.29 mg/dL). Intraoral examination revealed ulcerative lesions covered with pseudomembranes on the palate and on the complete gingival mucosa of anterior upper teeth as well as the frenulum liguae, tongue's ventral surface, and the region of sublingual caruncles (Figure 4,5). Initial diagnosis was US, and the treatment prescribed was symptomatic, including a chlorhexidine 0.12% mouthwash, topic anesthetic before meals to facilitate eating. Stabilization of the patient's clinical condition led to complete disappearance of lesions.

DISCUSSION

Though the prevalence of oral conditions associated with high salivary urea levels in CKF patients is low, these diseases may be observed in patients presenting sharp rise in urea levels in blood [3,4,8]. However, besides US, other oral changes have been described in these patients.

According to Oyetola et al., [14], the prevalence of oral lesions in CKF patients is 97%. Lesions described include abnormal pigmentation of lip, uremic halitosis, dysgeusia, xerostomia, US, gingival hemorrhage, periodontitis, candidiasis, oral burning sensation, and ulcerations. Oral ulcerations were present in patients with glomerular filtration rates below 57.6 mL/min per 1.73 m^2 surface area. The authors suggest that the presence of oral lesions in CKF patients may be a predictor of the severity of kidney disease.

Moreover, hyperparathyroidism induces the generation of intraosseous lesions that mimic central giant cell tumor, in addition to affecting normal bone formation (renal osteodystrophy). If kidney disease starts in childhood, delayed tooth eruption may be observed. Bone remodeling to heal dental alveolus after tooth extraction may also be abnormal. Presence of calculus, tooth abrasion, low prevalence of caries, and enamel hypoplasia have been described [3,8,10,12,13,15-18]. Chung et al. [15], observed that patients with CKF and diabetes mellitus had

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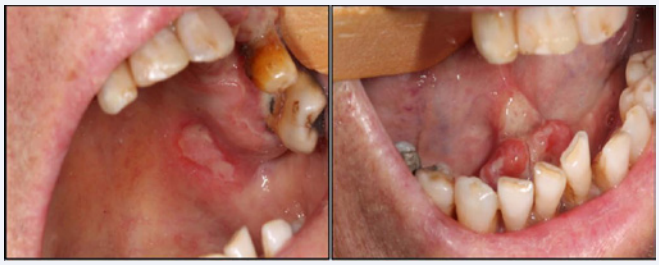

Figure 4 Ulcerative lesions affecting the hard palate mucosa, left maxillary gingiva, mouth floor on the region of sublingual caruncles, and frenulum linguae.

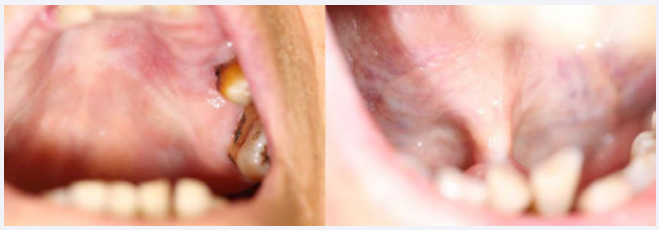

Figure 5 : Case 3 after the total remission of the lesions.

higher risk of oral complications compared with subjects without diabetes. No patient in the present case report had diabetes.

The evaluation of 458 patients in late kidney failure stage and undergoing hemodialysis showed that the most common lesions were stomatitis, xerostomia, gingivitis, and uremic halitosis, but those conditions were observed in only 13.1% of cases [19].

It has been suggested that US emerges when urea levels in blood are higher than 300 mg/mL. However, oral changes have been observed in patients with urea levels below 200 mg/mL [6,7]. Urea levels were 67 mg/mL, 61 mg/mL, and 99 mg/dL in the three cases included in the present report, respectively. Creatinine levels between 0.6 mg/dL and 1.3 mg/dL are considered normal, while values over 1.5 mg/dL or 1.6 mg/dL indicate kidney disease in most cases. High creatinine levels were observed in two of the cases described (4.09 mg/dL and 4.02 mg/dL), and only patient 3 had creatinine level near the top acceptable threshold (1.3 mg/dL).

Etiopathogenesis of US is poorly known, but the condition has been associated with urea degradation by urease in the oral cavity, manifesting a few days into the emergence of severe kidney disease, when urea levels are in excess of 30 mmol/L [3,4,7,8,11,15].

The numerous different characteristics of US make it more difficult to reach a final diagnosis. The three patients included in this report complained of pain and spontaneous hemorrhage, whose cause was platelet dysfunction caused by bacteria, anticoagulants prescribed, and capillary fragility [4,8,12]. Also, US manifests as multiple lesions in sites where saliva accumulates and therefore remains in contact with tissues for longer periods of time. Therefore, the lesions on the tongue's ventral surface, mouth floor, lips, and gingivae are often observed [1-4,8,11,12]. Importantly, since pseudomembranes in US may detach from lesions and subsequently accumulate on the oropharynx, the patient may experience difficulty to breathe, with risk of death [11]. In this case report, patients 1 and 3 presented the ulcerative manifestation of US, while patient 2 had the pseudomembranous as well as ulcerative forms of the condition.

Differential diagnosis should include any disease that induces the emergence of multiple lesions on the oral mucosa, such as candidiasis and lichen planus [18]. Vesicular bullous diseases and vitamin deficiency have also been included in the differential diagnosis of US [8], as well as pilous leukoplakia, carcinomas, and other acquired keratoses [4,18].

Management of US includes a few important measures, such as plaque control, removal of dental calculus to reduce the amount of urease and ammonia in the oral cavity, and the use of mouthwash containing hydrogen peroxide or sodium perborate. Aqueous chlorhexidine solutions are potent topical bactericides, inhibiting ammonia production by reducing bacterial counts in the oral cavity and preventing secondary contamination of ulcerations, which is a desired outcome in the healing of lesions. In addition, the pain caused by ulcerations in the oral cavity should be controlled with analgesics and topical anesthetics. However, total remission of lesions will take place only after serum urea levels return to normal, with the ensuing stabilization of the patient's clinical condition [1-4,7,8,11,20].

Once normal serum levels of urea and creatinine have been reached, a new oral examination has to be carried out to not only confirm the remission of US, but also to identify any other disease still present that went by undiagnosed or overlaps US. If any lingering lesion is observed, a biopsy should be conducted together with the appropriate treatment of the condition.

Though rare, US should be included in the differential diagnosis of multiple lesions on the oral mucosa in patients with CKF. In addition, the oral conditions of these patients may be used as indicators of how stable their clinical status is. In patients with no diagnosis of CKF, renal function tests like urea and creatinine serum levels may be useful to rule out or not US as suspected condition against other oral diseases that manifest as multiple lesions. Since stomatological complications are common and the presence of oral lesions may indicate that the clinical condition of kidney failure patients has actually worsened, a dental surgeon should be called to take part in the transdisciplinary team that usually treats CKF patients.

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