CASE REPORT

Ulcerative Uremic Stomatitis - Review of the Literature and A Rare Case Report

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Abstract:

Uremic Stomatitis (US) represents a comparatively uncommon intraoral complication seen, mostly, in cases of end-stage renal disease or undiagnosed or untreated chronic renal failure. Its frequency has diminished due to the advent of renal dialysis. Clinically uremic stomatitis is characterized by the presence of painful plaques and crusts that are usually distributed on the buccal and labial mucosa, dorsal or ventral surface of the tongue, gingiva, and floor of the mouth. Ultimate treatment consists of improvement of blood urea concentration and underlying renal failure is supported by enhancement of oral hygiene with antiseptic mouthwashes and antimicrobial/antifungal agents, if necessary. Here we report a rare case of ulcerative type of uremic stomatitis occurring in a patient of chronic renal failure due to sudden relapse of uremia and reviewed the possible pathophysiology of oral symptoms of chronic renal failure.

Keywords: Ulcerative uremic stomatitis, Chronic renal failure

Introduction:

It is a well-known verity that many systemic diseases are manifest in the oral cavity. Irrespective of the organ system involved, changes frequently occur in the oral cavity reflecting disease elsewhere in the body. So it is accurately said that oral cavity is the mirror of the general health and ideal management of such manifestations is by treating the underlying disease first and followed by providing local therapy, if it is necessary. One such systemic disease which dentist might encounter in his practice is Chronic Renal Failure (CRF) or End Stage Renal Disease (ESRD). Uremic Stomatitis (US) occurs in the oral cavity as a complication of uremia in patients with undiagnosed or untreated ESRD.

Kidneys are responsible for a wide range of important functions. They help to maintain a stable composition of the fluid-bathing cells by selective retention of water, electrolytes, and other solutes and they play a role in the renin-angiotensin system, the stimulation of red blood cell production and the metabolism, elimination of both drugs and hormones. The progressive loss of kidney function was caused by various pathologic disorders results in a clinical syndrome known as uremia. Uremia is responsible for the build-up of retained toxins and development of numerous problems disturbing virtually every organ system, in which failure to adequately perform necessary functions leads to the withholding of nitrogenous substances, accompanied by an elevation in blood urea, nitrogen, and non protein nitrogen [1-3]. So it becomes necessary to employ extra-renal blood-filtering techniques, mainly, hemodialysis [1, 4].

CRF affects a range of tissues and systems, leading to complications of nervous, cardiovascular, respiratory, endocrinological, hematopoietic, gastrointestinal, urological, skin, mucosa and craniofacial complex [3,4,5].

After the advent of renal dialysis, the incidence of severe uremia in CRF has decreased, hence a relatively small number of cases have reported in the literature [6]. A broad range of oral symptoms are reported in ESRD patients, including gingivitis, dry mouth, ammonia-like odour resulting from a high urea content, mucosal lesions, tooth mobility, malocclusion, and an increased risk of dental erosion because of frequent regurgitation [7,8]. In severe conditions, uremic stomatitis may be prominent oral lesion, occurs due to uremia, the accumulation of nitrogenous waste products in the blood may be caused by either acute or chronic renal failure. US was first mentioned by Lancereaux in 1887 and described by Barie in 1892 as a complication of uremia. Here we report a clinically diagnosed rare case of ulcerative uremic stomatitis in a patient with CRF, who also had concomitant diabetes mellitus [8].

Case Report:

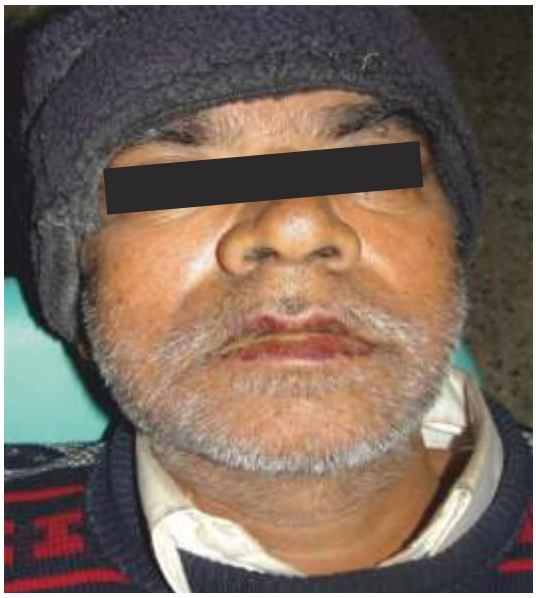
A 46 year old male patient reported to the Department of Oral Medicine and Radiology, with the complaint of inability to eat, difficulty in speaking due to peeling of the skin in the mouth with associated burning sensation (70% on Visual Analogue Scale (VAS) on taking hot and spicy food since one month. There were other symptoms such as xerostomia, nausea, vomiting, enlarged tongue, alteration in the taste, and foul odour from the mouth since 20 days.

Initially patient noticed adherent white lesions of the oral mucosa one month back in right and left cheek mucosa, later slowly spread to other parts of the mouth and lips, and after few days it started peeling off from the underlying tissues without any noticeable resolution. There was burning which was continuous and present all over the mouth. It was initiated and precipitated by taking hot and spicy food and relieved by sipping of cold water. In addition patient was unable to maintain his oral hygiene due to pain and bleeding from gums and other oral tissues during cleansing of the mouth. He had difficulty in speaking, swallowing due to pain, dryness of mouth and increase in size of the tongue.

The patient was a business man, married with three healthy children. His medical history revealed that he developed CRF 3 years earlier due to nonspecific nephritis and associated diabetes mellitus. At that time the patient was started with hemodialysis thrice weekly and renal transplantation was planned. But due to financial constraints he could not undergo for kidney replacement and therefore continued with hemodialysis and oral antidiabetic drugs. Subsequently patient developed hepatitis B infection as a consequence of hemodialysis and was treated for the same for three months.

On general physical examination, patient was moderately built and moderately nourished, dehydrated, drained, catatonic and slightly disoriented with slurred speech. Extra-oral examination revealed obvious signs of renal disease such as pallor, puffy and dull looking face, uremic oral malodor and crusting of lips with bleeding. Bilateral submandibular, submental lymph nodes were enlarged and tender on palpation (Fig.1 and 2).

Intra-oral examination revealed loosely adherent extensive creamy white pseudo membranes separating from the underlying mucosa leaving the erythematous base on the buccal and labial mucosae, palate, tongue, gingiva and floor of the mouth, bleeding was elicited from the crustings on stretching of the lips. On palpation the plaques were easily scrapable leaving erythematous base and mucosa was tender (Fig.3 and 4).



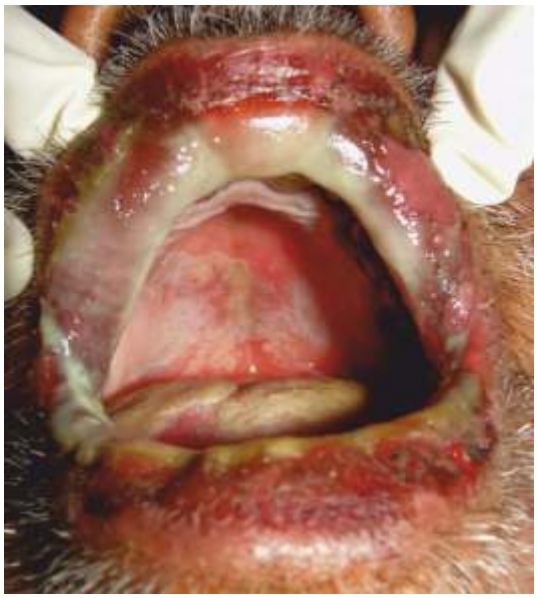
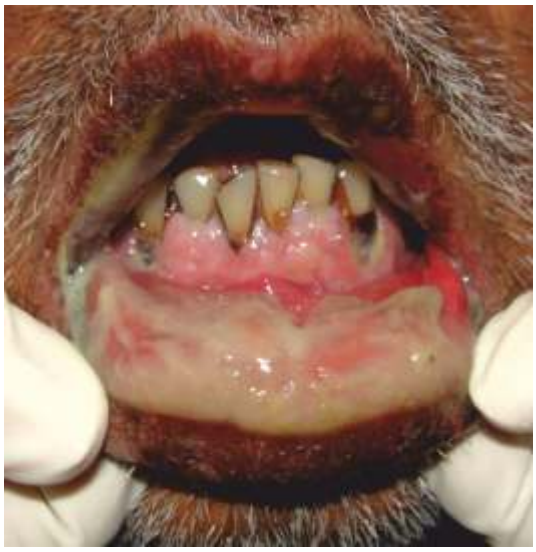


Fig. 1 and 2: Extraoral Photograph Showing Puffiness of Face and Crusting of Lips with Bleeding



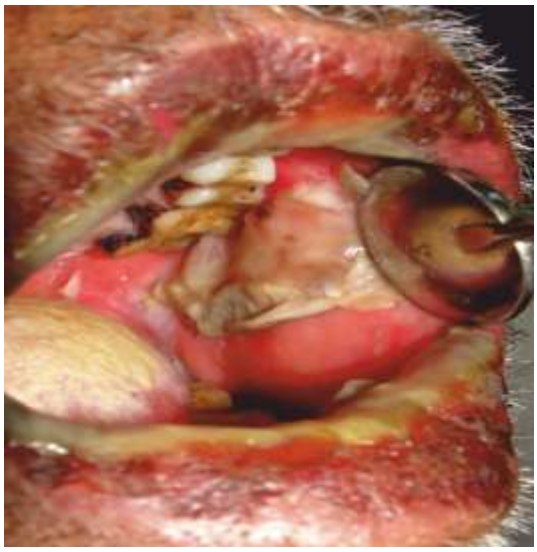


Fig. 3 and 4: Intra Oral Photographs Showing Pseudo Membranes with Underlying Ulcerations of Oral Mucosa

Hematological and biochemical profiles showed increased levels of blood urea-295mg/dl, serum creatinine- 5.8 mgs/dl and Alkaline phospatase-170 Ul/l, blood glucose levels FBS-150 mgs% & PPBS-304 mgs% and hemoglobin-10 gms%.

On the basis of history, extensive nature of the oral lesions, other clinical features and hematological and biochemical profile of the patient, the ulcerative uremic stomatitis was made, however, chronic pseudo membranous candidiasis was considered in the differential diagnosis, in view of the fact that patient was also suffering from diabetes mellitus.

Uremic stomatitis is often a clinical finding in cases of advanced stages of renal failure. We did not subject the patient to histopathological investigations for oral lesions, since the histopathological signs of uremic stomatitis are not specific and pathognomonic and the role of histopathology is only to exclude other pathologic conditions. The definitive diagnosis was made by combining history, clinical and hematological findings.

Oral lesions secondary to uremia does not require specific treatment and there is no need to modify the relevant systemic treatment and furthermore intraoral lesions are resistant to local treatment as long as blood concentration of urea remains high, hence in order to assist lesion healing, 10% hydrogen peroxide gargles (1:1 in water) 4 times a day was recommended and patient was referred back to the nephrology unit for control of blood urea, creatinine and glucose levels and for continued review of his renal disease.

Discussion:

CRF is a major health care problem throughout the world, the incidence increasing with age; men are more often affected than women. The most frequent causes of CRF are Diabetes mellitus (DM), hypertension (HTN), glomerulonephritis and renal polycystosis [9]. The diabetic nephropathy is the most frequent cause accounting to about 40-60%, of all patients with CRF that progressed to ESRD, as we see in our case. Arterial hypertension, which affects 15-30%; and glomerulonephritis, in less than 10% cases, only 2-3% of all CRF patients present renal polycystosis [10, 11].

The clinical signs and symptoms are related to the type of underlying renal or systemic problem, and to the rate of impairment of renal function. A frequent observation in CRF is anemia secondary to deficient erythropoiesis [12]. Hemostasis is altered as a result of diminished platelet adhesion, together with increase in prostacyclin activity, lesser availability of platelet factor3, increased capillary fragility and due to effect of anticoagulants used in hemodialysis leading to gingival bleeding, petechiae and ecchymosis. These patients also suffer dyspnea and gastrointestinal alterations such as anorexia, nausea and vomiting associated to the uremia, as reported by our patient [12,14].

About 90% of all patients with CRF suffer oral signs and symptoms [14] affecting both the bone and soft tissue structures [12]. Fetid odor (secondary to uremia) and metallic taste resulting from the increased concentration of urea in saliva and its posterior transformation into ammonium and subsequent breakdown to ammonia and carbon dioxide by bacterial ureases and secondary to xerostomia and poor maintenance of oral hygiene. The use of medications, diminished number of taste buds and changes in the salivary flow and composition are also possible causes [11, 13, 14].

Among oral mucosal lesions gingivitis and periondontitis are the common diseases because of chronicity of the disease, poor maintainace of oral hygiene. But uremic stomatitis is a uncommon clinical observation associated with severe cases due to uremia [12,14]. Previous studies have reported higher incidence of US in CRF patients with diabetes compared to non-diabetic CRF patients, similarly as we see in our case.

As many as four types of US have been described: erythemo-pultaceous, ulcerative [11, 12, 14, 15], hemorrhagic and hyperkeratotic. The lesions are very painful and most often appear on the ventral surface of the tongue and on the anterior mucosal surfaces. These lesions are resistant to treatment

as long as blood urea levels remain high and heal spontaneously within 2-3 weeks once the underlying renal disorder is resolved [14,15,16].

The incidence of US is very low, particularly if the disease process progresses gradually over a period of years and occurs usually in advanced renal failure. However, an acute necrotic pseudomembranous gingivostomatitis is occasionally observed in the patients who rapidly develop high blood urea nitrogen levels [8].

The exact pathophysiology of US remains unidentified. Most authors believe that oral lesions develop due to the irritation and chemical injury of mucosa by ammonia or ammonium compounds formed by the hydrolysis of urea in saliva by urease. According to this theory, when the intraoral concentration of urea exceeds 30 mmol/L (healthy individuals mixed stimulated saliva contains 2 to 6 mmol/L urea), the enzyme urease found in dental calculus and oral bacteria hydrolyzes salivary urea to free ammonia [17]. Poor oral hygiene, chronic gingivitis and periodontal disease, decayed teeth, xerostomia, and smoking are believed to further aggravate the reaction pattern [17,18, 19]. The fact that main lesions develop in sites that mucosa comes in contact with teeth and not underneath artificial dentures supports this theory. Bliss in 1937 experimentally proved that uremic lesions can be developed in mucosal sites by direct effect of ammonium hydroxide in association with calculus. Moreover, some of the uremic toxins may act directly against epithelial cells by altering cell membrane transport of sodium, potassium, or other electrolytes [20,21]. However, the description of similar forms of stomatitis in nephritis patients without uremia and the low incidence of uremic stomatitis in uremic patients raises the need for further investigation. The low incidence of uremic stomatitis in patients with CRF can be attributed to the advent of renal dialysis. A genetic substrate is also possible, since 40% of the population, according to review articles, shows a genetic tendency for oral ulcerative diseases [9, 18, 22].

Recent studies for CRF and toxic effects of uremic retention solutes support a more complicated mechanism for the development of uremic stomatitis. Abnormalities of the immune system involving both cellular and humoral immunity seem to play a crucial role [23,24]. Evidence suggests that uremic toxins like beta2-microglobulin, parathyroid hormone (PTH), advanced glycosylation products, and DIP I accelerate apoptosis of lymphocytes, monocytes, and polymorphonuclear leukocytes (PMNs) [27] or inhibit PMNs' metabolism and functions such as phagocytosis and chemotaxis [21, 23, 26-28]. Moreover, advanced glycosylation end products may cause an inflammatory reaction consisting of monocytes by the induction of interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), and interferon gamma (IFN-γ) [29].

Xerostomia (dry mouth), is also a common symptom as a result of the restriction in fluid intake, the side effects of drugs (fundamentally antihypertensive agents), possible salivary gland alteration, and oral breathing secondary to lung perfusion problems [11, 13 & 14] and it is a most frequent complaint in patients having both diabetes mellitus and CRF due to increased thirst and urination as a consequence of osmotic diuresis caused by sustained hyperglycemia. Diuresis results in loss of glucose, free water, and electrolytes in urine [29].

In our case we noted that patient had slurred speech and disorientation. Altered speech could be due to two reasons as uremia can affect the central nervous system (CNS) causing slurred speech and because of thick tongue coating and

disorientation is again secondary to CNS involvement associated with the development of metabolic acidosis and hyperkalemia [13].

Oral manifestations persist usually for 2 to 3 weeks and may heal spontaneously with resolution of underlying uremia and lowering of blood urea nitrogen (BUN) levels. Increase of fluid intake encourages salivation. Scaling of the teeth may be carried out to remove calculus deposits, which may contain urease. Hydrogen peroxide mouth rinses can contribute to the elimination of anaerobic bacteria producing ammonia, to neutralize ammonia and the condition of acidosis [30]. Additional treatment may include vitamin supplements, antiseptic mouthwashes and antimicrobial/antifungal agents against microbial or fungal infections [17, 30].

Conclusion:

The consequences of uremia and its complications in the oral cavity are higher in uncontrolled CRF patients especially in patients with advanced age, immune dysfunction and other comorbidities such as DM, HTN etc., These lesions interfere with routine oral functions and compromise food intake, and this might further make the patient more sick. Oral lesions secondary to uremia can be dramatically treated just by improving the blood urea levels. Further periodic dental follow-up and meticulous treatment of oral diseases and oral hygiene measures help the patient to maintain diet and intern good health. For this multidisciplinary approach by medical and dental professionals are desirable in order to render best possible treatment.

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