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CASE STUDY

# Uremic stomatitis mimicking oral squamous cell carcinoma associated with local and systemic factor

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**ABSTRACT**

Uremic stomatitis is an oral manifestation of chronic kidney disease due to increased levels of urea in the blood circulation. Patients often complain sore lesions accompanied by ammonia breath. Clinical manifestations of uremic stomatitis are not only influenced by high levels of urea in the blood and saliva but also related to local factors, the oral anatomy and parafunction habits. This study aimed to present a case report of clinical features of uremic stomatitis that mimic oral squamous cell carcinoma. A 51-year-old woman was referred from the Department of Internal Medicine to the Department of Oral Medicine at Hasan Sadikin Hospital, Bandung. The patient complained of pain in the tongue, and it hurt when swallowing. The clinical manifestation showed an ulcerated lesion on the right lateral of the tongue and a slightly raised hyperkeratotic area on the floor of the mouth. Exfoliative cheilitis occurred on the upper and lower lips. The treatment used 0.12% chlorhexidine digluconate mouthwash three times a day and followed by applying a thin layer of vaseline for the exfoliative cheilitis on the upper and lower lips. The patient was provided with instructions and education in relation to maintaining oral and tongue hygiene. The patient was scheduled for a follow-up check-up the following day and fourteen days later. The patient's oral lesion and masticatory function improved. Local factors, including macroglossia, bad habits, and systemic factors have effect on the clinical manifestation of uremic stomatitis. Clinicians must be able to carry out examinations, establish diagnosis and appropriate management to ensure the patient receives the most appropriate treatment.

**Keywords:** chlorhexidine; chronic renal failure; uremic stomatitis

## INTRODUCTION

Uremic stomatitis is a disorder of the oral mucosa associated with impaired kidney function and accumulation of urea. Uremic stomatitis can be characterized by increased levels of urea and other nitrogenous wastes in the bloodstream of patients with chronic kidney failure. Patients usually complain of pain in the oral cavity, accompanied by loss of appetite and weight loss. Uremic stomatitis is a rare case of the oral manifestation in patient with renal disease.[1–3]

Uremic stomatitis is divided into several types according to the clinical manifestations. These are ulcerative, pseudomembranous/erythematous, hemorrhagic, and hyperkeratotic uremic stomatitis. Ulcerative lesions are common features that often occur with clinical picture showing intense pain in the tongue, cheeks, lips and palate with irregular borders, and the presence of a thick, yellowish layer on the tongue. Patients also have a dry mouth, a metallic taste, a burning sensation in the mouth, and erythema of the tongue and palatal mucosa. Pseudomembranous lesions are characterized by the formation of a thick, sticky, and gray pseudomembrane that is accompanied by pain. Hemorrhagic uremic stomatitis is characterized by bleeding from the gingiva or other areas of the oral mucosa. Lesions of the keratotic type are rarely present with a clinical picture of a hyperkeratotic layer and are usually found in conjunction with the ulcerated type.[1]

Oral squamous cell carcinoma (OSCC) is one of the most common oral cancers in the oral cavity. This disease can be a persistent ulcer and asymptomatic. The lesions are shallow, with

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a reddish base, well defined and raised. Several studies have shown that prolonged inflammation may influence the development of OSCC. Various factors can cause chronic inflammation. Continuous mechanical trauma to the soft tissues of the oral cavity can induce OSCC, especially if the patient has genetic disorder and other risk factors, such as virus infection, lack of nutrition, and bad habit.[1,4–7]

Uremic stomatitis may mimic the clinical features of OSCC. Local and systemic factors, such as anatomy of the tongue, dental calculus and the uremic inside the blood vessels in a patient can be predisposing factors that exacerbate the occurrence of the disease. The purpose of this case report is to differentiate uremic stomatitis from OSCC and its appropriate management. Local and systemic factors in patients can aggravate this disease.

## METHODS

A 51-years-old woman was referred to the Oral Medicine Department of Hasan Sadikin Hospital from the Department of Internal Medicine. The patient complained of pain under the tongue and on the right side of the tongue accompanied by pain when swallowing for the last 4 days, resulting in difficulty to speak. The patient had no history of recurrent aphthous and never had this condition before. She also had no history of trauma to the tongue.

The lesion under the tongue was bleeding and sore. The patient had a history of systemic disease including stage IV chronic kidney failure, type 2 diabetes mellitus with complications of diabetic kidney disease (DKD). Currently the patient received folic acid, CaCO3, sodium bicarbonate, metoclopramide, ramipril, ceftriaxone, telmisartan, bisoprolol and omeprazole.

Extra oral examination showed that the patient was weak and had anemic conjunctiva and nonicteric sclera. An intraoral examination found 2 papules whose color was similar to the surrounding tissue. They were round, sessile, with a diameter of 4-5 mm, and the patient had no pain on the left buccal mucosa. On the lateral part of the right tongue, yellowish plaque was found, surrounded by a white hyperkeratotic layer. It could not be scrapped, with a size of 2 x 2 mm - 15 x 5 mm, teeth 43-47, was accompanied by pain, and tended to bleed. An examination of the floor of the mouth showed that multiple ulcers appeared along the surface of the floor of the mouth. These ulcers were covered with grayish, whitish, to blackish pseudomembranes, resembling impressions of the teeth, accompanied by erythema and pain, with induration and risk of bleeding. The blood tests showed an urea level of 83.5 mg/dL (H), which was four times the normal level (21-43 mg/dL), and a creatinine level of 5.39 mg/dL (H), about five times the normal level (0.56-1.11 mg/dL). The patient was diagnosed with uremic stomatitis with a differential diagnosis of OSCC and necrotizing sialometaplasia. Initially, the patient was instructed to maintain oral hygiene by brushing her teeth and tongue at least twice a day, in the morning and evening before going to bed. The patient was then given instruction to gargle with 10 mL of 0.12% chlorhexidine digluconate 3 times a day.

**Table 1.** Patient laboratory examination results

| Examination | November 08 2022 | November 09 2022 | November 10 2022 | November 11 2022 | November 27 2022 |
|---|---|---|---|---|---|
| Hemoglobin | 5.9 g/dL (LL) | 6.9 g/dL (LL) | 7.7 g/dL (LL) | 7.2 g/dL (LL) | - |
| Haematocrit | 16.1% (LL) | 18.4% (LL) | 21.0% (L) | 20.0% (L) | - |
| Erythrocyte | 2.14x10^6/uL (L) | 2.45x10^6 /uL (L) | 2.70x10^6 /uL (L) | 2.56x10^6 /uL (L) | - |
| MCV | 75.2 fL (L) | 75.1 fL (L) | 77.0 fL (L) | 78.1 fL (L) | - |
| MCHC | 36.6% (H) | 37.5% (H) | 36.7% (H) | 36.0% (H) | - |
| Ureum | 83.5 mg/dL (H) | - | 85.6 mg/dL (H) | - | 197.7 mg/dL (H) |
| Creatinine | 5.39 mg/dL (H) | - | 5.54 mg/dL(H) | - | 7.93 mg/dL (H) |

(A) (B) (C)

**Figure 1.** Lateral view of the tongue (A) first visit (a yellowish plaque was found, surrounded by a white hyperkeratotic layer on the lateral part of the right tongue) (B) first control (the lession were decreased) (C) second control (the lession were improved significanly)

(A) (B) (C)

**Figure 2.** The Clinical Manifestation of Floor of the Mouth (A) first visit (the floor of the mouth was raised with multiple ulcers covered with gray-white to blackish pseudomembranes) (B) first control (the lession were decreased) (C) second control (the lession were improved significanly)

The patient was re-examined at the second visit (the first follow-up check-up), or two days after the patient's first visit. The condition of the patient improved, and the lesion decreased. Currently the patient could consume more food, and no pain in the oral cavity was reported. There was improvement in the lesions on the lateral side of the patient's tongue (Figure 1 B) and on the floor of the patient's mouth (Figure 2 B). The patient explained that the medicine was taken as directed. The patient also maintained oral hygiene by brushing her teeth and tongue twice a day. However, the results of blood tests still showed high amount of urea and creatinine, at 85.6 mg/dL and 5.54 mg/dL, respectively.

The second follow-up check-up was 14 days after the first visit (Figures 1 C and 2 C). This time, the condition of the patient's oral cavity improved. She could consume more food and chew solid foods. The patient explained that the mouthwash was used 3 times a day, and she continued to apply vaseline 3 times a day on the upper and lower lips. However, the patient complained that the discomfort on tongue did not go away in the past 2 weeks. The clinical sign showed that the lesion on the lateral side of the tongue improved, but white plaques remained. The patient was instructed to continue cleaning the oral cavity by brushing the teeth and tongue at least twice a day, in the morning and evening before going to bed, and rinsing the mouth with 10 mL of 0.12% chlorhexidine digluconate 3 times a day. The patient was also required to continue to apply a thin layer of vaseline album at least 3 times a day on the upper and lower lips. Vaseline can protect the skin of lips by preventing moisture loss from the lips. She was also asked to continue drinking water little by little but frequently, accompanied

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by regular consumption of fruits and vegetables every day.

## DISCUSSION

Uremic stomatitis is an oral manifestation due to an imbalance level of urea in patient with renal disease. This disease is caused by a malfunction of the kidneys. Kidneys filter blood and regulate the various components that must be maintained and disposed of in the body. Disturbed kidney function may cause an imbalance of the blood filtration system and have a negative impact on the body.[1]

The incidence of uremic stomatitis is rare. Uremic stomatitis is an uncommon intraoral manifestation of the chronic kidney disease. This disease is usually found in undiagnosed or untreated end-stage kidney disease or chronic kidney disease. The etiopathogenesis of uremic stomatitis is not fully understood, but this may be caused by raised levels of ammonia. Ammonia is formed by bacterial urease that converts urea in saliva, which can affect the oral mucosa.[8,9]

The patient in this study was referred from the Department of Internal Medicine with complaints of pain under the tongue and on the right side of the tongue accompanied by pain when swallowing for the past 4 days. The patient had a history of chronic kidney failure or stage 5 chronic kidney disease (CKD). Chronic kidney failure has several stages of change. These are changes in signaling pathways in epithelial cells, increased induction of oxidative stress in mitochondria, changes in autophagy levels, and changes in kidney inflammation status, which can lead to vascular dysfunction, which affects blood vessels.[10–12]

Patients with renal impairment experiences hemorrhagic diathesis, a pathological condition caused by abnormalities in hemostatic function due to vascular disorders, deficiency or dysfunction of platelets and reduced coagulation factors. Hemorrhagic diathesis causes ulceration and pseudomembranes, resulting in a decrease in tissue viability and posing a risk of bacterial infection.[13]

The patient complained of discomfort in the floor of the mouth. The floor of the mouth raised, and multiple ulcers covered with grayish, whitish to blackish pseudomembranes appeared along the surface of the floor of the mouth. They resembled impressions of the teeth. This condition was accompanied by erythema, pain, induration, and bleeding. The patient's complaints resemble those of oral squamous cell carcinoma (OSCC). Symptoms of OSCC include pain, discomfort, swelling, dysphagia, and sore throat. OSCC has specific clinical manifestation. It appears as a white or reddish mixed proliferative lesion with raised margins and an ulcerated surface with yellowish-grey pseudomembranes, especially on the lateral and ventral sides of the tongue. OSCC also shows other clinical characteristics, such as exophytic (grows outward) or endophytic (grows inward), and leukoplakia or erythroleukoplakia on the surface. Additionally, the physician will feel the hard surface of the lesion during palpation.[14–17]

Lesions that mimic OSCC can be caused by a variety of local factors, such as dental, prosthetic and functional factors. Dental factors include dental malposition, diastema, sharp teeth, and restorations. Prosthetic factors include dentures that are rough or sharp, dental retainers, excessive tyrant wings, impaired retention, and denture stability. Functional factors include tongue interposition, sucking, biting and parafunctional habits.[4] Anamnesis showed that the patient had a habit of sucking her tongue and pressing it to the floor of the mouth. The patient also had enlarged tongue, or macroglossia, as seen from the clinical aspect of the tongue which showed that the size of the tongue was larger than normal. Macroglossia is a condition in which the tongue enlarges and protrudes beyond the dental arch and alveolar bone in the resting position. Analysis of the pathophysiology shows that macroglossia can be caused by excessive tissue growth or tissue infiltration. Macroglossia can affect oral cavity and the body as a whole. It can also cause edema or swelling in the area around the patient's tongue. Enlarged tongue can also cause systemic disorders, including airway obstruction. Macroglossia can lead to airway obstruction, and thus clinicians need to ensure that the patient's

**Table 2.** Difference between OSCC and uremic stomatitis[2,20]

| | OSCC | Uremic stomatitis |
|---|---|---|
| Etiology | Tobacco, alcohol, infection, sun exposure | Urea levels above normal |
| Incidence | Two to 3 percent, about 36,000 new cases/year | Rare among patient with renal disease |
| Clinical Description | Induration lesions, exophytic, endophytic, in the form of white or red patches | Sore superficial ulceration covered with necrotic pseudomembrane, Multiple painful white hyperkeratotic plaques, Ammonia-like bad breath, Thick and numb tongue, Diffuse erythematous covered with thick gray pseudomembrane |
| Histological Picture | Proliferation of squamous epithelial cells, atypia with deformity rete peg processus, abnormal formation of keratin, increase basaloid cell proliferation, cell arrangement becomes irregular, and forms tumor nests (daughter tumors) that infiltrate into the surrounding tissue | There is no specific pathognomonic features, epithelial acantolysis, hyperparakeratinization, basal cell hyperplasia are present. |

airway is not compromised by macroglossia. Macroglossia can be managed both surgically and non-surgically.

Non-surgical management includes administration of corticosteroid injections and application of bite blocks to avoid trauma to the patient's oral cavity.[18,19] For this case report, we only educated the patient to change her habit by not sucking the tongue and pressing it to the floor of the mouth.

Patients with chronic kidney failure must receive appropriate dental and oral care. In general, patients often have various complaints about the condition of their oral cavity. The patient in this case complained of pain under the tongue and on the right side of the tongue accompanied by pain when swallowing for the past 4 days. In this case study, 0.12% chlorhexidine gluconate mouthwash was advised 3 times a day. This mouthwash functions as an antiseptic with broad-spectrum antibacterial properties that are effective against bacteria and fungi. Chlorhexidine digluconate has bactericidal properties. This will inhibit the production of ammonia by reducing the number of bacteria in the oral cavity.[21] The patient also had exfoliative and dry upper and lower lips. This condition can relate to the dehydration and lack of the salivary flow. Dehydration of the stratum corneum is common in patients with chronic kidney disease. It can manifest as dryness on the skin. Furthermore, the decreased salivary flow may be due to direct uremic involvement of salivary glands.[2,22,23] The patient in our study was treated with vaseline album, a covering agent that functions to protect the outer skin. It protects the skin from the effects of weather and sun exposure and protects the inner skin by preventing moisture loss, keeping it moisturized. However, this material is not readily absorbed by the skin. The adverse effect of vaseline album is rare when used as topical preparation.[24] A previous study showed that application of vaseline album can heal exfoliative and dry lips of patients with vitamin D deficiency.[25] In our study, the patient was cooperative with positive attitude during the treatment. Lesions on the oral mucosa showed improvement in each follow-up check-up. The patient was declared cured in the second follow-up check-up, or 14 days after the first visit. The oral lesions found in the first visit improved, and the patient no longer had complaints. The patient could chew and swallow food comfortably without pain.

## CONCLUSION

Uremic stomatitis is an oral manifestation in patients with chronic renal failure that can mimic like oral squamous cell carcinoma (OSCC). Local and systemic factors influence the occurrence of uremic stomatitis lesions in patients. Therefore, clinicians

must be able to carry out examinations, establish a diagnosis and appropriate management, so patients receive appropriate treatment.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest with the data contained in the manuscript.

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