Pharmacotherapy And Behavioural-Modifying Lifestyle For Oral Lesions Management in Multimorbid Patient Post-Pyelolithotomy: A Case Report

Selviana Rizky Pramitha,**, Arissa Izzati***, Maharani Laillyza Apriasari*, Amy Nindia Carabelly****, Dewi Puspitasari*****

*Department of Oral Medicine, Faculty of Dentistry, ULM
**Oral Medicine Specialist, Siaga Surgical Hospital, Banjarmasin
***Sungai Andai Community Health Center, Banjarmasin
****Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, ULM
*****Department of Dental Material, Faculty of Dentistry, ULM

***Correspondence*: selviana.pramitha@ulm.ac.id**

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ABSTRACT

Background: Chronic kidney disease (CKD), a recognized complication of pyelolithotomy along with multimorbidity in the elderly population, presents a higher incidence of oral lesions. Further damage to the renal vasculature interchangeably affects oral-systemic conditions. We report oral lesions management in MCC patient post-pyelolithotomy for better outcomes.
Case: A 65-year-old male patient complained of painful ulceration on the atrophic dorsum of the tongue for two weeks with a fair oral hygiene score. The condition had been managed with various topical agents alternately with no improvement. There was a history of pyelolithotomy and emergency room admission. Laboratory examination presented type 2 diabetes mellitus, stage 3B kidney disease and anemia of chronic disease. A diagnosis of ulcerative-type uremic stomatitis with atrophic glossitis in multimorbid patient was obtained. Pharmacotherapy of oral lesion including aloe vera extract mouthwash and povidone-iodine mouthwash showed significant clinical improvement on the following day. Behavioural-modifying lifestyle involved physical activity, healthy eating, and adherence to treatment (oral hygiene maintenance and regular dental appointment). Systemic conditions were managed by multidiscipline treatment with Internal Medicine.
Conclusion: Pharmacotherapy and behavioral modifying lifestyle may support a better prognosis for oral manifestation in multimorbid patient post pyelolithotomy.

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INTRODUCTION

Non-communicable diseases (NCDs), also known as chronic diseases, are of increasing concern for society and national governments, as well as globally due to their high mortality rate. These are medical conditions that are associated with long durations and slow progress often identified in the elderly population.[1,2] One in three adults lives with more than one chronic disease, or multimorbidty, and accrues a disproportionate health and cost burden. As the number of chronic diseases increases, the proportion of people with multimorbidity has also increased. The prevalence of multimorbidity ranges from 16% to 81% of adults over 65 years old with the highest proportion observed with chronic kidney disease (CKD) as a secondary condition, and diabetes was more likely as the primary condition.[1,3]

One of the risk factors that may develop and contribute to multimotbidity is kidney stones or nephrolithiasis.[4] Kidney stones are the most common urinary tract problems after infection and prostate disease with a prevalence of 12% of men at the age 20-40 years than women (6%). Active stone removal is required when stone is larger than 10 mm in which most conditions cases are managed via open surgery or pyelolithotomy.[5,6] As kidney stones and pyelolithotomy take part of the kidney functional area, this significantly generates a reduction of kidney function.[4,7] Hence, over two-thirds of patients with CKD experience complications comprising acute and other chronic diseases, one of which is anemia.[8]

Oral health and systemic health share a profound bidirectional relationship where chronic diseases increase the risk of infection and inflammation that lead to significant oral health challenges.[9,10] Diabetes mellitus patients have been reported with a significant occurrence of oral health changes from dry mouth (xerostomia), tooth decay (including root caries), gingivitis, periodontal disease, oral candidiasis to defective wound healing.[11] Chronic kidney disease patients have been presented with uremic stomatitis to dysgeusia.[12] Meanwhile, anemic patients commonly presented with angular cheilitis and atrophic glossitis to generalized oral mucosal atrophy.[13] Over time, sustained localized inflammation in the oral cavity can trigger the initiation of a systemic inflammatory response that could contribute to the worsening of systemic conditions.[9,14]

When two or more chronic diseases coexist in the same patient, it will present multiple concurrent changes in the oral cavity.[15] Since oral diseases may influence the course and treatment of the general disease, they undoubtedly require a multidisciplinary approach for comprehensive diagnosis, evaluation, and treatment to prevent the risks of adverse health outcomes, consume more medical resources, and improve the patient's quality of life.[3,15,16] Each oral mucosal lesion in MCC may arise from different aetiologies and predisposing factors, therefore management should focus on the nature of each disease and combination of mulimorbidity management at an individual level.[2,17–20] Several studies have reported the management of oral mucosal lesions in multimorbid patients yet studies on multiple oral lesions management in patients with co-existing diabetes mellitus, anemia of chronic disease, and chronic kidney disease post nephrolithotomy have remained scarce and varied. In this report, we initiate the implementation of pharmacotherapy and behavioral modifying lifestyle as comprehensive treatment for oral lesions in multimorbid patients post-pyelolithotomy to expect better outcomes.

CASE REPORT

A 65-year-old male patient was first consulted to Oral Medicine Specialist Siaga Surgical Hospital Banjarmasin via teledentistry with a complaint of a very painful persistent ulceration of the tongue. The complaint

had been experienced for approximately two weeks since he was admitted to an emergency room for packed red blood cell transfusions and it had worsened that prevent him from consuming food and beverages. There was a history of outpatient treatment for diabetes mellitus from January 2023 up to recent days, complaints of lethargy and dizziness in the past years, and kidney stone surgical removal three months earlier. Oral lesions had been managed with nystatin, triamcinolone acetonide 0,1% in orabase and aloe vera extract gel yet no improvement was observed.

No history of allergy was recorded with oral hygiene practice twice daily without the use of mouthwash, tongue brush and dental floss. No history of smoking, alcohol consumption and tobacco use. There was a history of routine drug consumption for diabetes mellitus treatment once daily in the morning. No history of similar condition and systemic condition among family members.

General status presented a lethargic undernourished patient with spontaneous eye movement, oriented verbal response, and complied motor commands. Vital signs were stable. Extraoral examination exhibited pale lips while intraoral examination presented a 50 to 60 mm irregular painful ulceration with a yellowish surface surrounded by an erythematous area on the fully atrophic pale-in-color dorsum of the tongue.

Laboratory test had performed reporting a decrease in hemglobin (9.7 g/dL), MCV 78.5, MCH 27.8 while an increase in random blood glucose 260 mg/dL, blood urea nitrogen 45 mg/dL and creatinine 2.34. Gromerular filtration rate was at 31 ml/min/1.73m^2 which is classified as Stage 3B Kidney Disease.

Based on the history taking and overall examination, a diagnosis of ulcerative type uremic stomatitis with atrophic glossitis and reduced salivary production associated with multiple chronic conditions (diabetes mellitus, Stage 3B Kidney Disease, and anemia of chronic disease) was obtained.

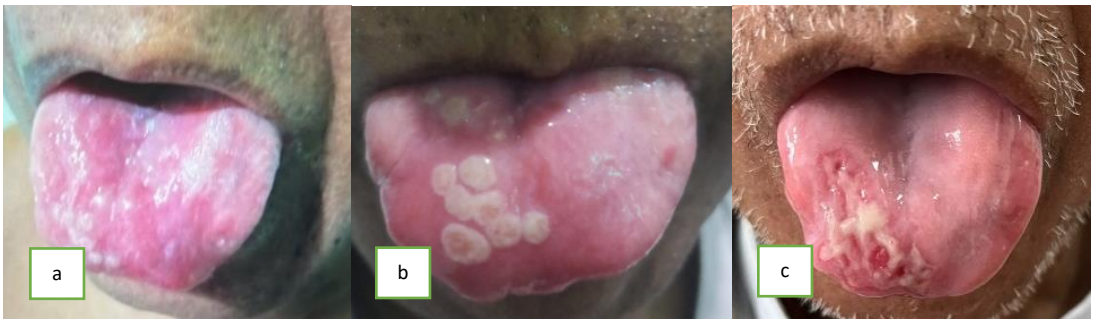

Fig 1. The first visit (day 1) presented a history of of burning and itchy sensation of the tongue on January 20th 2025 (a), progression into multiple ulcers on January 21st 2025 (b), and presently manifested as a very painful irregular solitary ulcer on the dorsum of the tongue since January 28th 2025 (c).

On the first consultation via teledentistry (January 30th 2025), patient had used aloe vera extract gel thrice daily for three days without any improvement so that additional antiseptic mouthwash of povidone-iodine 1% was prescribed. Patient was then instructed to apply aloe vera extract with an interval of thirty minutes after application of povidone iodine 1% four times daily. The patient's oral manifestation of systemic conditions were evaluated by an oral medicine specialist on the following day.

On the first direct appointment (January 31st 2025), the oral complaint had been diminished. Intraoral examination presented non-painful 40 mm x 20 mm irregular erosion surrounded by an erythematous area on an atrophic dorsum of the tongue.

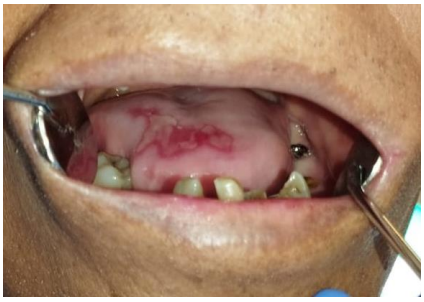

Fig 2. The second visit (Day 3) exhibited diminished ulceration after the application of aloe vera extract gel in combination with antiseptic mouthwash povidone iodine 1%

Treatment planning includes elimination of local factors (scaling and root planning, extraction of tooth radix, and fabrication of removable partial dentures), prescription of topical agent for oral ulcer healing promotion, and management of systemic diseases. The patient was informed of the result of the laboratory blood examination and instructed to keep on the current prescription with an addition of multivitamin per oral (Ferric gluconate, vitamin B1, vitamin B2, vitamin B6, nicotinamide, and biotin) for atrophic glossitis treatment. A referral to an internist was issued to manage diabetes mellitus, anemia of chronic disease, and Stage 3B kidney disease. Education of self-management comprising behavioral modifying lifestyle was mentioned to the patient and his family.

We presented a list of daily lifestyle goals including management of oral health, physical activity, and dietary choices. To prevent the recurrence of oral ulceration, the patient was educated to maintain oral hygiene by toothbrushing for two minutes twice daily, use antiseptic mouthwash for maintenance twice daily when no oral lesion exists, and oral health screening every 3 months for people with risk factors. Physical activity may be performed for non-endurance exercise such as walking or cycling 20 minutes at least thrice weekly.

Since no nutritionist was present and no daily intake instruction was provided previously to the patient, we emphasized the need for a balanced diet to maintain blood glucose level, urea metabolism, and support hematopoiesis. Total energy intake should be around 1900 to 2100 kcal including low carbohydrate 180 g, low protein 36 g (eggs/meat/fish 17 g, milk/nuts and seeds 4.8 g, vegetables 14.2 g), fats and oils 15 g, and fruit 200 g. Consumption of vitamins A C D E K should be avoided.

The patient reported via teledentistry that painful ulceration had ceased yet atrophic glossitis on the dorsal surface of the tongue has yet to be evaluated. The visit to the internist for his monthly diabetes checkup had been performed. The patient was instructed to continue the supplementation to be evaluated each month and reinforced to do a follow-up visit to assess their tongue condition.

DISCUSSION

MCC individuals have been reported with multioral and multidental problems that may persist in uncontrolled conditions.[15,21] Patients seek treatment mostly for more severe health conditions that disturb oral circumstances associated with eating, nutrition, social interaction, and emotional and psychological functions when related to discomfort, disability, and social and financial impact.[22,23] Diagnosis, evaluation, and treatment approaches are varied based on the nature of individualized diseases.[2,17–20] In this study, we report the pharmacotherapy and behavioral modification of lifestyle for ulcerative-type uremic stomatitis and atrophic glossitis management in an MCC diabetic coexisted with stage 3B kidney disease post pyelolithotomy and anemia of chronic disease.

Diabetes Mellitus (DM) is a hyperglycemic condition caused by a combination of defective insulin secretion and the inability of insulin-sensitive tissues to respond resulting in the accumulation of toxic metabolites in the body.[24,25] The main drivers of the DM epidemic are the global rise in obesity, sedentary lifestyles, high caloric diets and population aging. In this report, patient was elderly which may contribute to the progression of DM two years prior to the history of lethargy and kidney stone removal. Advanced age leads to the exacerbation of systemic chronic inflammation, oxidative stress, DNA damage, decline of mitochondrial function, cellular senescence, and tissue dysfunction, therefore promoting β-cell death by inducing mitochondrial dysfunction.[26] This will lead over time to damage to the heart, vasculature, eyes, kidneys, and nerves.[25]

The patient was also identified with Stage 3B kidney disease by Oral Medicine Specialist after a history of kidney stone removal was recorded and kidney function tests revealed an increase in blood urea nitrogen and creatinine levels. It is well known that Type 2 diabetes mellitus is characterized by insulin resistance, a metabolic derangement that may increase the risk of kidney stone formation. Although a low urinary pH plays a major role in the formation of uric acid kidney stones, a defect in renal acid excretion also could lead to hypocitraturia, an important risk factor for calcium stones. In addition, the compensatory hyperinsulinemia of insulin resistance may increase the urinary excretion of calcium.[27] However, the presence of the upstream influence of hyperglycemia may also lead to a dysregulated intracellular metabolism, inflammatory lesions, increased apoptosis processes and tissue fibrosis. These mechanisms lead to the worsening of kidney disease via glomerular basement membrane thickening, podocyte depletion, mesangial matrix expansion, and tubular damage.[28]

Kidney stone treatment itself may account for the excess risk of kidney damage.[4] (Shang et al., 2017). Nowadays, extracorporeal shock wave lithotripsy (ESWL), retrograde ureteroscopy, and percutaneous nephrolithotomy (PCNL) occupy an essential place in the treatment of urinary calculi as increasing technologic advancements allow easier access to stones in all parts of the kidney and ureter. Despite the less frequent indication, open surgery or pyelolithotomy currently holds an important role and is remained common in Indonesia because urologists still face patients with complex urinary stone disease due to the high stone burden and/or anatomical anomalies of the collecting system.[6,29] It has potential for renal injury yet is considered as a kind of neuron-sparing urinary stone removal therapy, causing less parenchyma damage than other techniques. However, it has higher incidence of postoperative new onset of ESRD in open pyelolithotomy patients.[30]

The patient reported that there was lethargy and dizziness three months post-kidney stone removal which led to his admission to the ER. Symptoms were confirmed by blood test presenting anemia microcytic hypochromic which is a common complication whether in the presence of diabetes mellitus and its complication of CKD. Diabetes mellitus may cause prolonged direct glucose toxicity of erythrocyte precursors cells in the bone marrow leading to disturbances in the erythrocyte production.[31] Meanwhile, CKD is associated with an adaptation of renal tissue to consume less oxygen where PHD enzymes remain active, the HIF heterodimer is not formed and the erythropoiesis (EPO) gene is not activated.[32] In addition, patients with CKD often lose large amounts of iron through blood loss and uremia. Both Diabetes Mellitus and CKD also presented with chronic inflammation that promotes hepcidin production, an acute phase protein, which decrease iron absorption from intestine and iron release from macrophages.[33] A lack of iron delivery to the heme group causes decreased hemoglobin production presenting smaller erythrocyte size.[34]

Oral findings in this study were identified as ulcerative-type uremic stomatitis that concurrently occurred on the atrophic dorsal surface of the tongue. Uremic stomatitis is an inflammatory condition of oral mucosa as an uncommon complication of uremia with the presence of markedly elevated BUN levels around 150–300 mg/dl.[35] The pathophysiology of the disease has not yet been established, but urea causes mucosa irritation and chemical injury when hydrolyzed by microbial urease in saliva. The mechanism for mucosal injury is through lysosomal pH increase and termination of lysosomal ammonia storage causing cell death after ammonia reflux into mitochondria. This not only contributes to liquefaction necrosis of epithelial cells.[35,36] Yet we reported the occurrence of uremic stomatitis at BUN level of 45 mg/dl presumably exacerbated by atrophic glossitis, which increases mucosal vulnerability. Atrophic glossitis is a diminished number and size of the lingual papilla or epithelial layer of the tongue with decreased cell size and tissue mass.[37] The epithelial cells of lingual papillae have a rapid turnover, resulting in their sensitivity to deficiencies in oxygen-carrying capacity to the dorsal surface mucosa of the tongue such as in chronic diseases.[30,38] Therefore, it is prone to ulceration which involves a breach in the epithelial covering of mucosa exposing the underlying lamina propria.[39] As the ulceration caused by ammonia from salivary ureum on the thinning of tongue mucosa, the diagnosis of ulcerative type uremic stomatitis was made.

The management for uremic stomatitis is by preventing the production of ammonia in saliva via reduction of oral microbe and maintenance of blood urea level. Povidone iodine is an antiseptic mouthwash that has a small molecule that can rapidly penetrate into microorganisms and oxidize key proteins, nucleotides, and fatty acids, eventually leading to cell death. PVP-I has a broad antimicrobial spectrum with activity against Gram-positive and Gram-negative bacteria, including antibiotic-resistant and antiseptic-resistant strains.[40]

To promote wound healing in this patient with chronic conditions that may hinder wound healing process, topical application of aloe vera extract gel is suggested. Aloe vera or commonly known as aloe vera contains several natural bioactive compounds including pyrocatechol, saponins, acemannan, anthraquinones, glycosides, oleic acid, phytol, and water-soluble polysaccharides, both simple and complex. The antioxidant properties of aloe vera along with its inhibitory effects on the production of prostaglandin E2 and interleukin-8 are other candidate mechanisms that indicate its potential curative benefits. Aloe vera produces growth factors that bind to the wound area with the IGF fibroblast receptor and subsequently produce collagen and proteoglycans resulting in increased tensile strength of the wound.[41]

Patient was also prescribed with multivitamin consisting Ferric gluconate, vitamin B1, B2, B6, nicotinamide, and biotin. Iron supplement 100 mg per day is in accordance with a study by Kumar et al. (2022) as the preferred dosing regimen in order to reduce the side effects and optimise the proportion of elemental iron absorbed in patient with very low ferritin (2.7 ng/ml).[42,43] Recently absorbed iron (or iron that is released from storage sites) is bound to plasma transferrin which distributes it around the body to sites of utilization. Steady-state erythropoiesis involves the production of 200 billion new red blood cells per day or 2.4 million per second that requires a daily supply of 20 to 25 mg of iron, in the form of holotransferrin. The body can only absorb 10–20 mg of iron per day and red blood cell with low hemoglobin synthesis will remain as the lifespan of erythrocyte is 120 days, therefore therapy should be continued for three months with monthly blood test evaluation after the anemia is corrected to shortallow iron stores to become replenished.[42,44] Aside of being the active center of hemoglobin, iron is actively implicated in cell metabolism, cell respiration, DNA synthesis, cell cycle control, and apoptosis triggering. Iron is also a regulator of the inflammatory response induced by epithelial cells through the

secretion of lactoferrin. In proliferation phase, it is actively involved in the maturation of pro-collagen into a stabilized collagen triple helix.[45]

Vitamin B has several functions to promote wound healing and eryhtropoiesis. Thiamin (B1) has been shown to play a role in pathways involved with proteins and fat metabolism. Riboflavin (B2) and nicotinamide/niacin (B3) are vital for maintaining skin integrity and mucous membranes' integrity, especially by supplying the needed coenzyme for the energy cycles. Nicotinamide (B3) plays role in restoring cellular energy, repairing DNA damage, and inhibiting inflammation by suppressing pro-inflammatory cytokines release.[46] All three of vitamin B2, B6, and B8 has been associated with collagen maturity.[47] In addition, vitamin B6 is a rate-limiting coenzyme that plays an important role in the biosynthesis of heme and the incorporation of iron into protoporphyrin. Its deficiency is often seen in chronic kidney disease (CKD), particularly those requiring dialysis and following administration of erythropoietin-stimulating agent (ESA).[48] Biotin (vitamin H or B7) serves as a vital coenzyme for the metabolism of fats, carbohydrates, and amino acids, supporting cellular proliferation with important roles in erythropoiesis. It is further important for growth, collagen synthesis, digestion, muscle function, and periodontal wound healing.[49,50] Through its anti-inflammatory and cell proliferation effect, multivitamin prescription was expected to accelerate the healing of epithelial breach in the ulcerative type of uremic stomatitis and the healing of the mucosal thinning in atrophic glossitis.

Patient with MCC requires multidisciplinary treatment including dental practitioner, oral medicine specialist, internist and nutritionist. General dental practice not only identify but also refer MCC patients with complex needs to appropriate specialist but provide preventive support to improve oral health status.[9] Presented with oral lesions associated with MCC, this requires personalized treatment of oral mucosal disease and dental treatment by accounting for the prioritization, goals, and complications of systemic conditions and dental therapy which are within the scope of oral medicine specialists.[51] For acute and long-term management of chronic conditions and its complications, a holistic approach to patient care is within the scope of internal medicine.[52] Patient with anemia of chronic disease in CKD require medication fo erythropoietin stimulating agents combined with iron supplementation until hemoglobin level reach 10-12 mg/dl, while diabetes mellitus requires medications and dose adjustment in the presence of declined kidney function.[53,54] However, long-term progression depends on daily lifestyle of the patients thus expecting behavioural change to support better treatment outcomes.

Behavioural modifying lifestyle is interventions to change and maintain healthier behaviours preventing morbidity and mortality in chronic diseases. These interventions involve physical activity; healthy eating/diet; smoking cessation; reducing excessive drinking; treatment adherence, including medication and attending medical appointments were eligible.[55,56] In diabetic nephropathy with anemic patients, the treatment goal was to manage blood glucose level and uremic solutes that contribute to organ damage. Physical activity has been associated with controlled glucose level as it increases skeletal muscle GLUT4 expression and augments insulin receptor signaling and oxidative capacity which optimizes insulin action and glucose oxidation and storage.[57] It should be supported by diet choice of carbohydrate 180 g per day as it is the threshold for gromeruli to filter. [58] This will prevent further progression of CKD because high glucose concentration reduces mesangial matrix degradation by affecting the activity of matrix metalloproteinases (MMPs) lead to further fibrosis of kidney tissue.[59] A renal diet or low protein diet limits protein intake from animal sources at the weight of 1.3 or 0.58 g protein/kg of standard body weight/day and 16–20 or 5–10 mg phosphorus/kg of standard body weight/day,

respectively. High protein intake may promote renal damage by chronically increasing glomerular pressure and hyperfiltration.[60,61] Vitamin A D E K should be avoided as it burdens glomerular filtration while vitamin C higher than 100-200 mg per day may increase oxalate formation that further accumulate in organ tissue causing inflammation, pain and stone formation within tissue.[62,63] However, it is ideally evaluated for 59 to 66 days in the forming of new habit.[64]

In oral lesion behavioural management, treatment adherence, including medication, oral hygiene maintenance and attending medical appointments were pivotal. Oral hygiene maintenance should be encouraged in patient with atrophic glossitis as atrophic tissue is lack of protective function due to reduced number of stratified cell, thus preventing colonization of normal microbe with ureolytic activity should be achieved to prevent mucosal irritation.[35,36,38,65,66] The removal of dental plaque reduces the number of bacteria in the saliva. Toothbrushing brushes off the plaque adhering to the teeth, causing the plaque to mix with saliva. As a result, the number of bacteria in the saliva may increase immediately after brushing. This temporary increase in the bacteria in the saliva after brushing is not a major problem for healthy people because they can wash away the saliva mixed with dental plaque by rinsing their mouths immediately after brushing and can normally swallow the saliva mixed with the remaining bacteria. However, when brushing older adult patients requiring nursing care or those on ventilators, the collection of bacteria during and after brushing is important.[67]

Although no current guidelines for regular appointments to evaluate oral conditions, appointment within 5 to 7 days is required to evaluate the inflammatory response in healing process of uremic stomatitis lesions and in addition of 7 days to evaluate the proliferation process.[68] For the atrophic tongue, improvement may be observed within 2 to 3 weeks after elimination of anemic condition as the oral epithelium turnover requires 14 to 21 days to achieve.[69] Meanwhile, a recall between every two to six months should be performed in the absence of oral mucosal lesion considering dental plaque and calculus formation with the presence of systemic diseases needs.[70]

CONCLUSION

In conclusion, the integration of pharmacotherapy and behavioral lifestyle modifications facilitates a more favorable prognosis for oral lesions management in multimorbid patients following pyelolithotomy-related renal complications. This case underscores the importance of a comprehensive, multidisciplinary approach in managing complex oral manifestations in MCC patients with diabetes mellitus, stage 3B chronic kidney disease post pyelolithotomy and anemia of chronic disease that may be a guide for patients with the same complaint in the future. However, the primary limitation lies in the focus on a single geriatric case with minimal external lifestyle risk factors. While the uremic stomatitis resolved within seven days, atrophic glossitis requires a more prolonged evaluation due to slower epithelial turnover. Meanwhile, a behavioral modifying lifestyle should be encouraged and assessed for 59 to 66 days to form a new habit.

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