Case Report

Smoking cessation induces rapid healing in elderly patient with traumatic ulcerative granuloma with stromal eosinophilia (TUGSE): a rare case report

Chivita Wulandari Febryna[1*]
Nanan Nur'aeny[2]

[1]Specialist Program Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia
[2]Department of Oral Medicine, Faculty of Dentistry, University Padjadjaran, Bandung, Indonesia

* Correspondence:
Chivita22001@mail.unpad.ac.id

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ABSTRACT

Introduction: Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) is a type of chronic traumatic ulcer. There are several factors that contribute to the development of TUGSE, but trauma is the primary one. If smoking or other risk factors are present, the condition may be exacerbated, as this may impede the healing of wounds. This case report will show the influence of smoking cessation on the recovery from TUGSE in patients and the resulting improvement in quality of life. **Case report**: A 64-year-old male patient presented to the dental hospital with a primary complaint of a painful sore on the tip of his tongue at the back for the past month. The patient had previously consulted a general practitioner and an ear, nose, and throat (ENT) specialist and was prescribed triamcinolone acetonide and povidone iodine mouthwash but no improvement was observed. An intraoral examination revealed an ulcer on the lateral side of the tongue. The patient had a cavity with sharp edges near the lesion, but it was ground down 2 days ago. The patient had a history of smoking clove cigarettes, consuming 24 sticks per day for more than five years. The patient was given chlorhexidine gluconate 0.2% mouthwash, to be used at a dose of 10ml, twice a day, and was instructed to apply a thin layer of triamcinolone acetonide 0.1% in orabase three times a day on the lesion. The patient recovered after seven days of treatment and reported their symptoms have decreased. The assessment using the Oral Health Impact Profile-14 (OHIP-14) indicated an improvement in the patient quality of life. **Conclusion**: Smoking cessation can improve the healing process of ulcers, thereby improving an individual's quality of life.

KEYWORDS

Smoking cessation, TUGSE, wound healing, quality of life

INTRODUCTION

In the oral cavity, traumatic ulcers are common lesions. Acute and chronic cases are distinguished in this instance based on several characteristics.[1,2]Some of the most common causes of these lesions are being bitten, having restorations that overhang, and having cavities that impact sharp portions of teeth.[2] Traumatic ulcers can be brought on by substances include chemical, electrical, and thermal factors. If the trauma causing the lesion is left untreated, the lesion will continue to be traumatized, which can result in the development of chronic traumatic ulcers.[1–4]

Based on its classification, chronic traumatic ulcers can be divided into single traumatic ulcers and multiple traumatic ulcers.[1] Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a type of chronic single traumatic ulcer.[4–6] This ulcerative lesion is benign and reactive, capable of healing on its own, but the process is slow, ranging from several weeks to two years. This case is rarely

encountered and is generally found in infants at the age of 2 years due to tooth growth. In adults, TUGSE occurs between the ages of 40 and 70. It can occur in both women and men with a ratio of 1.8:1.[1,4,5,7]

The region with the greatest incidence for TUGSE is the tongue, followed by the buccal mucosa, vestibule, gingiva, floor of the mouth, and retromolar area.[3,7] Various factors may be involved in this case, including trauma, which is responsible for approximately half of all cases.[1,7] Other possible contributing factors include toxins, viruses, microorganisms, and degradation from endogenous factors. One of the toxins that affect lesions is cigarette smoke.[1,7–9]

Cigarettes contain tobacco and have several other active substances such as nicotine, carbon monoxide, hydrogen cyanide, tar, polycyclic aromatic hydrocarbons (PAHs), metals, and nitrosamines.[10] Among these substances in cigarettes, nicotine, carbon monoxide gas, and hydrogen cyanide are the substances most significant in delaying the healing process.[11] These three substances can cause tissue hypoxia, which triggers a decrease in blood circulation, a reduction in the oxygen-binding capacity of the blood, and metabolic disturbances, thereby slowing down the wound healing process in the tissue.[9–11]

There are several stages of oral ulcer healing: hemostasis, inflammation, proliferation, and maturation.[12,13] The cigarette can cause damage in inflammation stage by disturbing the process of macrophage migration due to decreased of blood circulation.[12,14] On the other hand, the hydrogen cyanide and nicotine have the potential to interfere with the epithelium's capacity for repair. This condition can slow down the healing stages, particularly the proliferation stage, and the result is the ulcer takes longer to heal.[11,14,15]

The bad habit in this patient is smoking. After cessation of smoking, the patient's oral cavity ulcer showed significant improvement. Reducing smoking might enhance quality of life through psychological and economic factors. The purpose of this case report is to show how TUGSE was successfully treated by giving adequate treatment and minimizing bad habits that were thought to be escalating the patient's condition.

Treatment for TUGSE usually focuses on healing the ulcer without considering any worsening factors. Although the patient in this case report had previously received the same drug from another doctor without any improvement in the patient condition, our treatment was successful. Our treatment shown the successful because the patient smoked fewer cigarettes, which was thought to be a contributing factor in accelerating the healing process.

Case Report

A 64-year-old male patient presented to the Department of Oral Medicine at Padjadjaran University Dental and Oral Hospital with the main complaint of an ulcer at the back of his tongue for the past month. This ulcer was painful. It appeared due to contact with a sharp residual tooth root. The sharp tooth was polished about two days ago at the dentist. The patient has treated the thrush by visiting a general practitioner and an ear, nose, and throat (ENT) specialist, who prescribed an ointment containing triamcinolone acetonide 0,1%, to be applied three times a day to the ulcer and a povidone iodine 1% mouthwash twice a day. The patient reported that after using the medication as instructed, there was no improvement, so the patient stopped using the medication.

The patient's medical history shows that he denies any history of recurrent ulcer, drug and food allergies. He also denies a history of systemic diseases and family illnesses. The patient admits to brushing his teeth once a day without brushing his tongue. He also acknowledges inadequate consumption of mineral water, fruits, and vegetables. The patient consumes coffee two to three times daily, and has the habit of smoking clove cigarettes, 1.5 packs per day (24 sticks daily) for more than 5 years.

The patient is in good condition, with a weight of 57 kg, a height of 167 cm, a temperature of 36.7ºC, a blood pressure reading of 135/80 mmHg, a pulse 86 beats per minute, and a respiration rate of 23 breaths per minute. The extraoral examination shows no abnormalities, the face was symmetrical, non-anemic conjunctiva, non-icteric sclera, lymph nodes and temporomandibular joint and mouth opening normal. The patient's lips were dry, showing exfoliation and the presence of black macules, multiple and diffusely bordered along the vermilion of the upper and lower lips (white arrow); this condition is painless (Figure 1A).

Before performing the intraoral examination, we explained the procedure including taking a picture of intraoral and extraoral from the patient and obtained the patient's informed consent for publication. Intraoral examination (Figures 1B-L) revealed a single ulcer with a yellowish-brown base, approximately 1 mm deep, measuring 0.5x1cm, with diffuse borders surrounded by hyperkeratotic lesions, with induration. This lesion was painful. On the dorsal surface of the tongue, there was a presence of yellowish-black white plaque that can be scraped off without leaving any erythema on almost the entire dorsal surface of the tongue. This was accompanied by elongated, multiple, diffuse hair-like papillae that could not be scraped off and are not painful.

The dental examination revealed missing teeth 18, 14, 15, 24, 25, 38, 36, and 47; gangrene of the roots of teeth 13, 23, and 48; cervical caries on tooth 12; and pulp necrosis of tooth 37. The patient's gums are experiencing recession, and the presence of plaque and calculus in all remaining dental regions, along with findings of poor oral hygiene.

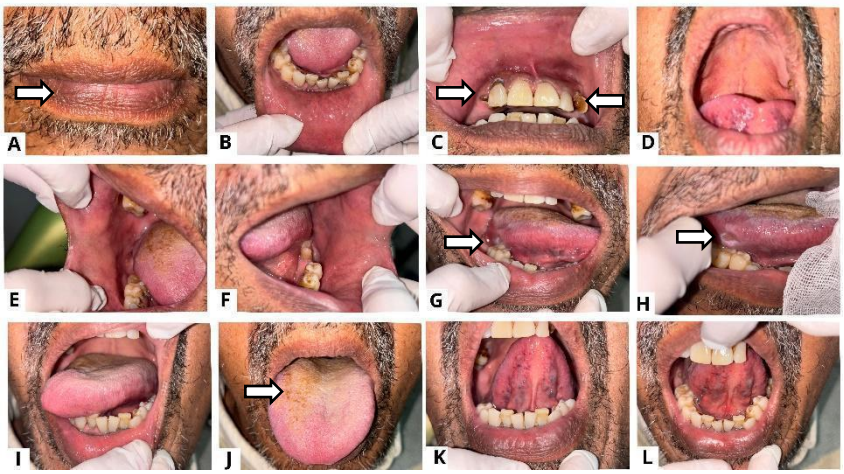

Figure 1. (A) extraoral examination; (B-L) intraoral examination.

Based on the clinical examination, the main complaint from the patient is a single ulcer with diffuse borders surrounded by hyperkeratotic lesions, with induration the diagnosis of this case is suspected traumatic ulcerative granuloma with stromal eosinophilia (TUGSE). Other oral manifestations found include oral

hairy tongue, smoker's melanosis, coated tongue scale 3 Miyazaki, chronic apical periodontitis with gangrene of the roots of teeth 13, 23, 48, and pulp necrosis of tooth 37 were found. Reversible pulpitis of tooth 12, along with chronic generalized marginal periodontitis.

The main diagnosis of this case is TUGSE with the differential diagnosis is oral squamous cell carcinoma.[3] Hyperkeratosis and induration are the clinical manifestation of TUGSE that can resemble OSCC.[3] The prognosis of TUGSE usually is good. Many of TUGSE cases showing healing withing months to years without any complication.

This patient was given both non-pharmacological and pharmacological treatment. The non-pharmacological treatment provided is through education about the patient's condition, including the causes and the effects that will occur if this condition continues. We explained how to clean teeth properly by brushing twice a day. We advised the patient to stop the habit of smoking and reduce coffee consumption, replacing it with an increased mineral water intake of 2 liters per day, as well as greater consumption of fruits and vegetables.

Pharmacological treatment included the use of chlorhexidine gluconate mouthwash at a concentration of 0.2%, administered at a dosage of 10ml, twice a day. The patient was instructed to apply a thin layer of triamcinolone acetonide 0.1% in orabase three times a day on the ulcer lesion on the tongue. After being applied to the tongue, the patient is asked to avoid eating and drinking for 30 minutes. The patient was scheduled to undergo a biopsy during the second visit as a supplementary examination for the diagnosis of TUGSE.

At this visit, we conducted a supplementary examination using the Oral Health Impact Profile-14 (OHIP-14). This evaluation was necessary considering the patient reveals severe disruption because the ulcer still has not healed. OHIP-14 showed a score of 50, indicating a poor outcome. We explained that in the second visit we would reassess to see if there is any improvement or worsening of the patient's condition.

During the second visit, the patient returned 10 days after the first visit, reporting that the oral ulcer had healed and there was no complaints of pain in the lesion area. The patient reported that he reduced his consumption of clove cigarettes to three times per day, after each meal. Initially, on the first and second days, the patient had stopped smoking, but he felt more anxious, experienced a sour taste in his mouth, and was easily irritated. The patient often unconsciously sought out cigarettes, but by the third day, they admitted to smoking more than five cigarettes again. Then, from the fourth day until now, the patient has reduced their intake to three cigarettes a day, with consuming 1 cigarette after each meal. Whenever the patient sought a cigarette, his wife assisted him by replacing it with low-sugar candies. The use of these candies helped the patient to divert his smoking habit after several days.

The patient also reduced his coffee consumption and increased mineral water intake, but still rarely consumed vegetables and fruits. The patient underwent an OHIP examination, which resulted in a score 32, indicating a moderate level. This situation showed that the patient was much better compared to their condition upon arrival.

Based on the results of the intraoral examination (Figure 2), the lesion on the lateral side of the tongue had healed (white arrow), and the dorsum of the tongue showed improvement, although there is still plaque in the posterior area (white arrow). The patient was again educated about the importance of

maintaining oral hygiene, including brushing the tongue, and to continue to stop smoking. The patient was shown images of his condition from the initial visit and after the follow-up. The patient reported that his condition had improved significantly (black circle). (Figure 3 and Figure 4).

The patient admitted that he had not yet received treatment for his remaining root teeth or his cavities, but had already been scheduled for extraction. The initial plan for a biopsy was ruled out because the ulcer had already healed. This presented a challenge in diagnosing the case as TUGSE without biopsy. However, the clinical manifestation of persistent ulcer with induration and hyperkeratotic areas surrounding the lesion are characteristic of ulcers in TUGSE. This became the basis for diagnosis.

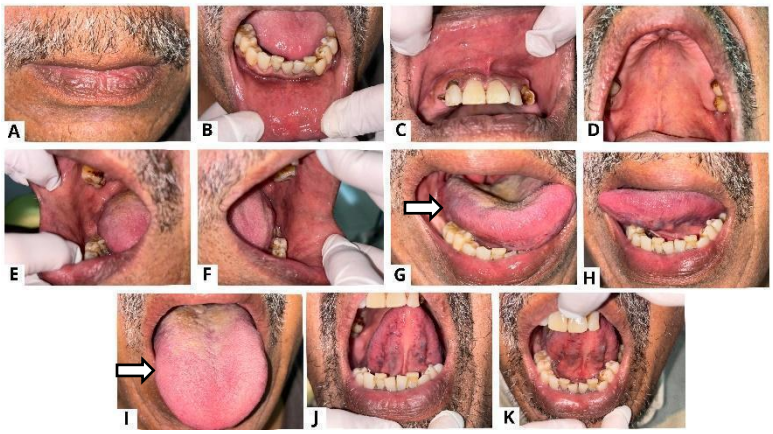

Figure 2. Patient (A) extra oral and (B-K) intra oral condition after 10 days treatment

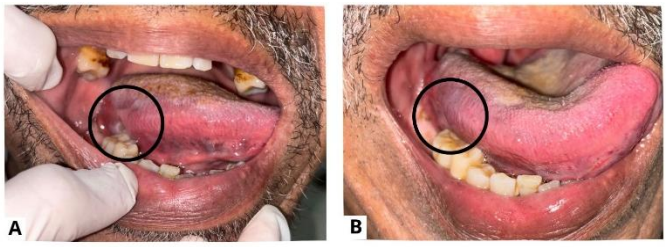

Figure 3. Condition of the lateral tongue during (A) the first and (B) the second visits.

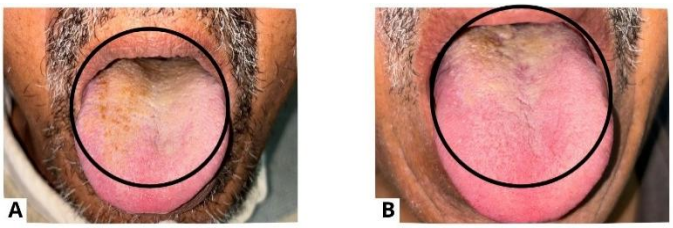

Figure 4. Condition of the patient's tongue during (A) the first and (B) the second visits.

DISCUSSION

In elderly patients, wound healing is worse than in younger patients.[16,17] This can happen when aging leads to a decrease in cellular function. An altered inflammatory response, delay in angiogenesis, collagen synthesis, and re-epithelization are all linked to delayed wound healing in elderly patients.[16,17]

According to Florina (2024), every stage of the healing process is affected by aging, including changes in platelet aggregation, increased inflammatory mediator secretion, delayed lymphocytic infiltration and decreased collagen turnover rate.[16]

An elderly man has had a smoking habit for over 5 years. The patient works as a shopkeeper, which allows him to have plenty of free time to smoke in significant amounts. Smoking is a habit of consuming tobacco products including filter cigarettes, electronic cigarettes, rolling tobacco, clove and also cigars. According to the World Health Organization (WHO), there are over 1 billion smokers, with an average age ranging from teenagers to elderly, specifically between 18 and 65 years old.[10,14] Based on gender, men smoke more than women, with a ratio of 20%:14%.[14] Almost 34% Indonesia citizens is smokers.[18]

According to the 2023 Indonesian Health Survey (SKI), there are 70 million active smokers in Indonesia and from World Health Organization perspective, Indonesia has the highest number of smoking-related death, with more than 200.000 mortalities or approximately 15% of all the deaths.[18,19] In Indonesia, there is currently a shift in the age of cigarette consumers. It is known that smoking has many negative effects, including increasing the risk of death by more than 10% in men and 6% in women.[18,19]

Considering cigarettes are addictive, dropping the habit requires careful consideration of a variety of factors.[10] This is linked to the patient's condition, as he reports smoking more cigarettes than they did six months prior. This condition has multiple causes, one of which is that smoking affects men more frequently than women.[10] In terms of employment, people who work part-time or are unemployed generally smoke more than people who work full-time, this is because they have more time to smoke. Individuals who have lower incomes also tend to smoke more.[10,14] The prevalence of smoking is also influenced by factors such as low education, disregard for health, and limited access to medical facilities.[10,14,19] Additionally, unsupervised promiscuity due to disharmonious family relationships is one of the factors contributing to the high rate of smoking among young people.[10,14,19]

Smoking has negative effects on the wound healing process in various ways, including reducing the role of neutrophils and macrophages in the inflammatory process. Bacteria that are supposed to be eliminated may persist due to immune system disturbances during the healing process. This will increase the bacterial activity in the ulcer area. Pandit (2024) mentions that smoking cessation can help restore blood flow and enhance natural healing mechanisms and leading to the improvement of wound recovery.[20]

The active substances in cigarettes are very diverse, one of which is nicotine, which is part of alkaloids.[11,19] When nicotine enters the body, it can travels to the brain and affect the central nervous system (CNS).[14] Once in the brain, nicotine triggers an increase in stimulation of the adrenal glands, leading to the release of epinephrine, acetylcholine, and dopamine. Dopamine plays a role in movement, hormone release, emotional balance, and happiness.[14,21] Acetylcholine is related to synapses in the body, which will influence various interactions within the body, including cardiovascular and psychological aspects, leading patients to feel more energized to carry out their tasks.[10,22,23] In addition to acetylcholine, nicotine binds with dopaminergic receptors, triggering serotonin release, which makes patients to feel calmer and happier when smoking.[10,14,21]

The inhalation of cigarettes will form a bond between nicotine and acetylcholine receptors (nAChRs).[14] Patients do not experience cravings as long

as they smoke since their nAChR levels will be steady. However, when the patient sleeps, the amount of nicotine in the plasma will drop; as a result, when the patient wakes up, nAChR activity will increase, leading to cravings and withdrawal symptoms. Patients typically have psychological difficulties during this phase, including anxiety, frustration, and an inability to manage their anger. Meanwhile, this circumstance also leads to an increase in food intake.[14,21,23]

Both of these phases indicate that the patient is beginning to enter the chronic smoker phase. During these two phases, there will be an increase in the number of cigarettes consumed due to the need to stabilize the nicotine levels in the body.[10,14,19] This increase in quantity leads to more frequent contact between the active ingredients and the oral cavity. Individuals who smoke frequently experience various types of lesions in the oral cavity, including nicotine stomatitis, smoker's melanosis, and are prone to ulcers due to irritation, known as traumatic ulcers.[1,19,21]

Traumatic ulcer is an ulcer that forms due to trauma, whether acute or chronic.[1,2] Traumatic ulcers are classified into several types based on whether they are acute or chronic, as well as their clinical characteristics. TUGSE is one of the chronic traumatic ulcers that occurs in a solitary or single form.[1,3,5] This case presents a typical clinical picture characterized by slow healing of ulcers with a rolled white border, surrounded by a reddish color or the presence of keratosis.[1,7,9] This condition is generally asymptomatic, but it is not uncommon for patients to complain of discomfort.[1,6,24]

According to the research by Shen et al. (2015), TUGSE is most commonly found on the tongue, accounting for about 67.6%, and is more prevalent in males at approximately 64.7%, with an average age of 49 years.[24] This situation reflects the same findings as this case report, which indicate male patient with lesions found on the tongue.

TUGSE has a main characteristic of delayed self-healing caused by a decrease in the synthesis of transforming growth factor (TGF) by eosinophils during the inflammatory process.[6,25,26] It is well known that the complex process of tissue healing consists of the inflammatory phase, proliferation, restoration, and remodeling. At this stage of the healing process, disruptions can occur due to various factors, one of which is smoking. Exposure to nicotine induces fibrosis and leads to fibroblast damage because of α7-nAChR. Injury on the fibroblast disturbs collagen accumulation.[25–27]

Individuals who smoke experience a condition known as hypoxia due to the nicotine content that stimulates the release of catecholamines, which leads to peripheral vasoconstriction and a decrease in perfusion rate.[14,26] This hypoxia disrupts the ability of cells to regenerate during the tissue healing process. In addition to causing hypoxia, vasoconstriction reduces monocytes and macrophages in the wound area, thereby increasing the risk of bacterial infection.[26,28] An increased risk of infection will slow down of the wound healing process.[14,26,28]

In addition to causing hypoxia, the bond between nicotine and non-neuronal cells will lead to changes in the cells, particularly affecting collagen expression, collagen activity, and DNA synthesis.[21,27] Disruption in collagen will lead to impaired activation of fibroblasts. At the inflammatory stage, this disorder causes disturbances in cell differentiation, migration, and mitogenesis, leading to a slowdown in the wound healing process. Disruption of proteoglycans leads to

disturbances in protein binding, which is essential for the formation of new cellular matrix in areas that have been injured.[26,29]

Other contents in cigarettes include carbon monoxide and hydrogen cyanide.[15,29] Both of these substances negatively affect the healing process. Carbon monoxide in the blood forms a complex called carboxyhemoglobin (CoHb), which disrupts the blood exchange process in the lungs, preventing oxygen that should have been delivered to the injured areas.[15,29] This disturbance will lead to the formation of reactive oxygen species (ROS), resulting in a prolonged inflammatory process. Hydrogen cyanide inhibits oxidative phosphorylation, thereby triggering disturbances in the mitochondria. This disturbance will lead to the occurrence of hypoxia and depletion of ATP, resulting in acidosis. This condition will disrupt the healing process of tissues, especially during the inflammatory and proliferative stages.[15,29,30]

In this case report, the patient was advised to stop smoking from 1.5 packs of cigarettes or 24 cigarettes per day. However, the patient admits to still having difficulty quitting entirely, so he reduced the number of cigarettes consumed. This is in line with the theory that individuals experiencing a decrease in nicotine levels in plasma develop cravings and withdrawal symptoms, leading the patient to have a desire to smoke.

The patient admitted that in the end, he smoked only three cigarettes per day after meals. This decline in smoking is acknowledged to be difficult for the patient, leading him to seek alternative options such as consuming low-sugar candies as a substitute for cigarettes. In the process of reducing cigarette consumption, there are several factors to consider, namely the help of the 5A: ask, advise, assess, assist, and arrange.[31] The first step is to "ask", which means to request the patient to stop smoking. "Advise" emphasizes the importance of why the patient should quit smoking, both in relation to the condition of oral lesions and overall health for the patient. Then "assess", which means asking for the smoker's sincere involvement in order to become a healthier individual. "Assist" involves the patient's family to always remind and ensure that he does not return to smoking. The last step is to "arrange" for the patient to have a follow-up regarding their smoking habits.[18,31]

These five aspects, ask, advise, assess, assist, and arrange will help reduce dependence on cigarettes.[32] With the reduction of dependence, the patient can become healthier because of the decrease in the amount of nicotine in the body, which will aid the binding process between oxygen and blood, thus preventing vasoconstriction from occurring.[10,25,31] The oxygenase in tissues, tissue proliferation, immune cell capability in the injured area, activation of fibroblasts, and re-epithelialization are expected to improve optimally. This condition will help hasten the healing process of the patient's ulcer.[10,26,28]

Considering that the condition of the patient's mouth cavity has improved, the patient's quality of life has also improved as a result of smoking cessation. Oral health-related quality of life (OHRQoL) is a multifaceted concept that encompasses various aspects related to oral health status.[32,33] There are several types of instruments are available to assess an individual's OHRQoL, and the Oral Health Impact Profile-14 (OHIP-14) is one of many assessments.[32] The OHIP-14 contains 14 questions designed to evaluate an individual's condition resulting from oral health anomalies.[32–35] The use of OHIP-14 is generally performed before and after treatment, with the results being compared. A decrease in OHIP scores indicates an improvement in the patient's condition following treatment. In this

case, there is a decrease in the OHIP-14 score. During the first visit the score was 50, and after treatment, it dropped to 32. The results of this score indicate an improvement in the patient's quality of life. At this stage, the patient was satisfied with the treatment because the ulcer had healed.[32–35]

Smoking cessation provides numerous health advantages that start immediately and get better with time.[38] In a few days after smoking cessation, the body begins to detoxify carbon monoxide from the bloodstream, which enhances the delivery of oxygen to tissue including oral mucosa tissue.[36,37] The increase of wound healing greatly increase longevity and quality of life. Other than wound healing, smoking cessation at any age helps lowering the mortality from vascular, respiratory and neoplastic diseases.[36,38]

The primary lesson from this case report is the importance of changing harmful habits. Patient education and motivation are crucial to achieve smoking cessation. Family involvement is important in supporting patients through the process to stop harmful habits.

The limitation of this article is that we did not perform a biopsy as the standard supporting examination for TUGSE. Because the patient feared that receiving a biopsy in the ulcer area could lead to additional pain. Another reason was the cost of the examination, which the patient would have to pay.

CONCLUSION

The exact cause of TUGSE is not yet known, but one of the predisposing factor is smoking. In cigarettes, there are various substances such as nicotine, carbon monoxide and hydrogen cyanide. All the substances had a role in delaying the wound healing process. A non-healing oral ulcer produces pain, which can disturb the quality of life and psychological well-being of the patient. Along with the proper medication for TUGSE, smoking cessation is a crucial factor in the wound healing process. The implication of this case report is to show the importance of medical practitioners constantly emphasizing the value of stopping smoking to help improve wound healing in the oral cavity.

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