SWISS DENTAL JOURNAL SSO

Science and Clinical Topics

ISSN 2296-6498
swissdentaljournal.org

Scientific article

Oral squamous cell carcinoma misinterpreted as reaction to chronic mechanical trauma: report of two cases and critical review of the literature

Accepted: December 12, 2025
DOI: 10.61872/sdj-2025-04-03
2025, Vol. 135

Fariba Ashrafi[1], Lisa Velte[1], Martina Schriber[1], Daniel Baumhoer[2], Michael M. Bornstein[1*]

[1] Department of Oral Health & Medicine, University Center for Dental Medicine Basel (UZB), University of Basel, Basel, Switzerland
[2] Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland

*Correspondence: Michael M. Bornstein
UZB | University Center for Dental Medicine Basel
Department of Oral Health & Medicine
Mattenstrasse 40, CH-4058 Basel
Telephone number: +41 61 267 25 45
email: michael.bornstein@unibas.ch

Keywords

Chronic mechanical trauma, Oral Potentially Malignant Disorders, Leukoplakia, Oral Squamous Cell Carcinoma, Epithelial Dysplasia, Biopsy, Histopathology

Abstract

Traumatic and reactive lesions of the oral mucosa, caused unintentionally by mechanical, thermal, or chemical irritation, may develop either acutely or chronically. In most cases, traumatic ulcerations heal within two weeks once the causative irritant is removed. However, persistent irritation can lead to chronic hyperkeratosis or mimic oral potentially malignant disorders (OPMDs). According to the World Health Organization (WHO), OPMDs such as leukoplakia, erythroplakia, proliferative verrucous leukoplakia, and oral submucous fibrosis carry an increased risk of malignant transformation into oral squamous cell carcinoma (OSCC). Clinically, reactive and potentially malignant lesions often present with overlapping features, rendering biopsy with histopathological evaluation essential for accurate diagnosis.

This article presents two clinical cases that were initially misdiagnosed as lesions resulting from chronic mechanical trauma (CMT). Histopathological examination revealed high-grade epithelial dysplasia (carcinoma in situ) in one patient and a moderately differentiated OSCC in the other. These cases highlight the importance of a structured diagnostic approach—including removal of mechanical irritants, histopathological assessment, and regular clinical follow-up to ensure early detection and appropriate management of suspicious lesions of the oral mucosa.

Introduction

Traumatic and reactive lesions of the oral mucosa can be caused unintentionally by mechanical, chemical, or thermal factors that may present acutely or chronically. They result in localized tissue damage due to single or repeated irritation. Mechanical trauma commonly arises from sharp or fractured teeth, poorly fitting dentures, orthodontic appliances, or parafunctional habits such as cheek or tongue biting. Thermal or chemical injuries occur following exposure to acids or excessively hot foods and beverages. Furthermore, an injury or irritation can be caused by a patient's manipulation or self-mutilation in the context of a psychiatric illness.

According to the latest World Health Organization (WHO) classification (1), oral potentially malignant disorders (OPMDs) comprise leukoplakia, erythroplakia, erythroleukoplakia, proliferative verrucous leukoplakia, oral submucous fibrosis (OSF), oral lichenoid lesions, oral lichen planus, smokeless tobacco-associated keratosis, oral graft-versus-host disease, lupus erythematosus, palatal changes from “reverse smoking,” and several hereditary cancer syndromes such as Fanconi anemia, dyskeratosis congenita, xeroderma pigmentosum, Li-Fraumeni-syndrome, Bloom syndrome, ataxia telangiectasia, and Cowden syndrome. All OPMDs carry an elevated risk of malignant transformation into oral squamous cell carcinoma (OSCC)(2), which can be increased by additional risk factors such as tobacco use, alcohol consumption, betel nut chewing, viral infections, or immunosuppression.

Clinically, traumatic lesions often present as painful ulcers with erythematous borders. They typically heal within 7–14 days, usually after eliminating the irritant. However, persistent trauma may induce chronic hyperkeratosis, resulting in whitish mucosal thickening that may mimic leukoplakia. Histopathologically, traumatic ulcers display acute to chronic inflammation, while eosinophilic ulcerations (3, 4)—also known as traumatic ulcerative granulomas with stromal eosinophilia (TUGSE)—are rare, benign, and self-limiting lesions that might be caused by immune-mediated processes.

Oral leukoplakia manifests as non-wipeable white plaques ranging from simple hyperkeratosis to epithelial dysplasia, whereas erythroplakia appears as red or mixed red and white (“speckled”) patches of the oral mucosa with a higher likelihood of underlying dysplasia or even invasive carcinoma. Proliferative verrucous leukoplakia (PVL) is a multifocal, progressive disease that often affects elderly female patients and has a high rate of malignant transformation. As chronic mechanical trauma (CMT) can clinically exhibit similar features as leukoplakia (white patches) and / or erythroplakia (red patches), a differential diagnosis of OPMD should always be included for suspected traumatic lesions. Another frequent OPMD is oral lichen planus (OLP), a chronic, immune-mediated inflammatory disorder that usually presents with whitish, lace-like striae (Wickham striae), and also areas, with atrophic or erosions and even ulcers (more reddish component of OLP). Due to the systemic nature of the disease, OLP can usually be differentiated more easily from localized lesions stemming from CMT. Generally, for whitish, redish or mixed mucosal lesions, the most important differential diagnosis is epithelial dysplasia and oral squamous cell carcinoma (OSCC).

The aim of this article is to present and discuss two clinical cases initially misdiagnosed as traumatic oral lesions, which were ultimately found to represent carcinoma in situ and OSCC. The article highlights the importance of early diagnosis of suspicious mucosal findings when dealing with atypical oral mucosal lesions.

Report of two cases

Both patients included here in this report have given their permission to use their clinical data by signing the institutional consent form of the University Center for Dental Medicine Basel (UZB).

Case 1

Medical history
A male patient, born in 1973, has no relevant medical findings and is a non-smoker. During his initial consultation at the Department of Oral Health & Medicine (OHM) in March 2024, he reported to have noted superficial changes on his tongue for the past 2 to 3 years. Initially, the lesion had been painful. When he first visited his private dentist, bruxism and related craniomandibular disorder (CMD) were suspected and a respective therapeutic approach was initiated. The patient had then undergone various occlusal splint therapies, but none were successful in reducing or healing the tongue lesion. Recently, he had noticed a worsen-

ing of the condition and therefore had contacted OHM directly for a second opinion.

Clinical findings
During the initial oral examination at OHM, an inhomogeneous, partially ulcerated red and white ("speckled") mucosal lesion (erythroleukoplakia) measuring approximately 3 cm in diameter and that felt slightly indurated upon palpation was observed on the left side of the tongue (Figure 1). To rule out dysplasia, an excision of the lesion was recommended and discussed with the patient.

Diagnostics and Histopathology
The lesion was completely excised with a safety margin under local anesthesia with a scalpel on the same day of the initial consultation. The histopathological analysis revealed a moderately differentiated squamous cell carcinoma, which focally reached the resection margin (Figure 2).

Figure 1. Clinical presentation at the initial visit: an inhomogeneous, partially ulcerated erythroleukoplakia on the left border of the tongue.

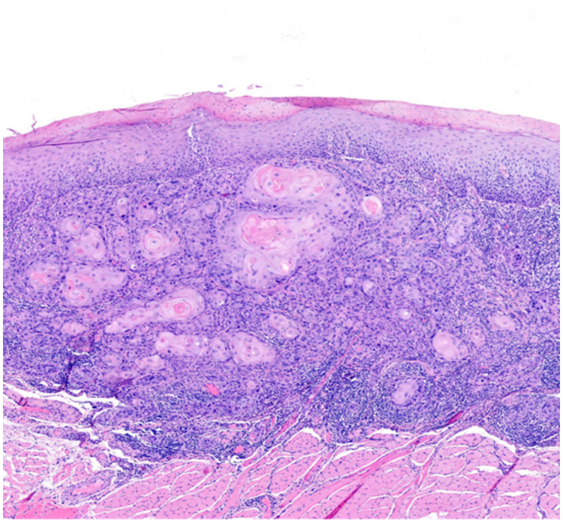

Figure 2. The histology of the excisional biopsy shows infiltration of the subepithelial stroma by a moderately differentiated and keratinizing squamous cell carcinoma. The overlying epithelium demonstrates marked hyperkeratosis and moderate epithelial dysplasia (H&E, 50x).

Follow up and further procedures
The patient was followed up one week after the excision, and all sutures were removed. He was informed of the histopathological findings, including the need for a secondary excision for further diagnosis at the university hospital including an evaluation by the interdisciplinary head and neck tumor board.

At the university hospital, approximately five weeks after the first excision at OHM, the patient underwent a left partial glossectomy, a reconstruction of the resulting defect with a split-thickness skin graft from the left thigh, and a neck dissection of levels I–III on the left side. The final diagnosis for the lesion was a $pT_1\ pN_0\ M_0$ OSCC (Stage I). The patient was subsequently scheduled for regular follow-up examinations at the university hospital.

Case 2

Medical history
A male patient, born in 1983, presented to OHM in September 2022 with a persistent, burning sensation on the right side of his tongue. The patient did not take any medication, was in good general health and a non-smoker. He reported noticing a change on the right side of his tongue in spring 2021 and reported that this lesion had been excised elsewhere and the histopathological assessment concluded a non-specific hyperkeratosis. However, the lesion quickly recurred and an orthodontic assessment to determine if the tooth 47 was the potential cause of the lesion due to CMT was initiated. As the lesion continued to grow and had also become symptomatic (burning sensation), the patient contacted OHM for a second opinion prior to initiating orthodontic therapy for the tooth 47.

Clinical findings
At the initial examination at OHM, there was an extended whitish area measuring about 2 to 3 cm with verrucous aspects and a central ulceration that felt slightly indurated upon palpation. The overall clinical aspect was irregular and inhomogeneous (Figure 3). The patient was informed that an excision of the inhomogeneous lesion was recommended to rule out dysplasia.

Diagnostics and Histopathology

In October 2022, the erythroleukoplakic lesion was completely excised under local anesthesia using a scalpel and ensuring a safety margin. The histopathological examination revealed a high-grade dysplasia with clear resection margins.

Follow up and further procedures

After suture removal and discussing the histopathological diagnosis, follow-up oral medicine examinations were scheduled in an interval of three months in the first year. The wound healed without irritation or complications and the right side of the tongue exhibited only minimal scarring (Figure 5).

Figure 3. Extended whitish, irregular, inhomogeneous lesion with central ulceration on the right side of the tongue.

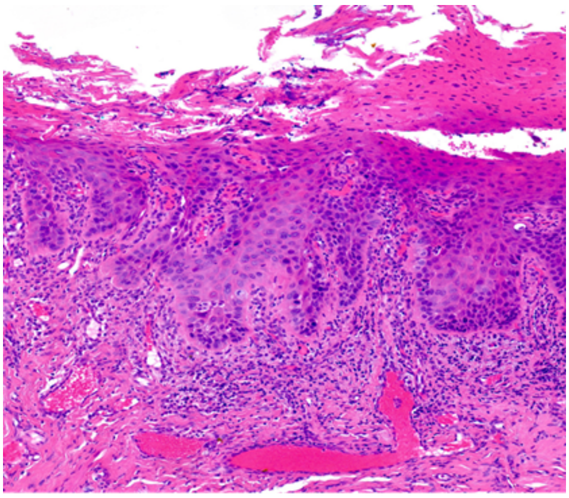

Figure 4. The histology of the excisional biopsy reveals high-grade dysplasia of the oral mucosa with ulceration and marked secondary inflammation (H&E, 100x).

During the follow-up examinations, the mucosa remained clinically stable for several months. However, after approximately eight months, a small whitish, exophytic lesion (about 3–4 mm in diameter) appeared at the same location on the right lateral tongue (Figure 6). The lesion was excised under local anesthesia using a scalpel, and the specimen was submitted for histopathological evaluation. The analysis revealed squamous epithelium with mild epithelial dysplasia and slight chronic subepithelial inflammation, without any signs of malignancy. Healing again proceeded without complications.

Figure 5. Healed region 3 months after the excisional biopsy at the right border of the tongue exhibiting only minimal scarring.

Figure 6. Former site of the excisional biopsy at the right border of the tongue before the second excisional biopsy (eight months after the initial intervention).

Subsequent follow-up visits were conducted every 3–6 months. In early 2024, mild recurrent leukoplakic changes were noted at the previous excision site (Figure 7). For diagnostic clarification, another excisional biopsy was performed under local anesthesia. Histopathological examination again demonstrated mild epithelial dysplasia, discrete lichenoid inflammation, and parakeratosis.

The patient continued to attend regular follow-up examinations at six-month intervals (Figure 8). As of the most recent clinical evaluation in early 2025, the right lateral tongue showed a stable, homogeneous mucosal surface with only minimal scarassociated whitish changes and no clinical signs of recurrence.

Figure 7. Former site of the excisional biopsy at the right border of the tongue before the third excision (appr. 1.5 years after the initial intervention).

Figure 8. Former site of the excisional biopsy at the right border of the tongue 6 months after the third intervention.

Discussion

The two cases presented here highlight that oral lesions initially thought to be related to chronic mechanical trauma (CMT) can in fact represent epithelial dysplasia or even squamous cell carcinoma (OSCC). The findings presented here emphasize the importance of early biopsy assessment in all persistent, ulcerated, or inhomogeneous oral mucosal lesions to avoid diagnostic delay. The cases represent common diagnostic challenges in dental and oral medicine practice, where benign-appearing lesions can mask underlying malignancy.

According to the current literature, chronic mechanical irritation has long been discussed as a potential etiological factor in oral carcinogenesis. However, systematic reviews have demonstrated only weak or inconsistent evidence supporting a direct causal relationship between CMT and OSCC (5). Instead, chronic trauma may act as a co-factor in the presence of additional carcinogenic influences such as tobacco or alcohol use, poor oral hygiene (6, 7), viral infections, particularly due to human papillomavirus (HPV)(8), or pre-existing oral potentially malignant disorders (OPMDs) (9-11).

From a pathophysiological standpoint, chronic irritation of the mucosa may disturb normal wound healing mechanisms, leading to increased cellular proliferation, impaired apoptosis, and DNA damage (12, 13). Inflammatory mediators including cytokines, matrix metalloproteinases (MMPs), and cyclooxygenase-2 (COX-2) play important roles in this process (14, 15). These molecular alterations may, in turn, create a microenvironment facilitating malignant transformation (16, 17). The World Health Organization (WHO) currently does not include chronic trauma as an OPMD (1). Nevertheless, in the presence of persistent mucosal irritation, clinicians should maintain diagnostic vigilance. Traumatic ulcers usually heal with-in 7–14 days once the irritant is removed (18-20), and this is happening without the necessity to use further topical ointments or gels. If a lesion persists beyond this period or shows irregular, indurated or inhomogeneous (“speckled”) features, further diagnostic evaluation including histopathology is warranted (21, 22) without further delay. In highly suspicious cases, biopsy taking even at the initial examination is also a valuable option to reduce potential delay of the diagnosis as it had been performed for the first case described here. For the second case presented, the excisional biopsy was scheduled two weeks after the initial examination as the patient did not want the intervention upon his first visit.

A structured diagnostic approach is therefore recommended for clinical practice when CMT is suspected: (a) identification and elimination of potential irritants, (b) short-term follow-up within 1–2 weeks, (c) biopsy of non-healing or atypical lesions, and (d) referral to an oral medicine specialist when in doubt (23). The two cases presented underline the necessity of such a structured process as both mucosal lesions were initially misinterpreted as traumatic but were later confirmed histopathologically as dysplasia and invasive carcinoma, respectively. It should be noted that for malignant lesions, histopathologically clear margins of 5 mm in the specimens are needed (24). Thus, clinically highly suspicious mucosa lesions should be ideally excised with a safety margin of approximately 1 cm.

For lesions under surveillance, a regular follow-up is crucial. After excision of low to mildly dysplastic lesions, a 6-month interval seems adequate, whereas lesions with moderate to severe dysplasia should be followed every 3 months (23). The relevance of this approach can also be seen in the second case presented here, where two further biopsies were taken during follow-up after the initial excision of the lesion on the right border of the tongue. In anatomically challenging or multifocal cases, cytopathology using a brush biopsy technique may be considered to complement histopathological assessment, balancing greater area coverage with lower diagnostic precision (23).

Even after excision or laser ablation, the risk of recurrence and subsequent malignant transformation cannot be completely eliminated (25, 26). Therefore, long-term clinical monitoring remains indispensable. Clinically homogeneous lesions classified as mild dysplasia may be observed, e.g. do not need to be excised with histopathologically clear margin, while all medium to high-grade dysplastic or histologically suspicious lesions should be excised exhibiting clear tissue margins. If clinical and histopathological findings are incongruent, a second biopsy from another site or referral for a second opinion to a specialist in oral (and maxillofacial) surgery or oral medicine should be pursued without delay.

Conclusions

Persistent lesions of the oral mucosa with an inhomogeneous aspect should always be carefully assessed. Once the source of irritation has been removed and there is no clear improvement within 7 to 14 days, a biopsy must be performed to avoid unnecessary delay. Early identification of dysplasia or malignancy is a key factor in minimizing diagnostic delays and improving outcomes for patients with oral cancer and its precursors.

Acknowledgements

The authors do not report any possible conflict of interest related to this study.

Zusammenfassung

Einleitung

Traumatische Läsionen der Mundschleimhaut entstehen durch mechanische, thermische oder chemische Reize und können sowohl akut als auch chronisch auftreten. In den meisten Fällen heilen traumatische Ulzerationen innerhalb von zwei Wochen nach Entfernung der auslösenden Ursache vollständig ab. Persistierende Irritationen hingegen können zu einer chronischen Hyperkeratose führen oder klinisch potenziell maligne Erkrankungen der oralen Mukosa (Oral Potentially Malignant Disorders, OPMD) imitieren. Zu den OPMDs zählen laut Weltgesundheitsorganisation (WHO) unter anderem die orale Leukoplakie, die Erythroplakie, die proliferative verruköse Leukoplakie und die orale submuköse Fibrose; allen gemeinsam ist ein erhöhtes Risiko für die Entstehung eines oralen Plattenepithelkarzinoms (Oral Squamous Cell Carcinoma, OSCC). Da sich traumatische und potenziell maligne Läsionen häufig klinisch ähneln, ist die histopathologische Untersuchung von entscheidender Bedeutung, um eine Fehldiagnose und daraus resultierende Diagnose- und/oder Therapieverzögerungen zu vermeiden.

Material und Methoden

In dieser Arbeit werden zwei klinische Fälle aus der Klinik für Oral Health & Medicine (OHM), Universitäres Zentrum für Zahnmedizin Basel (UZB) vorgestellt, bei denen initial von einem chronischen mechanischen Trauma (CMT) ausgegangen wurde. Beide Patienten waren männlich, Nichtraucher und allgemeinmedizinisch gesund. In beiden Fällen bestanden seit längerer Zeit persistierende Läsionen an der Zunge, die trotz Beseitigung potenzieller Irritationsquellen und diverser konservativer Behandlungsansätze keine Heilungstendenz zeigten. Aufgrund des inhomogenen Erscheinungsbildes und des Verdachts auf eine dysplastische oder maligne Veränderung erfolgte jeweils eine vollständige Exzision der Läsion unter Lokalanästhesie mit anschliessender histopathologischer Untersuchung.

Resultate

Im ersten Fall zeigte die Histopathologie ein mässig differenziertes orales Plattenepithelkarzinom. Der Patient wurde ans Universitätsspital überwiesen, wo eine partielle Glossektomie, eine Spalthauttransplantation sowie eine selektive zervikale Lymphknotendissektion durchgeführt wurden. Die postoperative Heilung verlief komplikationslos, und der Patient befindet sich seither in regelmässiger onkologischer Nachsorge am Zentrumsspital.

Im zweiten Fall ergab die histopathologische Untersuchung eine hochgradige Epitheldysplasie mit dysplasiefreien Resektionsrändern. Während der Nachsorge – zunächst in dreimonatigen, später in halbjährlichen Abständen – traten an derselben Stelle rezidivierende leukoplakische Veränderungen mit milden Dysplasien auf, die zweimal exzidiert wurden. Etwas mehr als zwei Jahre nach der Erstdiagnose zeigte sich die Schleimhaut stabil und ohne klinische Hinweise auf ein Rezidiv.

Diskussion

Die vorgestellten Fälle verdeutlichen die diagnostische Herausforderung, klinisch benigne erscheinende Läsionen korrekt zu beurteilen. Chronisch mechanische Traumata können in Einzelfällen mit dysplastischen oder malignen Veränderungen verwechselt werden oder sogar deren Entstehung begünstigen. Ein strukturiertes diagnostisches Vorgehen ist daher essenziell: Nach Beseitigung möglicher Irritationsquellen sollte eine kurzfristige klinische Kontrolle nach ein bis zwei Wochen erfolgen. Persistierende, ulzerierte oder inhomogene Läsionen sollten dann biopsiert werden. Bei Nachweis von Dysplasien sind regelmässige Nachkontrollen angezeigt – bei milden Dysplasien alle sechs Monate, bei moderaten oder schweren Dysplasien alle drei Monate. Trotz chirurgischer Entfernung bleibt ein Restrisiko für Rezidive oder maligne Transformationen bestehen, weshalb eine langfristige klinische Überwachung notwendig ist.

Résumé

Introduction

Les lésions traumatiques de la muqueuse buccale résultent d'une irritation mécanique, thermique ou chimique involontaire et peuvent se développer de manière aiguë ou chronique. Dans la majorité des cas, les ulcérations traumatiques guérissent spontanément en deux semaines après l'élimination du facteur causal. En revanche, une irritation persistante peut entraîner une hyperkératose chronique ou imiter des troubles potentiellement malins de la cavité buccale (Oral Potentially Malignant Disorders, OPMD). Selon la classification actuelle de l'Organisation mondiale de la santé (OMS), les OPMD comprennent la leucoplasie, l'érythroplasie, la leucoplasie verruqueuse proliférative, la fibrose sous-muqueuse buccale et le lichen plan buccal, toutes associées à un risque accru de transformation maligne en carcinome épidermoïde buccal (Oral Squamous Cell Carcinoma, OSCC). Comme les lésions traumatiques et les OPMD présentent souvent des similitudes cliniques, l'examen histopathologique est essentiel pour établir un diagnostic précis et éviter des retards thérapeutiques.

Matériels et méthodes

Cette étude présente deux observations cliniques issues du département de médecine orale (Oral Health & Medicine, OHM), initialement interprétées comme des traumatismes mécaniques chroniques (Chronic Mechanical Trauma, CMT). Les deux patients, des hommes non-fumeurs et en bonne santé générale, présentaient depuis plusieurs années des lésions persistantes de la langue, malgré la suppression des sources d'irritation et diverses tentatives thérapeutiques conservatrices. En raison de l'aspect inhomogène et persistant des lésions, une excision complète a été réalisée sous anesthésie locale, suivie d'une analyse histopathologique. Les patients ont ensuite bénéficié d'un suivi clinique régulier afin de dépister précocement toute récidive ou nouvelle altération muqueuse.

Résultats

Dans le premier cas, l'analyse histopathologique a révélé un carcinome épidermoïde buccal modérément différencié. Le patient a été orienté vers le service de chirurgie maxillo-faciale de l'hôpital universitaire, où une glossectomie partielle, une greffe de peau mince et un curage ganglionnaire cervical (niveaux I–III) ont été effectués. La cicatrisation postopératoire a été satisfaisante, et le patient reste sous surveillance oncologique régulière.

Dans le second cas, l'examen histologique a mis en évidence une dysplasie épithéliale de haut grade (carcinome in situ) avec des marges d'excision saines. Durant le suivi à intervalles trimestriels, puis semestriels, de petites lésions récidivantes à type de leucoplasie avec dysplasie légère ont été observées et excisées. Deux ans après la première intervention, la muqueuse linguale demeure stable, sans signe clinique de transformation maligne.

Discussion

Ces deux observations illustrent la difficulté diagnostique que représentent les lésions buccales d'apparence bénigne. Un traumatisme mécanique chronique peut être confondu avec une lésion précancéreuse ou maligne, voire favoriser leur développement. Une approche diagnostique structurée est indispensable: (a) identification et élimination des irritants, (b) contrôle clinique à court terme
(1 à 2 semaines), (c) biopsie des lésions non cicatrisées ou atypiques, et (d) orientation vers un spécialiste en médecine orale en cas de doute. Après exérèse de lésions dysplasiques légères, un suivi semestriel est suffisant, tandis que pour les dysplasies modérées à sévères, un suivi trimestriel est recommandé. Malgré le traitement chirurgical, le risque de récidive ou de transformation maligne ne peut être totalement exclu, justifiant une surveillance clinique à long terme.

References

1. Baumhoer D, Reichert TE. Aktuelle WHO-Klassifikation der oralen potenziell malignen Erkrankungen (OPMD). Die MKG-Chirurgie. 2024;17(2):72-81.

2. Pérez MA, Raimondi AR, Itoiz ME. An experimental model to demonstrate the carcinogenic action of oral chronic traumatic ulcer. J Oral Pathol Med. 2005;34(1):17-22.

3. Hamie L, Hamie M, Kurban M, Abbas O. Eosinophilic ulcer of the oral mucosa: An update on clinicopathologic features, pathogenesis, and management. International Journal of Dermatology. 2022;61(11):1359-63.

4. Segura S, Pujol RM. Eosinophilic ulcer of the oral mucosa: a distinct entity or a non-specific reactive pattern? Oral Dis. 2008;14(4):287-95.

5. Pentenero M, Azzi L, Lodi G, Manfredi M, Varoni E. Chronic mechanical trauma/irritation and oral carcinoma: A systematic review showing low evidence to support an association. Oral Dis. 2022;28(8):2110-8.

6. Kawakita D, Lee YA, Li Q, Chen Y, Chen CJ, Hsu WL, et al. Impact of oral hygiene on head and neck cancer risk in a Chinese population. Head Neck. 2017;39(12):2549-57.

7. Hashim D, Sartori S, Brennan P, Curado MP, Wünsch-Filho V, Divaris K, et al. The role of oral hygiene in head and neck cancer: results from International Head and Neck Cancer Epidemiology (INHANCE) consortium. Ann Oncol. 2016;27(8):1619-25.

8. Farsi NJ, Rousseau MC, Schlecht N, Castonguay G, Allison P, Nguyen-Tan PF, et al. Aetiological heterogeneity of head and neck squamous cell carcinomas: the role of human papillomavirus infections, smoking and alcohol. Carcinogenesis. 2017;38(12):1188-95.

9. van der Waal I. Oral lichen planus and oral lichenoid lesions; a critical appraisal with emphasis on the diagnostic aspects. Med Oral Patol Oral Cir Bucal. 2009;14(7):E310-4.

10. Brennan M, Migliorati CA, Lockhart PB, Wray D, Al-Hashimi I, Axéll T, et al. Management of oral epithelial dysplasia: a review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103 Suppl:S19.e1-2.

11. Holmstrup P, Vedtofte P, Reibel J, Stoltze K. Long-term treatment outcome of oral premalignant lesions. Oral Oncol. 2006;42(5):461-74.

12. Schottenfeld D, Beebe-Dimmer J. Chronic inflammation: a common and important factor in the pathogenesis of neoplasia. CA Cancer J Clin. 2006;56(2):69-83.

13. Singhvi HR, Malik A, Chaturvedi P. The Role of Chronic Mucosal Trauma in Oral Cancer: A Review of Literature. Indian J Med Paediatr Oncol. 2017;38(1):44-50.

14. Tampa M, Mitran MI, Mitran CI, Sarbu MI, Matei C, Nicolae I, et al. Mediators of Inflammation – A Potential Source of Biomarkers in Oral Squamous Cell Carcinoma. J Immunol Res. 2018;2018:1061780.

15. Patel JB, Shah FD, Joshi GM, Patel PS. Clinical significance of inflammatory mediators in the pathogenesis of oral cancer. J Cancer Res Ther. 2016;12(2):447-57.

16. Mameli A, Murgia M, Orrù G, Casu C. Correlation between chronic mucosal trauma and oral cancer: a case report and review of the literature. WORLD CANCER RESEARCH JOURNAL. 2021;8:1-5.

17. Piemonte ED, Lazos JP, Gilligan GM, Panico RL, Werner LC, Yang YH, et al. Chronic mechanical irritation enhances the effect of tobacco and alcohol on the risk of oral squamous cell carcinoma: a case-control study in Argentina. Clin Oral Investig. 2022;26(10):6317-26.

18. Orbak R, Bayraktar C, Kavrut F, Gündogdu C. Poor oral hygiene and dental trauma as the precipitating factors of squamous cell carcinoma. Oral Oncology Extra. 2005;41(6):109-13.

19. Rotundo LD, Toporcov TN, Biazevic GH, de Carvalho MB, Kowalski LP, Antunes JL. Are recurrent denture-related sores associated with the risk of oral cancer? A case control study. Rev Bras Epidemiol. 2013;16(3):705-15.

20. Fan H, Yoon KY, Kim SM, Myoung H, Lee JH, Kim MJ. Relationship between squamous cell carcinoma of the tongue and the position of dental prosthesis. J Adv Prosthodont. 2015;7(2):129-37.

21. Dayal, Reddy R, Anuradha Bhat K. Malignant potential of oral submucous fibrosis due to intraoral trauma. Indian J Med Sci. 2000;54(5):182-7.

22. Fitzpatrick SG, Cohen DM, Clark AN. Ulcerated Lesions of the Oral Mucosa: Clinical and Histologic Review. Head Neck Pathol. 2019;13(1):91-102.

23. Kunkel M, Bengel W, Blume M, Boehme P, Buchholz GE, Follmann M, et al. S2k-Leitlinie: Diagnostik und Management von Vorläuferläsionen des oralen Plattenepithelkarzinoms in der Zahn-, Mund- und Kieferheilkunde. Der MKG-Chirurg. 2011;4:206-12.

24. Shapiro M, Salama A. Margin analysis. squamous cell carcinoma of th oral cavity. Oral Maxillofac Surg Clin North Am. 2017;29:259-267.

25. Lodi G, Sardella A, Bez C, Demarosi F, Carrassi A. Interventions for treating oral leukoplakia. Cochrane Database Syst Rev. 2006(4):Cd001829.

26. O'Shaughnessy JA, Kelloff GJ, Gordon GB, Dannenberg AJ, Hong WK, Fabian CJ, et al. Treatment and prevention of intraepithelial neoplasia: an important target for accelerated new agent development. Clin Cancer Res. 2002;8(2):314-46.