Actinic Cheilitis vs Squamous Cell Carcinoma of the Lip: Two Case Reports and a Brief Review

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Abstract

Lip squamous cell carcinoma (Lip SCC) and actinic cheilitis are chronic lip lesions with quite similar clinical features that can be induced by ultraviolet radiation. This report aimed to describe the differences between lip SCC and actinic cheilitis, and the importance of early diagnosis of both diseases. Case 1, a 78-year-old man visited the Oral Medicine Clinic with a chief complaint of persistent ulcers on the lower lip for 2 months. He has received various topical medications, but there was no improvement. He is a heavy smoker and alcoholic, and frequently exposed to direct sunlight daily in his workplace. Extraoral examination showed a yellowish ulcer with indurated border on the lower lip. A diagnosis of lip SCC was confirmed by histopathological examination. He had surgical removal of the lesion. Case 2, a 24-year-old female caddie admitted to the Oral Medicine Clinic with a chief complaint of painful and persistent dryness and scaly on her lower lip for 3 months. Extraoral examination showed erosions and yellow crusts on the lower lip. A diagnosis of actinic cheilitis was made. The patient was prescribed 0.2% chlorhexidine digluconate gel, ibuprofen, and multivitamins. The lesion showed significant improvement after 14 days of treatment. History taking and response to initial treatment have an important role in the diagnostic process of Lip SCC and actinic cheilitis.

Dental practitioners should be aware and competent enough to identify patients with chronic lip lesions that may be malignant lesions or potentially malignant disorders.

Keywords: Actinic cheilitis, chronic inflammation, lip SCC, ultraviolet.


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Introduction

It is well known that the lips are frequently exposed to a variety of irritants and carcinogenic agents, such as ultraviolet (UV) radiation and tobacco, which are the major cause of lip cancer. Chronic lesions of the lips induced by UV radiation and tobacco should be considered a potential malignant lesion or has a potential for malignant transformation.¹ ² Chronic lesions of the lips such as squamous cell carcinoma of the lip (Lip SCC) and actinic cheilitis, have an identical clinical appearance. History taking is very important in identifying the risk factors to establish the diagnosis and proper treatment plan. The malignant lesions must be diagnosed early since a delayed diagnosis can lead to progression to more advanced stages, more extensive treatments, lower chance of recovery, and greater psychological morbidity.³

Squamous cell carcinoma of the lip (Lip SCC) is a malignant tumor that develops from stratified squamous epithelium. Lip cancer occupies up to 25%-30% of all malignant tumors in the oral cavity, especially on the lower lip. Squamous cell carcinoma is usually caused by many risk factors, including long-term sun exposure, smoking (especially pipes and cigars), alcohol, and many other factors. The clinical signs of SCC on the lower lip can be determined by examining the presence of ulcers and erythema with elevation at the edges of the lesion.⁴ ⁵ ⁶

Actinic cheilitis, which can be characterized by various changes in the epithelial

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lining of the lips, are mainly caused by long-term and chronic sun exposure. The previous studies showed that prevalence of actinic cheilitis range from 5.6% to 38.8%.[7,8,9,10,11,12,13,14] The prevalence of actinic cheilitis is higher among fair-skinned populations and those closer to the equator where there is more UV exposure. Men are affected more than women, likely due to their comparatively increased work in the sun and less use of protective lip balm and cosmetics.[7]

Actinic cheilitis is known to have the potential for malignant transformation, and estimated 95% of SCC of the lip originate from AC.[2,15] Clinically, AC can cause lip atrophy, erythema, and ill-defined vermilion borders. The presence of mouth ulcers that fail to heal efficiently, bleeding, and hardened borders may suggest malignant transformation. This condition can be found in various clinical signs, therefore it is often disregarded by dentists.[1,16,17,18,19]

In this report, we present 2 cases of lip chronic lesions, OSCC dan AC, and we review the literature regarding the differences of the etiopathogenesis and clinical characteristics between the two oral diseases.

Case Report

Case 1

A 78-year old man visited to the Oral Medicine Department with a chief complaint of painful mouth ulcer on the lower lip that was extending for the last 2 months. The ulcer caused discomfort when eating and talking.

The patient had previously prescribed some medications, such as acyclovir cream, steroid ointment, and antibiotic, but there was no significant improvement. For the last 62 years, the patient has had a habit of smoking 30 cigarettes and drinking 1-1.5 liters (2-3 bottles) of alcoholic beverages per day.

Extraoral examination revealed a yellowish ulcer, painless, measuring about 1 x 1.5 cm in size, roughly oval in shape with elevated and indurated borders on the lower lip (Figure 1). A working diagnosis of Lip SCC and the differential diagnosis of actinic cheilitis were made. The blood test revealed no abnormalities. Moreover, ultrasound examination of the right and left thyroid showed no enlargement, and no intralesional vascularization. Histopathological examination of the incisional biopsy showed the presence of a tumor mass that was formed by the proliferation of squamous epithelial cellular anaplasia cells accompanied by the formation of keratin, necrosis, bleeding, and inflammation (Figure 2). Based on these findings, a definitive diagnosis of keratinized squamous cell carcinoma on the lower lip was made. The patient was referred to oncologist. We gave advice and support for effective smoking cessation and alcohol consumption to the patient 14 days later, the vermilionectomy was performed by oncologist. The patient was recommended to do regular check-ups for the next three-six months.

Figure 1. Clinical features of SCC of the lip in 78-years old man (A). A yellowish ulcer, about 1 x 1.5 cm in size, roughly oval in shape with elevated and indurated borders on the lower lip. (B, C) Lip condition after surgery. (D) Histopathologic feature of the lesion showing the presence of keratinization and cellular anaplasia (40x magnification). (E) a. Mitotic; b. Eosinophilic cytoplasm; c. Large nuclei; d. Intercellular nuclei; e. Bizarre nuclei (200x magnification).

Figure 2. Clinical features of actinic cheilitis a 24-year old female caddie (A). At the First visit, erosions and yellow crusts on the lower lip. (B). At the second visit, the lesions were completely resolved after 2 weeks of treatment.

Case 2

A 24-year old woman admitted to the Oral Medicine Clinic with a chief complaint of painful and persistent dryness and scaly on her lower lip for 3 months, and a mild fever for a day 3 weeks.
ago. Her occupation is a golf caddy who was exposed to prolonged sunlight throughout the day for five years. She did not give history of tobacco and alcohol use.

Extraoral examination showed erosions and yellow crusts on the lower lip. Intraoral examination showed no abnormalities. A working diagnosis was suspected actinic cheilitis, and the differential diagnosis include Lip SCC, herpes-associated erythema multiforme (HAEM), and herpes labialis. The patient was prescribed a topical application of 0.2% chlorhexidine digluconate gel, 400mg ibuprofen 3 times daily, and multivitamin as supportive therapy for 1 week.

The patient was also instructed to use petroleum jelly when working in the direct sunlight. After 2 weeks of follow up, the ulcers on the lower lip was recovered significantly. The patient is recommended to continue the treatment and do regular check-ups for the next six months.

Discussion

Lip SCC and AC are chronic lesions on the lip that can be caused by direct exposure to sunlight. However, tobacco and alcohol consumption routinely may be associated with an increase in the risk of lip SCC in elderly patients as seen in the first case. Other similarities and differences in the characteristics of these two oral diseases can be seen in Table 1.

According to several studies, exposure to ultraviolet light can cause lip SCC which is characterized by DNA damage, inflammation, immunosuppression, and carcinogenesis. Exposure to UV light induces membrane tyrosine kinase phosphorylation, triggers a change in epidermal growth factor (EGFRs), activates Ras and Raf, as well as activates and dissociates nuclear factor-kB from inhibitor B complexes. These events trigger the production of cytokines, interleukin (IL)-1, tumor necrosis factor, and IL-6. This signaling cascade can also cause arachidonic acid cascade activation, which stimulates oxidative and phosphorylation reactions. These reactions induce signal transduction and trigger secondary histamine release from mast cell degranulation and keratinocytes. This pathway causes the transcription factors to translocate into the nucleus and changes the gene expression.

Actinic cheilitis, which is an OPMD lesion, is caused by degenerative changes in the vermilion of the lips, especially on the lower lip. This lip condition is usually caused by chronic exposure to ultraviolet (UV) light. This lesion causes the epithelial tissue to be altered and associated with the potential for increased immune cell infiltration that can develop into oral squamous cell carcinoma (OSCC). UV light is absorbed by DNA, phospholipid membrane, and trans urocanic acid (UCA). The presence of DNA photoproducts can cause a mutation of p53 and tumor suppressor genes (TSG), a production of lipid-derived mediator membranes such as arachidonic acid, platelet-activating factor, and cis-UCA that can alter intracellular signaling. Dysregulation of the cytokine environment can lead to inflammation, alteration in T cell homeostasis, and immunosuppression. The absence of a p53-induced protective mechanism results in the accumulation of additional mutations and chromosomal instability that culminate in abnormal keratinocyte proliferation.

Alcohol consumption was also considered as the risk factor of lip SCC in the first case. Alcoholic beverages, such as wine, beer, and liquor, seem to mediate a synergistic effect. The alcohol concentration in saliva and blood circulation appears to be quite similar. Alcohol consumption seems to enhance the effect of carcinogens by: (1) dehydrating the oral mucosa, (2) increasing mucosal permeability through

<table>
<thead>
<tr>
<th>RISK FACTORS</th>
<th>OSSC</th>
<th>ACTINIC CHEILITIS</th>
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<tbody>
<tr>
<td>Age</td>
<td>&gt;50 years old</td>
<td>&gt;45 years old</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Etiology</td>
<td>Alcohol, tobacco, sunlight exposure</td>
<td>Prolonged sun exposure</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian</td>
<td>Caucasian</td>
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<td>Pathogenesis</td>
<td>Mutations in the TP53 gene make p53 unable to control cell proliferation, resulting in inefficient DNA repair, and allowing many cells exposed to mutagens to replicate damaged genetic material, spreading changes incorporated into the genome</td>
<td>Exposure to ultraviolet light can cause lip SCC which is characterized by DNA damage, inflammation, immunosuppression, and carcinogenesis. Exposure to UV light induces membrane tyrosine kinase phosphorylation, triggers a change in epidermal growth factor (EGFRs), activates Ras and Raf, as well as activates and dissociates nuclear factor-kB from inhibitor B complexes.</td>
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<tr>
<td>Clinical Features</td>
<td>Plaque keratosis, ulceration, indurated lesion margins, and redness</td>
<td>Lip atrophy, dryness, erythema, and unclear vermilion margins.</td>
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<td>Treatment</td>
<td>Surgery, chemotherapy, radiation</td>
<td>Topical cream/gel, limiting further sun exposure, applying lip balms or moisturizers, vermilionectomy, photodynamic therapy, CO2 laser, cryosurgery.</td>
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Table 1. A comparison of lip OSCC and actinic cheilitis.
changes in the physicochemical properties of cell membranes (fluidity and membrane shape), and (3) causing liver dysfunction and impaired mineral metabolism (retinoid, zinc, etc.). The effect of ethanol on the oral tissues seems to be dependent on the 100 g/day dosages, indicating a strong relative risk. Mutations caused by smoking and tobacco are essentially mediated by reactive oxygen and nitrogen species (ROS, NOS). Mitochondrial electron transport is the main source of ROS. Alcohol reacts to alcohol dehydrogenase and is converted to acetaldehyde (AcH), which is a strong carcinogen. Acetaldehyde (AcH) is activated by acetaldehyde dehydrogenase (ADH) and converted into acetate. Mutations in ADH enzymes can also result in the accumulation of AcH, which can lead to mutations and chromosomal aberrations.6,27,28,29

The management of lip OSCC involves the control not only of the primary tumours but also the possible metastatic spread to the neck. Early stage tumours have good prognostic and functional results after surgery.22 as long as the diagnosis can be established as early as possible as seen in the first case.20

In the management of AC, the patient was treated with chlorhexidine digluconate which has antimicrobial and anti-inflammatory properties. Considering AC is a potentially malignant lesion, preventing secondary infection and reducing the inflammation are important in treating AC. In addition, applying lip balm when working outside is an important treatment in the management of AC for preventing direct sunlight exposure or any other causative factors.30,31

It is also important to prevent long-term sunlight exposure that can cause a chronic lip inflammation leading to epithelial carcinogenesis. It is well known that chronic inflammation is a cause of tumor development and progression.32

Conclusions

Lip SCC and actinic cheilitis are chronic lesions that have similar clinical characteristics. History taking is the most important part of the diagnostic process for both diseases. Appropriate initial therapy has also an important role in the course of the diseases and determining the prognosis of the diseases. Dental practitioners should be aware and competent enough to identify patients with chronic lip lesions that may be malignant lesions or potentially malignant disorders.

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Declaration of Interest

The authors declare that there is no conflict of interest.

References


