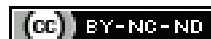


Oral Squamous Cell Carcinoma arising from Pre-existing Actinic Cheilitis: A Case Report

VANDANA SEKIZHAR¹, NANDINI VELLMURUGAN²

ABSTRACT

Oral Squamous Cell Carcinoma (OSCC) is considered one of the most prevalent cancers globally. A significant number of OSCC cases arise from pre-existing potentially malignant disorders, among which Actinic Cheilitis (AC) is uncommon. AC occurs most commonly on the lower lip with symptoms ranging from pale, dry and scaly lips to ulcerations, burning sensation and crusting. Due to the malignant potential, AC necessitates immediate evaluation and treatment. The present case report discusses a 70-year-old female patient who presented with a painful ulcer on the lower lip of one month's duration. A provisional diagnosis of AC was made and an incisional biopsy was recommended. However, the patient did not show willingness for the biopsy and reported four months later with a non healing ulcer. A provisional diagnosis of OSCC of the lower lip was established. Histopathological analysis revealed hyperparakeratinised stratified squamous epithelium exhibiting significant dysplasia. Surgical excision of the lesion was performed and follow-up after two weeks showed satisfactory healing. This paper highlights the critical importance of timely diagnosis and management of AC to prevent its progression into malignancy thereby emphasising the importance of early diagnosis and timely intervention.

Keywords: Lip, Oral cancer, Sun, Ultraviolet

CASE REPORT

A woman in her 70s came to the Outpatient Department with the chief complaint of a painful ulcer on her lower lip, persisting for the past one month. She gave a history of gradual-onset pain with moderate intensity and continuous in nature. The pain was exacerbated by the intake of hot and spicy foods and no relieving factors were noted. The patient also reported that the ulcer had remained of the same size since its onset and was associated with occasional bleeding. The patient's medical history revealed she had diabetes mellitus and hypertension for the last two years and was under medication for the same. The patient reported no recent dental treatment. Recent medical reports indicated she had good control of her diabetes. The patient gave a history of chewing betel nut along with tobacco for the past 40 years, with a frequency of four times per day. She worked as a farmer and spent an average of 5-6 hours every day in the sun without protection. Extraorally, inspection revealed a single well-defined ulcer evident over the vermilion border of the lower lip, measuring approximately 1×1.5 cm. It was roughly oval in shape with well-demarcated margins. The floor of the ulcer was covered with granulation tissue and surrounded by an erythematous border; encrustations were also present [Table/Fig-1].



[Table/Fig-1]: Ulceration evident over the lower lip.

On palpation, the lesion was tender, non indurated and bleeds upon pressure. On lymph node examination, a left submandibular lymph node was palpable, measuring approximately 0.5 cm in size, roughly oval in shape, tender and soft in consistency, with a freely mobile texture. Intraorally, the patient had a complete edentulous mandibular arch and partially edentulous maxillary arch with severe tobacco stains. The patient reported consuming betel nut along with tobacco and habitually retained the mixture in the lower labial sulcus for approximately five minutes. Based on history and clinical examination, a provisional diagnosis of AC involving the left-side of the lower lip was arrived. Differential diagnosis included exfoliative cheilitis and squamous cell carcinoma of lip. Exfoliative cheilitis has been considered to be less probable as it was a chronic lesion with granulation tissue rather than superficial desquamation. Squamous cell carcinoma was considered less likely in the initial presentation due to the absence of induration, well-defined margins and relatively stable lesion size, although it was not completely ruled out. To confirm the diagnosis, an incisional biopsy was advised which the patient refused. Haematological investigation was done to assess anaemia and result revealed a haemoglobin level of 9 g/dL. The patient was advised with a compounded topical preparation of prednisolone (Tablet Prednisolone 20 mg crushed and mixed with sucralfate suspension applied twice daily for 15 days), vitamin supplements (Syrup Haem up 5 mL once daily for 15 days, Capsule Becosules once daily for a month) and antioxidant (Capsule Alpha lipoic acid once daily for 15 days) to provide symptomatic relief. The patient was advised to report for review after two weeks. After 2-week follow-up, the patient reported a reduction in pain which was documented using Visual Analogue Scale (VAS) [1]. The VAS score reduced from 8/10 to 5/10 with slight reduction in erythema of the lesion but the overall clinical appearance of the lesion remains the same. However, she was lost to follow-up for the next three months.

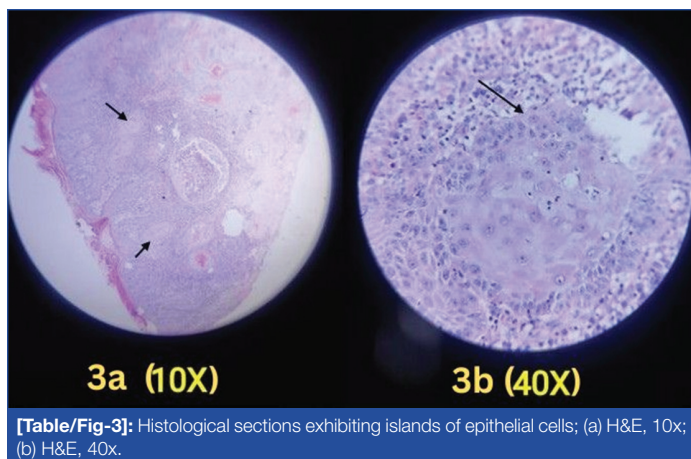
By the end of fourth month, the patient reported back with severe pain and a non healing ulcer in the same site of the provisionally diagnosed AC. On examination, a single well-defined ulcer was evident over the vermilion border of the lower lip, now enlarged to approximately 3×2 cm, with irregular margins. The floor of the ulcer was covered with granulation tissue, pseudomembranous slough,

encrustations and bleeding spots [Table/Fig-2]. On palpation, the lesion was tender, non indurated and bled on pressure. The left submandibular lymph node remained palpable, soft and freely mobile. Based on the clinical presentation, a provisional diagnosis of OSCC of the lower lip was given. After explaining the clinical importance and relevance of the present diagnosis, the patient consented for an incisional biopsy.



[Table/Fig-2]: Ulceration of lower lip after four months.

After routine blood investigations, incisional biopsy was performed under local anaesthesia in the lower lip region, including the margin and floor of the ulcer. The specimen was sent for histopathological examination. Haematoxylin and Eosin (H&E) staining at 10X and 40X magnification revealed stratified squamous epithelium which is hyperparakeratinised. The epithelium was proliferating into the connective tissue and infiltrating the muscle layer. The epithelium showed severe dysplasia with features of dyskeratosis. The subepithelial layer exhibited islands of epithelial cells exhibiting features of pleomorphism and the presence of invading epithelial cells into the underlying connective tissue. The subepithelial layer exhibited dense inflammatory cell infiltration. These findings were suggestive of moderately-differentiated OSCC [Table/Fig-3].



[Table/Fig-3]: Histological sections exhibiting islands of epithelial cells; (a) H&E, 10x; (b) H&E, 40x.

CECT of neck: Bony window (50 HU) revealed soft tissue thickening in the lower lip with no obvious focal enhancing lesion detected [Table/Fig-4]. No radiological evidence of lymph node involvement. Magnetic Resonance Imaging (MRI) was not performed due to patient-related constraints and financial considerations.

Following the diagnostic confirmation, the patient underwent a surgical excision under general anaesthesia by the oral and maxillofacial surgery team led by a well experienced oral surgeon. The surgery consisted of wide excision of the lesion with a 1 cm clinically safe margin extending into the vermillion border, lower lip mucosa and underlying submucosa, including part of the orbicularis oris muscle as needed to achieve adequate clearance. The previously palpable lymph node was assessed intraoperatively and no neck dissection was performed as it was clinically and radiologically uninvolved. Histopathological examination of the excised specimen confirmed moderately-differentiated OSCC with clear surgical margins. Postoperatively, the patient was instructed



[Table/Fig-4]: CECT (axial view) of neck at the level of the mandible. The bony window (50 HU) reveals the soft-tissue thickening in the lower lip with no obvious focal enhancing lesion or radiological evidence of cervical lymphadenopathy.

to continue her antidiabetic medications, with regular monitoring of blood glucose levels due to her prior history of diabetes, along with vitamin supplementation and antioxidants for symptomatic support. Follow-up was scheduled at two weeks, one month and monthly thereafter for the first six months. The patient reported after two weeks for review and showed satisfactory healing with no signs of infection [Table/Fig-5].



[Table/Fig-5]: Postoperative follow-up of the surgical site after two weeks, showing satisfactory healing with no clinical signs of infection.

DISCUSSION

The AC is a potentially malignant disorder primarily resulting due to chronic injury to the lip caused by Ultraviolet (UV) radiation. It occurs highly in farmers, fishermen, lifeguards and construction workers who are exposed to excessive sunlight radiation [2]. Although AC is predominantly seen in fair-skinned men aged over 40 years, recent evidence of occurrence among women and dark skin individuals in tropical regions has been reported [3,4]. The worldwide prevalence of AC is reported to be between 15.5% and 43.2% [5].

The pathogenesis of AC occurs by chronic UV radiation exposure leading to Deoxyribonucleic Acid (DNA) damage in keratinocytes, mutations in the TP53 (p53) gene and progression of epithelial dysplasia [6]. Along with the primary aetiological factor of chronic exposure to UV radiation, the other risk factors are tobacco use, genetic predisposition and alcohol intake which act synergistically leading to increased risk of malignant transformation [4,5]. In the present case, the patient was a female farmer in her 70s whose occupation exposed her to extensive sunlight along with chronic history of tobacco and betel nut use, which are both known risk factors that are susceptible to epithelial damage and malignant transformation [5].

The AC is clinically characterised by a poorly defined lip border featuring a white scaling plaque, oedema, atrophy, erythema, erosions and hyperkeratosis [3]. The AC was clinically graded by Poitevin NA et al., as shown in [Table/Fig-6] [7].

Grade I	Dryness and desquamation affecting the vermillion
Grade II	Atrophy and an unclear distinction between lip and skin/a melanotic line as the vermillion limit
Grade III	The presence of squamous and hyperkeratotic regions extending into the wet mucosa
Grade IV	Ulceration or leukoplakia, along with areas of induration, suggests a malignant transformation

[Table/Fig-6]: Clinical grading of Actinic Cheilitis (AC) [7].

In the present case, a single well-defined ulcer of size 1×1.5 cm was evident over the left-side of the lower lip surrounded by an erythematous border with encrustations. In the present case, although the lesion exhibited ulceration and encrustation, the absence of induration and other features suggestive of malignant transformation led to an initial clinical consideration of Grade III AC.

It is well known that the poor prognosis of the disease results from the delayed diagnosis, with nearly half of OSCC cases being diagnosed at an advanced stage (III-IV) [8]. The histopathological investigation remains the gold standard method to confirm AC and to assess its malignant potential, which presents with findings of epithelial hyperplasia or atrophy, parakeratosis, dysplasia and solar elastosis [6]. In the present case, the histopathological investigation revealed severe dysplastic epithelium with features of dyskeratosis and chronic inflammatory infiltrate, confirming the malignant transformation.

The AC has a reported malignant transformation rate of approximately 3.07% to squamous cell carcinoma, which is reported only in a few cases [9]. A similar case was reported in a 66-year-old male who reported an erosive area in the lower lip diagnosed as AC and treated with cryosurgery. However, after 30 months, the lesion underwent a malignant transformation to OSCC with lymph node metastasis and was treated with surgical excision and adjuvant radiotherapy [10].

Previously documented cases in India also reveal similar clinical patterns but no malignant transformation. A 65-year-old female farmer suffering from chronic keratotic plaques, crusting and bleeding of the lower lip, which was attributed to extended outdoor sun exposure and histopathological analysis showed hyperkeratosis, dyskeratosis and chronic inflammatory infiltrate [11]. Likewise, a 45-year-old female shepherd with painful crustations and ulceration of the lower lip, clinically consistent with AC, emphasises the elevated risk of malignant transformation associated with persistent lesions [4].

The present case is distinct as it documents a histopathologically confirmed malignant transformation of AC into OSCC in an elderly Indian female farmer, which has been reported rarely in the literature. Unlike previously documented Indian cases where malignant transformation was not observed, the present case highlights the combined effects of chronic sunlight exposure, tobacco with areca nut habit, loss to follow-up and patient non compliance in malignant progression. This progression highlights the critical importance of timely biopsy and rigorous monitoring in all suspected AC cases.

Furthermore, the present case highlights the clinical consequences of delayed intervention, emphasising the importance of early biopsy, timely management, sustained clinical vigilance and patient compliance. AC should therefore be regarded as an occupational hazard, especially in regions receiving excessive sunshine. A non healing ulcer on the lip in such individuals warrants clinical suspicion and histopathological evaluation for AC.

Public education and preventive strategies, such as lifestyle modifications and the consistent use of sunscreen with a Sun Protection Factor (SPF ≥30), are essential components of risk reduction. Future implications underscore the importance of having structured screening initiatives and standardised protocols to facilitate early identification and timely intervention for AC.

CONCLUSION(S)

As a potentially malignant disorder, AC demands early recognition and confirmation through histopathological evaluation. Timely diagnosis and intervention significantly enhance prognosis and reduce the likelihood of malignant transformation. The present case demonstrates how a delay in diagnosis and inconsistent follow-up can lead to malignant transformation, ultimately resulting in OSCC. By underscoring the significance of immediate evaluation, effective patient counselling and strict follow-up, this report illustrates that early diagnosis and timely intervention are the most effective approaches for decreasing morbidity and enhancing patient outcomes in lesions with malignant potential.

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PARTICULARS OF CONTRIBUTORS:

1. Professor and Head, Department of Oral Medicine and Radiology, Sri Balaji Vidyapeeth (Deemed to be University), Indira Gandhi Institute of Dental Sciences, Puducherry, India.
2. Postgraduate Student, Department of Oral Medicine and Radiology, Sri Balaji Vidyapeeth (Deemed to be University), Indira Gandhi Institute of Dental Sciences, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Nandini Vellmurugan,
Postgraduate Student, Department of Oral Medicine and Radiology, Sri Balaji Vidyapeeth (Deemed to be University), Indira Gandhi Institute of Dental Sciences, Puducherry-607402, India
E-mail: nandini13897@gmail.com

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