

WHAT LIES BENEATH

Upper lip squamous cell carcinoma arising from discoid lupus erythematosus treated with standard wide excision

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ABSTRACT

Introduction: Squamous cell carcinoma (SCC) is a rare complication of long-standing discoid lupus erythematosus (DLE). The reported risk factors associated with the malignant transformation include chronic inflammation, scarring, immunosuppression, and the dysfunctional healing already evident in discoid lesions. If underdiagnosed and left untreated, this may lead to higher rates of recurrences, metastases and death.

Objective: The main objective of this article is to report the diagnosis and management of a DLE-associated SCC on the upper lip of an elderly Filipino female. A short discussion on the pathogenesis and treatment of this disease entity is also presented. Topical medications, family history and accompanying systemic symptoms were reviewed and analyzed.

Case: A 78-year-old female, pawid maker, developed a rapidly growing verrucous tumor measuring 4.0 x 2.0 x 2.0 cm from a depigmented atrophic plaque located on the upper lip. Initial histopathologic findings were consistent with SCC and DLE. Considering the tumor size and the challenging anatomical location, the surgical oncology and plastic surgery team carried out a wide excision with 5 mm margin of the entire upper lip mass and surrounding plaque, followed by lip reconstruction. Biopsy findings of the excised mass were consistent with the initial findings. Three months post-operation, there was significant wound healing with no recurrences.

Conclusion: Although the incidence is rare, SCC occurring in DLE is considered to be high-risk and should warrant early recognition and prompt treatment. In this paper, the authors also highlight the use of a standard wide excision in lieu of Mohs Microscopic Surgery as an alternative option where resources are limited.

Key words: squamous cell carcinoma, discoid lupus erythematosus, wide excision, surgical flaps

INTRODUCTION

Discoid lupus erythematosus (DLE), a subtype of chronic cutaneous lupus erythematosus (CCLE), develops from loss of self-tolerance. It also

involves the interplay of genetic and environmental factors, where ultraviolet (UV) radiation has been a well-documented risk factor.⁽¹⁻³⁾ Incidence of malignant transformation to squamous cell carcinoma (SCC) is rare ranging from 2.2 to 3.3%.⁽⁴⁾ In DLE-related SCC, the lower lip has been the most commonly affected site with the upper lip involved in only 2.3% of the total number of cases.⁽⁵⁻⁶⁾ The recurrence rate, metastasis and mortality rates of DLE-related SCC were 10 to 20% higher than conventional SCC.⁽⁷⁾ For this reason, SCC tumor arising from DLE warrants aggressive therapy, close monitoring and stringent follow-up. We report a 78-year-old female who presented with SCC arising from a long-standing DLE lesion on the upper lip, and treated with wide excision followed by lip reconstruction.

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CASE REPORT

A 78-year-old Filipino female, *pawid* maker from Catanduanes, consulted at the Jose R. Reyes Memorial Medical Center Dermatology Out-Patient clinic due to a 4 x 2 x 2 cm verrucous exophytic black-brown tumor on the upper lip (Figure 1).

Two years prior to consult, few well-demarcated reddish to violaceous plaques developed over the upper lip, bilateral preauricular area, conchae, upper back and vertex of the scalp (Figure 2). This was associated with mild to moderate pruritus on sun exposure. The lesions later evolved with central atrophy and hyperpigmented borders. Six months prior to consult, a whitish papule developed over the atrophied lesion on the upper lip. This rapidly progressed into a verrucous tumor extending into the oral mucosa. There were no palpable submental, occipital, cervical, supraclavicular and axillary lymph nodes. The patient denied weight loss, anorexia, presence of oral ulcers, gum bleeding, dysphagia, dysuria and joint pains. There was no history of trauma, immunosuppression nor exposure to radiation on the face. For the past 50 years, the patient was a regular alcoholic beverage drinker (2 shots of gin/day), and has been practicing betel nut quid chewing. As a *pawid* maker, she assembles nipa palm roof during the day with frequent sun exposure.

Incisional biopsy of the verrucous tumor was consistent with SCC (Figure 3). Punch biopsy of the atrophic lesion, with special stain using Alcian blue, revealed DLE. Her antinuclear antibody (ANA) titer was negative. Ultrasound (UTZ) of the neck showed subcentimeter lymph nodes in the submentum, and bilateral jugular chains. Chest radiography and UTZ of whole abdomen were negative for distant metastases.

A team composed of surgical oncologist and plastic surgeon carried out a wide excision with a 5 mm margin. This was followed by lip reconstruction employing abbe lip switch technique with reverse fan flap on the left upper lip and advancement flap on the right upper lip. The microscopic examination of the excised mass was consistent with a well-differentiated squamous cell carcinoma. The lines of resection were negative for malignant cells. There were no significant post-operative morbidities and complications. The subcentimeter lymph nodes were managed with close observation and strict follow up. To address the concomitant DLE, she was started on hydroxychloroquine 200 mg/day, betamethasone valerate cream twice a day over the discoid lesions and daily use of sunscreen with SPF 50. Avoidance of betel nut quid chewing and alcohol beverage drinking

were advised. At 3 months post-operation, there was significant wound healing with no speech defect, drooling of saliva nor changes in eating habits (Figure 4). A formal referral to hospital/ clinician of choice in their locality was made for continuity of care and management. Strict follow up was advised every 3 months for the next 12 months.



Figure 1. Squamous cell carcinoma on top of discoid lupus erythematosus. Black-brown verrucous exophytic mass measuring 4.0 cm in its widest diameter on the upper lip. Well-delineated pinkish-whitish plaque with atrophy and hyperpigmented borders surrounds the tumor with extension to the entire upper lip.



Figure 1. DLE lesion. White atrophic plaque on the conchae of the right external ear.

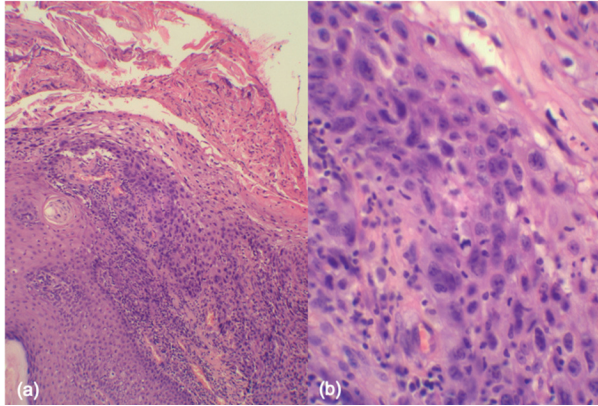


Figure 3. (a) Histologic sections from the verrucous tumor showing irregular epidermal acanthosis with thick scale crusts and full thickness loss of maturation. (Hematoxylin-eosin stain x 100) (b) Close up view showing atypical keratinocytes with marked nuclear pleomorphism characterized by large irregularly shaped hyperchromatic nuclei and prominent nucleoli surrounded by abundant pale cytoplasm, with occasional mitotic figures. (x 400)



Figure 3. Three months post-operation with significant wound healing.

DISCUSSION

Squamous cell carcinoma is a rare, but well-recognized complication of longstanding DLE since 1953, with an estimated incidence of 2.3 to 3.3%.^(4,8) Latency period may vary from 7 to 41 years.⁽⁹⁾ In a study made by Tao et. al. among Chinese patients with DLE-associated SCC, epidemiologic data showed a male to female ratio of 2.2:1, and age peak-prevalence between 40 to 49 years.⁽⁴⁾ The lip (74%) has been the most commonly involved site followed by the cheeks, dorsal surface of the hands, and forearms. In most cases of lip involvement, the lower lip was

more commonly affected than the upper lip, which is only involved in 2.3% of the cases.⁽⁴⁻⁶⁾ Contrary to the published epidemiologic data, our patient was an elderly female who developed an upper lip malignancy with a latency period of 2 years.

The mechanism by which DLE progresses to SCC is not yet well-established. Risk factors include the use of immunosuppressive therapy, exposure to environmental carcinogens, and chronic ultraviolet (UV) light exposure.⁽¹⁰⁾ In a study by Mulwafu et. al., decreased level of melanin confers less protection to the skin causing p53 tumor suppression gene inactivation, which ultimately leads to development of SCC in discoid lesions.^(11,12) Moreover, the presence of pro-inflammatory cytokines and dysfunctional T regulatory lymphocytes in DLE may play a part in the malignant alteration of DLE keratinocytes.⁽²⁾ The preference for the lip as a site for tumor growth relates to its constant exposure to the sun, food irritation and tobacco use.⁽⁴⁾ The patient's long-term alcohol drinking, betel nut quid chewing, and her occupation as a pawid maker predisposed her to chronic cellular damage which may have led to the malignant transformation.

Complete surgical removal with histologic clear margins is the current mainstay of treatment for conventional and high-risk SCC.⁽¹³⁾ Mohs microscopic surgery (MMS) is the treatment of choice for high-risk SCC and for tumors located on critical areas where tissue preservation is desired.⁽¹³⁾ Wide local excision with appropriate margins is generally acceptable making it an alternative option in advanced cases. However, the lack of on-site histologic evaluation of margins may lead to gross removal of normal skin leading to poor cosmesis and function. Furthermore, the infiltrative nature of high-risk SCC were observed to have higher proportions of positive histologic margins after being treated with wide excision.^(13,14)

DLE-associated SCC, mainly those on the face, is considered to be high risk, and is best treated with MMS. However, few cases have been reported where only standard wide local excision was employed. In a case reported by Kim et al, a standard wide excision of an upper lip mass (measuring 4.0 x 2.2 cm) in a 49-year-old male with DLE has been carried out. This was followed by a bilateral nasolabial orbicularis oris myocutaneous flap and cervical lymph node dissection.⁽⁶⁾ In a case reported by Gamble et al, a 55-year-old female underwent wide excision of an exophytic mass (measuring 8 x 10 cm) arising from a discoid lesion on the scalp. This was then repaired with a local tissue rotation flap and full thickness skin graft.⁽¹⁵⁾ Molomo et. al. published a case report on a 44-year-old male who

underwent excision biopsy of a lower lip mass arising from a discoid lesion.⁽²⁾ The histologic examinations of tissue specimens from all three studies were consistent with squamous cell carcinoma. Unfortunately, follow up care was not discussed on the cases cited.

With the anatomical location of the tumor and the lack of Mohs Microscopic Surgery facility during the time the patient was managed, the cosmetic, functional and prognostic outcome became primary concerns placing a challenge in this case. The team carried out the surgical plan which resulted in a lip defect but with good functional capacity. Moreover, lines of resection were negative for tumor cells on post-operative histologic sections. Available data demonstrates that histologic clear margins are of significance in achieving cure and preventing recurrences.⁽¹⁴⁾

DLE-related SCC has a higher rate of recurrence, metastases and death by 10 to 20%.^(7,8,15) The tumor recurrence, metastasis, and death ratios were 29%, 16.1%, and 19.4% higher than the 20%, 0.5% to 6%, and 1% reported for non-DLE-related SCCs.⁽⁴⁾ The imaging modality of choice for regional and distant metastases is not yet well-established for cutaneous SCC.⁽¹⁴⁾ With variable specificity and sensitivity, the most frequently used procedures are computed tomography, positron emission tomography and magnetic resonance imaging.^(14,16) In Europe, the utility of ultrasound is favored because this can detect extra-nodal spread of head and neck SCC with comparable accuracy and higher specificity than magnetic resonance imaging.^(14,16) Given the low cost, patient's financial limitation, and easy accessibility, UTZ of the neck was

performed in this case to investigate regional lymph node metastases. Chest XRAY and UTZ of the whole abdomen were performed to screen for liver and lung metastases being the most common sites of distant spread.⁽¹⁷⁾ Along with the review of systemic signs and symptoms suggestive of distant spread, diagnostic procedures done showed normal findings.

Follow-up every three to six months for five years is encouraged among treated high-risk SCC patients. Ninety five percent of local recurrences and metastases occur during this time interval.⁽¹⁶⁾ Each visit should include total body skin examination. Close examination of tumor site, palpation of lymph nodes and review of systems.

CONCLUSION

Reducing the risk of malignant degeneration of DLE is paramount. This involves early diagnosis and aggressive treatment of DLE lesions as well as avoidance of modifiable risk factors such as alcohol beverage drinking, tobacco use and excessive sun exposure. In health institutions where Mohs microscopic surgery is not available, a standard wide excision with acceptable margins is an alternative option. Close monitoring and regular follow up are highly recommended and prompt biopsy of any new suspicious lesions is highly encouraged.

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