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All Variants of Lichen Planus are a Possible Triggering Factors for Squamous Cell Carcinoma

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Lichen planus is a common dermatological disorder where oral lichen planus is the most commonly incriminated to have the possible risk to change into squamous cell carcinoma.
Objective: To realize squamous cell carcinoma as a possible complication of all variants of lichen planus and to raise dermatologists' awareness about this complication.
Patients and Methods: All patients with lichen planus who developed squamous cell carcinoma during the period from July 2012 –July 2021 were collected and included in this case series descriptive observational study. Full history and clinical, systemic and cutaneous, examinations were performed .Lymph nodes were inspected and palpated and biopsy was carried out to confirm the diagnosis.
Results: The data of eight patients were evaluated with 5 (62.5%) males and 3 (37.5%) females, and their ages at presentation were ranged from 45-71 years with mean 58.3±8.3 years. All patients were suffering from squamous cell carcinoma complicating previously diagnosed lichen planus during nine years time period. The variants of lichen planus that observed in the present study were as follow: 3 (37.5%) classic lichen planus, 2 (25%) oral lichen planus, 2 (25%) lichen

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planus actinicus and one(12.5%) with hypertrophic lichen planus. Also this study revealed that the sites of squamous cell carcinoma were observed in oral in 5 (62.5%) patients ,nose in 1 (12.5%)patient, penis in 1(12.5%) patient, and dorsal foot in1 (12.5%) patient.

Conclusion: Squamous cell carcinoma as a complication of lichen planus in its mucosal and cutaneous variant is a rare and non-documented issue but according to daily clinical practice, it can present and can complicate all variants of lichen planus on contrary to previous reports where the main site was oral cavity. This observation should be kept in mind while evaluating longstanding non-healed or poorly responding lesions of all varieties of lichen planus.

Keywords: Oral squamous cell carcinoma; penile squamous cell carcinoma; oral lichen planus; actinic lichen planus; hypertrophic lichen planus.

1. INTRODUCTION

Lichen planus (LP) is a relatively common, chronic, inflammatory and idiopathic dermatosis of the skin, nail, hair and mucous membrane including oral and genital mucosa. Although its rare, esophageal and conjunctival lichen planus had also been reported [1]. The worldwide prevalence of LP is estimated to be in the range of 0.22% to 5%. It usually affects middle-aged adults with slight female predominance in some reports [2]. The etiology of LP remains not clarified and several hypotheses had been suggested, including genetic, infective and autoimmune factors. The disease is thought to be the result of a cell-mediated reaction [3]. Although many factors had been proposed as a potential trigger to the development of LP ,none of these factors had been confirmed .An association between hepatitis C virus infection and lichen planus had also been reported in some geographic locations, such as Japan and Mediterranean regions. In United States, hepatitis C virus antibodies had been detected in limited but statistically significant percentage of patients with cutaneous lichen planus .Also, Hepatitis C virus sequences had been identified in the serum of patients with oral LP and in oral tissue samples. The HLA-DR6 allele had been identified as a potential risk factor for Hepatitis C virus -associated oral LP in an Italian study. Although the association between Hepatitis C virus and LP may be influenced by many factors, such as geography, screening for Hepatitis C virus has been recommended in LP patients to prevent transmission of undetected Hepatitis C virus [4]. In Iraq, screening for hepatitis B virus surface antigens and hepatitis C virus antibodies was negative in all patients diagnosed with different clinical forms of LP in a study done by Sharquie et al.[2].

Lichen planus can be divided into cutaneous and mucosal disease. Furthermore, cutaneous lichen planus can be subdivided into many variants including the classic (papular) LP which usually characterized by pruritic, purplish, flat-topped, papules and plaques with a whitish streak on its surface called Wickhams striae [5]. The hypertrophic LP presented as intensely pruritic, thick hyperkeratotic purplish or reddish plaques and nodules observed primarily on the shins or dorsal feet [6]. Actinic LP primarily affects young adults and older children in spring and early summer presented as a dark brown hyperpigmented patches affecting the face particularly the cheeks, nose, and around the eyebrows with mild to severe itching aggravated by sun light [7,8]. The other variants of cutaneous LP include: annular, linear,atrophic, follicular, LP pigmentosus and LP pigmentosus-inversus [5].

In the mucosal LP, oral LP is the most common form with risk of malignant transformation in 0.4-3.7% of cases [9]. It has more chronic course and commonly affects females. The buccal mucosa, tongue, and gingiva are the commonly affected sites. Oral LP is sub classified into six variants: reticular,papular,plaque, atrophic, erosive, and bullous with reticular variant being the most common type [4]. The other mucosal sites that can be involved by LP is the vulvovaginal area , esophagus, larynx, and conjunctiva [5].

Development of squamous cell carcinoma(SCC) on cutaneous LP is rare with estimated incidence between 0.4% and 1.74% .It developed mostly on the lower legs in hypertrophic or verrucous LP lesions [10].

Although the malignant potential of oral LP lesions has been a subject of debate [5]. An increased incidence of oral SCC had been reported in oral LP patients, particularly those with erosive lesions, and should be followed regularly [11].

So the aim of the present study is to realize the SCC as a possible complication of all variants of LP and to raise dermatologists' awareness about this complication.

2. PATIENTS AND METHODS

In this case series descriptive observational study where eight patients who were previously diagnosed with many variants of LP who developed SCC on various body regions were enrolled during the period from July 2012 – July 2021 . Oral consent was obtained from each patient after an explanation of the nature of the study. Close-up photographs were taken at the same place with constant distance and illumination. A full history concerning the duration and progression of disease, cutaneous and systemic associated diseases, smoking, alcohol drink and treatment history was obtained.

Complete cutaneous examination for any skin lesions was done in each patients. The mouth and genital mucosae were carefully examined. Careful inspection of oral mucosal site including tongue, buccal mucosa and palate for any persistent non-healed lesions were performed. The draining lymph nodes were also inspected and palpated. Biopsy was done in each case to confirm the diagnosis.

2.1 Statistical Analysis

Statistical package for social science (SPSS) version 23 was used for data input and analysis. Data were statistically described in terms of mean, frequencies (no.of cases), standard deviation (SD), male to female ratio and percentage (%).

3. RESULTS

Eight patients, 5 (62.5%) males and 3 (37.5%) females suffering from SCC complicating previously diagnosed LP patients during nine years' time period were enrolled in the present study. Their age at presentation was ranged from 45-71 years with mean 58.3±8.3 years. The mean duration of LP in the affected patients was 11 years.

The variants of LP observed in the present study were as follow: 3 (37.5%) classic lichen planus , 2 (25%)oral LP, 2 (25%)LP actinicus and one(12.5%)with hypertrophic LP. The variants of LP in correlation with patients' demographic features and diagnosed squamous cell carcinoma were shown in Table 1.

Oral SCC was observed in 5 (62.5%) of patients (Figs. 1, 2).of them, 2 patients previously diagnosed with predominantly oral LP and 2 patients had classic LP affecting oral mucosa with typical LP lesions on the skin (Fig. 3 A) and the fifth patients had actinic lesions affecting forehead, bilateral cheeks, nose and lip. Biopsy of the lesions showed hydropic degeneration of the basal layer, with severe epithelial atypia and dysplasia (Fig. 3 B). The oral mucosal sites affected by SCC in relation to the no. and gender of the patients were illustrated in Table 2. The lip was the commonly affected site in 2 (40%) oral LP patient. In all 5 patients, the lesion starts as asymptomatic, small and slowly growing plaques or nodules that were underestimated by the patient trying only over the counter medications, until they interfered with mouth function, with bleeding and pain in many patients, then the patients seek medical professional help.

The variants of oral LP in the presented patients were erosive in 3 patients, plaque in 1 patient, and reticular type in one.

One (12.5%) old aged female with light skin and history of chronic sun exposure presented with slowly growing non healed erosion of the nose on chronic patch of actinic LP with no response to different treatment approaches given the diagnosis of SCC in this patient.

One (12.5%) patient with history of classic LP involving the glans penis for long duration presents with long history of slowly progressive verrucous penile plaque with later erosion and ulceration. The diagnosis of penile SCC was finally documented (Fig. 4).

One (12.5%) patient who was previously diagnosed with hypertrophic LP for 11 years duration, presented with slowly growing, verrucous plaques and nodules on the dorsum of the right foot, ulceration with pain developed later in the course of disease. Biopsy of the lesion showed epidermal hyperplasia, hyper orthokeratosis with squamous proliferation, a finding consistent with diagnosis of SCC (Fig. 5. A,B).

Table 1. The variants of lichen planus in correlation with patient demographic features and diagnosed squamous cell carcinoma

Variant of lichen planus	No. of patients (%)	SCC and patient characteristics			
		Primary site involved	No. (%)	Gender	
				Male	Female
Classic lichen planus	3(37.5%)	- Oral SCC	2(25%)	1	1
		- Penile SCC	1(12.5%)	1	
Oral lichen planus	2(25%)	Oral SCC	2(25%)	1	1
Actinic lichen planus	2(25%)	- SCC of the nose	1(12.5%)		1
		Oral SCC of the lip	1(12.5%)	1	
Hypertrophic lichen planus	1 (12.5%)	SCC of the dorsum of the right foot	1(12.5%)	1	
Total	8 (100%)		8(100%)	5(62.5%)	3(37.5%)

Table 2. Lichen planus squamous cell carcinoma of oral mucosal sites

Patients	Gender	Extra oral	Primary location for oral squamous cell carcinoma
1	Male	Actinic lesions	Lip
2	Female	None	Lip
3	Male	None	Buccal
4	Male	Skin ,Genital	Tongue
5	Female	Skin	Floor of the mouth

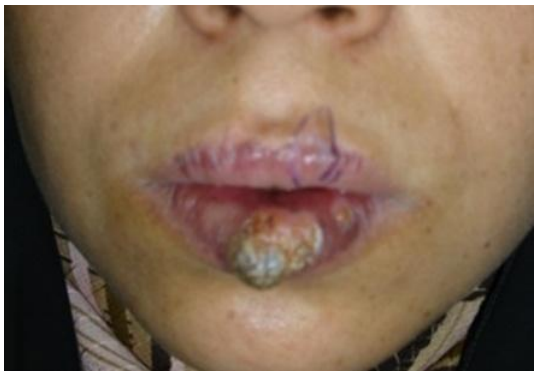

Fig. 1. Patient with squamous cell carcinoma showing slowly growing large nodular crusted and verrucous lesion on the lower lip in 45 years old female

Fig. 2. Patient with tongue squamous cell carcinoma showing longstanding mildly painful with minimal bleeding hypertrophied erythematous lesion of the dorsum of tongue with poor response to different topically applied medicine

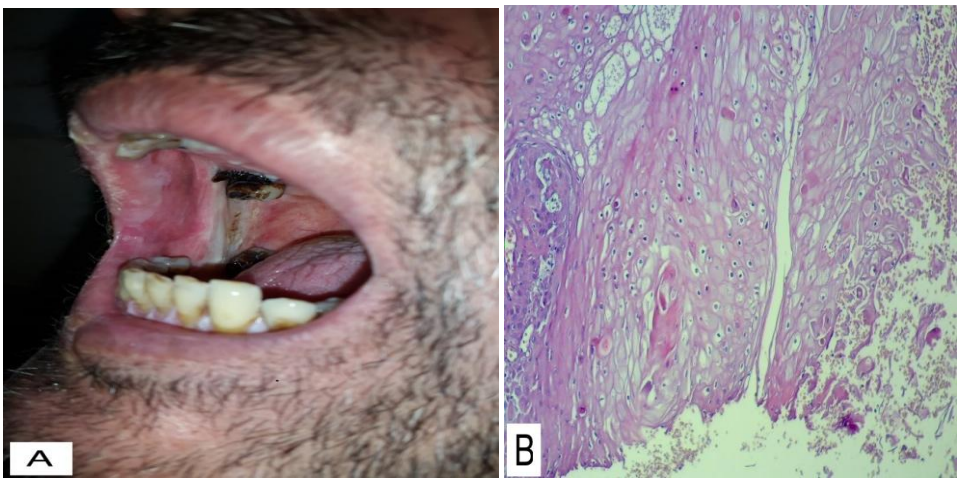

Fig. (3. A&B): A. Showing leukoplakic plaque with erosion on buccal mucosa and lip. B. Showing hydropic degeneration of the basal layer, with sever epithelial atypia and dysplasia (1 x 40)

Fig. 4. Patient with squamous cell carcinoma showing longstanding verrucous lesion on the glans penis in 57 years old patient with classic lichen planus

Fig. (5.A&B). A. Patient with squamous cell carcinoma showing large hypertrophied verrucous lesion with ulceration and bleeding upon walking in patient with hypertrophic lichen planus B. Showing epidermal hyperplasia, hyper orthokeratosis with squamous proliferation, a finding consistent with diagnosis of squamous cell carcinoma in patient with hypertrophic lichen planus (1 x 10)

4. DISCUSSION

Lichen planus (LP) is an idiopathic dermatosis with proposed immune-mediated etiology with chronic course that affects the skin, nails, hair, and mucosa commonly of middle-aged adults. The main forms of LP are cutaneous and mucosal lichen planus [2].

Although still controversial, many studies suggest an increased risk of malignant transformation in patients with oral LP [11,12]. World Health Organization (WHO) defines oral LP as a "potentially malignant disorder", and recommends close monitoring of oral LP patients [13].

While cutaneous LP does not associated with an increased risk of malignancy, still neoplastic transformation of cutaneous LP lesions can occur very rarely and should be considered in non-healed longstanding lesions [14].

In the present study, oral LP was responsible for the majority of SCC patients as affecting 5 (62.5%) patients,3 of them had erosive LP, this finding in agreement with other studies where the oral LP particularly the erosive lesions have the higher risk for malignant transformation [5,11]. Also in the present study, the lip was the commonly affected site in 2 (40%) lichen planus patients with oral involvement in contrary to other reports where the tongue was the mostly affected site followed by buccal mucosa [12,15]. The sunny climate of Iraq all over the year and little, if any, health orientation regarding sun screen might explain in part the higher frequency of lip involvement in the present study as both can be additive factors for earlier development of SCC on the lip [16].

Lichen planus actinicus is an inflammatory disease possessing important etiology of facial melanosis affecting mainly female patients. The rash mainly facial in butterfly distribution . Sun exposure plays a role in pathogenesis of the disease [17]. None of the available studies reported actinic LP as a cause of SCC except in one published study by Sharquie et al. where SCC of the lip had been recorded in 2 patients with actinic lichen planus which was assumed by the author as to be a risk rather than causal factor and this report corroborates our observation in the present study [16]. While the patient with SCC was elderly light skinned female with prominent sign of photoaging in form of lentigines and wrinkles. One can speculate that the SCC may be coincidental finding as both conditions can be precipitated by sunlight [16,17].

Although no clear association between penile LP and penile SCC can be confirmed, it had been reported in extremely limited case reports [18,19,20,21]. As far as we know, the first reported case of SCC arising on the LP lesion of the penis presented by Leal khouri et al.in 1994 [21]. In the present study, penile SCC developed in 1 (12.5%)patient with classic LP ,a finding consistent with previous report [18,19,20,21].

Hypertrophic LP is a variant of LP with chronic course presents with itchy, hyperkeratotic, or verrucous plaques that usually affects the lower extremities. The development of SCC in hypertrophic LP had been reported in few studies [22].

In the present study, 1 (12.5%)male patient developed biopsy proven SCC in longstanding lesion of hypertrophic LP on the dorsum of the right foot, a finding that is in line and also can be added to other reported literature [22].

5. STUDY LIMITATION

The Limited number of patients with only one ethnic background minimized the ability to provide any recommendations regarding the optimum screening program in LP patients.

6. CONCLUSION

Although SCC as a complication of LP in its mucosal and cutaneous variant is a rare and non-documented issue but in daily clinical practice, it presents and can complicate all variants of LP. This observation should be kept in mind while evaluating longstanding non-healed or poorly responding lesions of LP.The present study provides new information regarding the malignant potential of different variants of LP, not the oral variant only, where all variants had been associated with development of SCC either directly or with other additive factors. This finding should initiate a new larger study to confirm or to abort our observation.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICS COMMITTEE APPROVAL

The study followed the Declaration of Helsinki Principles and it was approved by the Ethics Committee of Fallujah Teaching Hospital (approval number 1170, date:29/7/2021).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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