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Original Article

The frequency of different types of squamous cell carcinoma according to their triggering factors in patients with dark complexion skin

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Abstract

Objective To gather all patients with squamous cell carcinoma and try to classify them according to their triggering factors.

Methods This is a cross-sectional study that was carried out during the period from 2014-2023 where all patients with squamous cell carcinoma were collected and analyzed into groups according to their triggering factors. Nearly all patients were Fitzpatrick skin type III and IV. Full demographic and clinical data were studied and evaluated. A histopathological assessment was done as a confirmatory measure.

Results Full analysis and evaluation were carried out for 95 cases of squamous cell carcinoma and classified into the following groups: lower lip sunlight-induced SCC in 44 (46.3%) cases, ordinary SCC without triggering factor in 22 (23.1%), lichen planus induced SCC in 17 (17.89%) and burn-induced in 12 (12.63%) patients with SCC.

Conclusion Cutaneous squamous cell carcinoma is not a common tumor but is frequently triggered by sunlight exposure, lichen planus and old burn scar.

Key words
Squamous cell carcinoma; Triggering factors; Sunlight exposure; Lichen planus; Old burn scar.

Introduction

Squamous cell carcinoma (SCC) of the skin is the second most common skin cancer, characterized by atypical, faster growth of squamous cells.[1] Two major presuming triggering factors: Firstly, endogenous mutagens result in spontaneous variations of DNA, like free radical damage due to depurination, deamination, or reactive oxygen species.[2] Secondly, exogenous mutagens like ultraviolet sunlight, smoking, dietary components, and Epigenetic alterations.[3]

The most common malignant proliferation of the keratinocytes originating from the burn scar is SCC, and it is an unavoidable probability.[4] Deep burns, unstable burned scars that commonly ulcerate due to frequent trauma and those which never cured completely, will advance into malignant alteration. The lower limbs, particularly around joints are commonly affected.[5,6] In Iraq, the occurrence of SCC

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among old burn scars is about 6.97% of male patients, where SCC is triggered by ulcerations, frequent infection, recurrent trauma, and contracture near the joints.[7]

Development of SCC over cutaneous lichen planus (LP is rare with an estimated frequency between 0.4 - 1.7%, the hypertrophic LP of the lower legs is commonly involved.[8] Concerning mucosal LP, the most common type with risk of SCC in 0.4-3.7% of females with oral LP. The commonly affected sites are the tongue, buccal mucosa, and gingiva.[9] Sharquie provides new observation regarding the malignant latency of different types of LP, where all kinds of LP had been accompanied by the development of SCC.[10]

In a recent study,[11] SCC of lower lips is not uncommon progressively realized tumor in middle age men that frequently present with solitary nodular ulcerative vegetating lesion without regional lymphadenopathy or distant metastases. In only 16.66% of cases, preexisting risk factors were observed.

SCC is the most common type of lip cancer, affecting the vermilion portion, with a distinguishing feature of being violently metastatic and having a higher relapse.[12] Epidemiological researches reveal that individuals with lower lip malignancy are more prevalent than those with upper lip.[13] The well-known cause for the advance of lip cancer is heavy exposure to sunlight.[11] Many studies discovered that UVR activated immune suppression in the skin over diverse signaling molecules, including the Fas/FasL system, interleukins, TNF, or initiation of apoptosis of T cell.[14] Ultraviolet radiation raises the TNF-α, IL-6 and IL-10 points in epidermal skin cells, which leads to down-regulating the actions of Langerhans cells, thus impeding the immune response of the involved skin.[15]

Also, it had been shown that autoimmune diseases like pemphigus, vitiligo, alopecia areata, lupus erythematosus and psoriasis had decreasing frequencies of skin malignancies like BCC and SCC. Hence these autoimmune diseases are protective against these tumors but through what mechanism? it is not well elucidated.[16-19] On the other hand, it has been well elucidated that patients with kidney transplants receiving cytotoxic therapy have a great tendency to develop skin management especially in cases with SCC.[18,20]

Over the last 10 years, Sharquie documented interesting findings and published many studies, regarding the different types of SCC and its propagating factors, but without available classification, like long-standing burn scars,[7] lichen planus,[10] lip cancer due to heavy exposure to sunlight.[11]

Thus, initial diagnosis and treatment of SCCs, and their premalignant conditions, are critical to diminish the morbidity and mortality of this type of skin cancer. The aim of the present work is to do gathering trial for all patients with SCC and challenging to classify them into groups proportional to their provoking triggering factors.

Patients and methods

This is a cross-sectional study that was carried out in a dermatology private clinic, Baghdad, Iraq, during the period from 2014-2023 where all patients with SCC were collected and analyzed into groups according to their recognized triggering aspects. Full demographic and clinical data were studied and evaluated. Nearly all of them were skin types III and IV. The name, age, gender, onset of disease, site of SCC, associated skin illness or internal problems, history of a long period of sun exposure, or history of burn were recorded. All

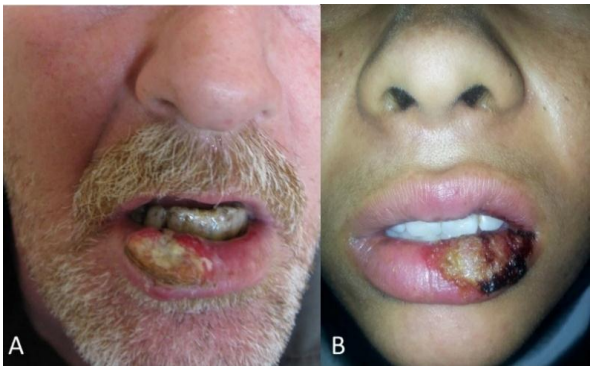

Figure 1 (A) Fifty-five years old man, (B) and twenty years old male patient with SCC of the lower lip, characterized by slowly growing nodular crusted and verrucous lesions.

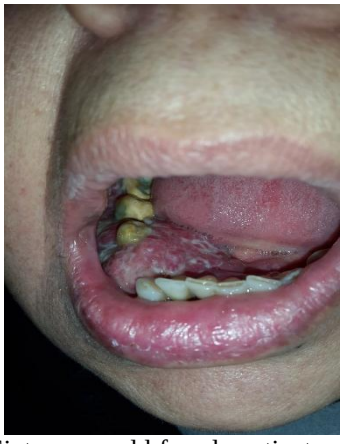

Figure 2 Sixty years old female patient, complaining of lichen planus induced SCC at the base of the oral cavity that is characterized by a slowly growing nodular tumor, with Wickham striae of LP.

patients were immunocompetent and nonsmokers but mostly had outdoor activities. Cases of SCC that are not related to the theme of the present work were excluded.

Biopsies from lesions were processed and stained for HE stains and then histopathological evaluation was carried out to confirm the clinical diagnosis.

Written consent regarding publication and photographs were taken from each subject before enrollment in the study.

Results

Complete analysis and assessment were carried out for 95 cases of SCC, 76 (80%) males and 19 (20%) females, with male to female ratio was 4:1. The mean (ranged) ages were 42 (20-78) years. They are classified into the following groups:

SCC of the lower lip, sunlight-induced in 44 (46.3%) cases, their ages ranged from 20-78 with a mean of 50 years, with 36 (83.7%) males and 6 (13.6%) females and only two (4.65%) patients showed associated solar keratosis of the face **(Figure 1)**.

Ordinary SCC without obvious triggering factor This included 22(23.1%) patients, the mean (ranged) ages were 50(24-60) years, 18 (81.8%) males and 4 (18.1%) females where different sites were involved.

Lichen planus induced SCC in 17 (17.9%) individuals, their ages ranged from 30-60years, with 12 (70.6%) males and 5 (29.4%) females. The type of lichen planus was an either oral cavity, body lichen planus or lichen planus actinicus. Oral SCC in 5 (29.4%) cases, all males, SCC of the lips in 11 (64,7%) cases, 9 males (81.8%) and 2 (18.1%) females. While one (5.8%) female case with foot involvement **(Figures 2, 3)**.

Burn-induced SCC in 12 (12.6%) patients, who complained of long-standing burn scars, their ages ranged from 25-50 years with a mean of 42 years, were 10 (83.3%) males and two (16.7%) females. The sites involved were 5 (41.7%) patients for the lower limbs and 5 (41.7%) cases for the upper arms, one (10%) patient on the buttock, and one (10%) case on the scalp. The burn scars are characterized by deep, ulcerative, located around the joints that had repeated trauma, and sometimes with secondary infection **(Figure 4)**.

The clinical examination of the regional lymph nodes and other parts of the body showed no metastasis.

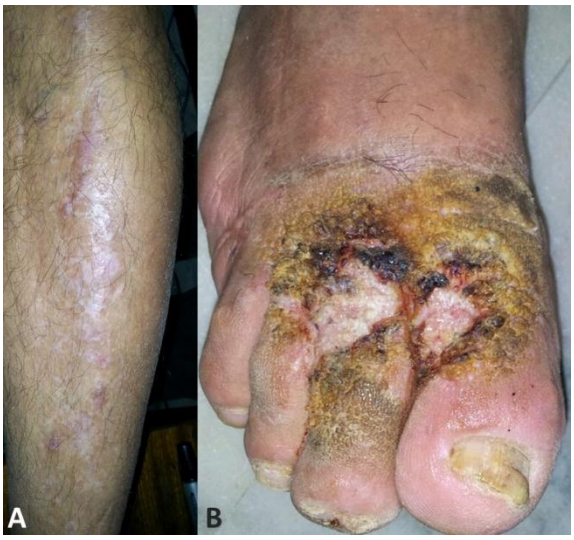

Figure 3 Fifty years old male patient showing (A) lichen planus of the leg, (B) SCC of the left foot.

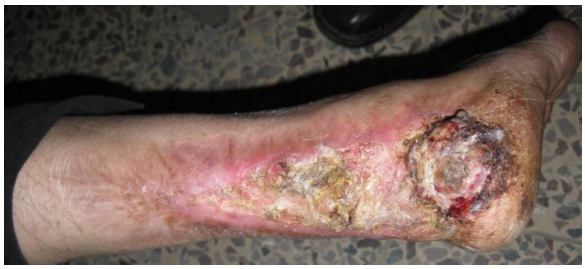

Figure 4 Showing SCC of the lower limb, triggered by a long-standing burn scar in 42 years old male patient.

Discussion

SCC is the second non-melanoma skin cancer[1] but unfortunately, they are managed separately in clinical practice hence the actual incidence of these different types of SCC is not well established. The present study provides, for the first time, an update on the frequency of SCC according to the different triggering factors. This is essentially required, as the risk factors of skin cancer continues to rise dramatically, and this needs to be judged to report the undergoing changes in the biological mechanisms happening in the human body. Few previous studies reported the ratio of BCC to SCC was nearly equal. However, an increasing incidence of SCC in the studied population younger than 65 years with heavy, chronic sunlight exposure may be an underappreciated evolving trend.[1, 21]

The current study mentioned that the male-to-female ratio in SCC was 4:1 and this could not be well explained as most people whether males or females have outdoor activities as they are living in the sunny atmospheres all over the year but males probably have more sunlight exposure, especially among workers. Although the people there have a dark complexion with Fitzpatrick skin types III and 1V. This ratio is considered to be slightly higher than many preceding studies in other countries, where male to female ratio was 2.85:1.[22,23] But the ratio in Iranian patients by Sadri's study was nearly equal and was dissimilar from the present work.[24]

One of the fixed causes for the development of lower lip SCC is exposure to sunlight, because of the longtime of exposure to the sunlight compared to the upper lip which is sloping downward and is protected by the nose region.[11] In the present study, SCC of the lower lip, as sunlight-induced SCC are reported up to 46.3% of cases without closely related skin disease, like solar keratosis as only 4.7% of patients showed associated solar keratosis of the face.

Overall, chronic and cumulative exposure to UVR is the single most significant etiological environmental issue-induced skin carcinogenesis for both non-melanoma skin cancer and melanoma, the oncogenic pathway, mutation ranges and tumor suppression genes are relatively cell-specific.[25] UVB is directly absorbed by DNA and thus causes DNA injury and changes in gene expression by intracellular signaling transduction, which leads to skin cancer. UVA irradiation can yield reactive oxygen free radicals, which cause secondary harm to DNA, and thus develop skin cancer.[26,27]

In the present work, ordinary SCC without

obvious triggering factors is elucidated in 23.1% of patients. The interpretation is related to other exogenous mutagens including dietary components, plus epigenetic alterations, leading to changes in gene manifestation, and facilitating inappropriate transcriptional initiation and quieting of genes. Thus, enhancing the rate of mutation, proliferation, and drop in cell death. however, DNA repair passes through the wrong way due to genetic or environmental aspects, therefore mutations in tumor suppressor genes and proto-oncogenes may happen, which lead to the development of tumor.[3,28]

The current study demonstrated similar information to what had been published by Sharquie *et al.*,[10] regarding the development of SCC following all variants of LP, either directly or with other additive influences. Herein, LP derived SCC is observed in 17.9% of patients. The oral cavity and actinic LP of the lips were involved in 29.4%, and 64.7% of cases respectively, while body lichen planus in 5.8% of individuals. Especially when evaluating poorly responding lesions or longstanding non-healed LP. Though SCC as a complication of LP is a sporadic and non-documented problem, this observation should be kept in mind during daily medical practice. But, on contrary, many preceding kinds of researches suggest a greater risk of malignant transformation in subjects with oral LP. [29,30] World Health Organization (WHO) describes oral LP as a potentially malignant illness, and close monitoring of oral LP patients was recommended.[31]

Also, this study showed that 12.6% of patients are well recognized as burn-induced SCC. It was somewhat higher than other published studies.[4,7,32] Our participants complained of long-standing burn scars, where the main sites involved are the lower limbs and the upper arms in about 41.7% of patients for each site, while nearly 10% of cases involved the buttock and 10% of cases for the scalp. The burn scars are characterized by deep, ulcerative, located around the joints getting repeated trauma, and sometimes with secondary infection. The most important correlation with the development of SCC in burn scars is the early job time, prolonged sunlight exposure during outdoor work, and sunny climatic situation during the whole year time.[33] Important advice for patients with old burn scars for preventing skin cancer development is the avoidance of repeated infection of the burned skin, protect the burn scars from frequent trauma, and start medical treatment like skin grafting for burn scars as soon as possible.

Conclusion

This is the first study that documented the actual frequency and incidence of different cutaneous SCC according to their triggering factors. Their frequency was lower lip sunlight-induced SCC in 44(46.3%) cases, ordinary SCC without triggering factor in 22(23.1%), lichen planus induced SCC in 17(17.89%) and burn-induced in 12(12.63%) patients with SCC. It is essential to treat and or prevent these triggering factors to avoid these different SSC variants.

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