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Research Paper

Squamous cell carcinoma: a comprehensive review on causes, clinical presentation, diagnosis, prognosis, and prevention

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ABSTRACT

Background: Squamous cell carcinoma (SCC) is one of the most common skin cancers and represents a significant public health concern. Its development is strongly associated with cumulative exposure to ultraviolet (UV) radiation from sunlight and tanning beds.
Objective: This review summarizes the epidemiology, risk factors, clinical features, diagnosis, prognosis, and prevention of cutaneous SCC.
Methods: Current evidence concerning SCC etiology, risk factors, clinical presentation, diagnostic approaches, prognostic factors, and preventive strategies was reviewed and synthesized.
Results: Chronic UV exposure is a major risk factor for SCC. Additional factors include fair skin, previous sunburn, immunosuppression, and inherited disorders that impair protection against UV-induced skin damage. Clinically, SCC commonly presents as raised, scaly, crusted, erythematous, ulcerated, or tender lesions. Biopsy with histopathological examination remains essential for definitive diagnosis, while dermoscopy and imaging may assist in selected cases. Prognosis is influenced by tumor stage, metastasis, tumor characteristics, and overall patient health. Early diagnosis is generally associated with favorable outcomes, whereas metastatic disease and immunocompromise are linked to poorer prognosis. Prevention primarily involves UV protection, protective clothing, sunscreen use, shade-seeking, self-skin examination, and regular dermatological surveillance.
Conclusion: SCC remains an important dermatological and public health problem. Early recognition, appropriate diagnosis, sun-protective behaviors, and routine skin surveillance can reduce disease burden and improve clinical outcomes. Patient education and preventive care remain essential components of SCC management.

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1. INTRODUCTION

1.1 Definition and Overview of Squamous Cell Carcinoma (SCC)

Squamous cell carcinoma (SCC) is a common type of skin cancer that arises from the squamous cells, which are thin, flat cells that form the outer layer of the skin. These cells are found in various parts of the body, including the skin [1], lips, mouth, esophagus, lungs, and other organs [2], [3]. SCC primarily affects the skin [4], [5], [6] and it typically develops on areas exposed to the sun, such as the face, neck, hands, and arms. However, it can also occur on non-sun-exposed areas and mucous membranes. SCC is characterized by [7], [8], [9] the uncontrolled growth and division of abnormal squamous cells [10]. These cells may form a scaly, red patch, an open sore, or a raised growth with a crusted surface [2]. In some cases, SCC can progress beyond the skin and invade nearby tissues, including lymph nodes, or spread to distant organs, leading to metastatic SCC.

1.2 Brief Explanation of SCC's Prevalence and Significance as a form of Skin Cancer

Squamous cell carcinoma is the second most common type of skin cancer, after basal cell carcinoma (BCC). According to global estimates, SCC accounts for approximately 20% of all skin cancers [11], [12]. It affects both men and women, and its incidence tends to increase with age. While SCC can occur in individuals of any skin type, people with fair skin [3], light-colored eyes, and a history of sun exposure are at higher risk. The prevalence of SCC varies geographically, with higher rates reported in regions with sunny climates and populations engaged in outdoor activities. For instance, in Australia, SCC is considered a major public health issue, given the high rates of ultraviolet (UV) radiation exposure and the country's fair-skinned population. Moreover, SCC has been associated with certain risk factors, including chronic sun exposure [4], tanning bed use, exposure to chemicals, immunosuppression, and specific genetic conditions such as xeroderma pigmentosum. The significance of SCC lies in its potential to invade surrounding tissues and metastasize [13]. While most SCCs are localized and can be successfully treated with early detection and appropriate intervention, advanced or neglected cases can lead to significant morbidity and mortality. Therefore, understanding the risk factors, recognizing early signs, and seeking prompt medical attention are crucial in managing SCC effectively [14].

1.3 Causes and Risk Factors

- **Discussion of Common Causes, Such As Exposure to Ultraviolet (UV) Radiation from the Sun or Tanning Beds:** The primary cause of squamous cell carcinoma (SCC) is prolonged or excessive exposure to ultraviolet (UV) radiation from the sun or artificial sources like tanning beds. UV radiation damages the DNA in skin cells, leading to genetic mutations that can trigger the development of SCC. The two types of UV radiation that are most relevant to skin cancer are UVA and UVB. UVA radiation penetrates deep into the skin and is associated with long-term damage, including premature aging and wrinkling. UVB radiation is more intense and primarily affects the superficial layers of the skin, causing sunburns. Both UVA and UVB radiation contribute to the development of SCC, although UVB is considered more carcinogenic. Tanning beds emit UVA and UVB radiation, and their use has been strongly linked to an increased risk of developing SCC. Studies have shown that indoor tanning significantly raises the likelihood of developing SCC, especially when started at a young age and with frequent or prolonged exposure.

1.4 Explanation of Risk Factors, Including Fair Skin, History of Sunburns, and Certain Genetic Conditions

- **Fair Skin:** Individuals with fair skin, particularly those who have light-colored hair and eyes, are more susceptible to developing SCC. Fair skin has less melanin, which is the pigment that provides some protection against UV radiation. Therefore, people with fair skin tend to burn more easily and have a higher risk of developing skin cancer, including SCC.
- **History of Sunburns:** Experiencing severe sunburns, especially during childhood or adolescence, increases the risk of developing SCC later in life. Intense and repeated sunburns lead to cumulative damage to the skin cells' DNA, elevating the chances of malignant transformation.
- **Genetic Conditions:** Certain genetic conditions can predispose individuals to an increased risk of SCC. One notable example is xeroderma pigmentosum (XP), a rare inherited disorder that impairs the body's ability to repair DNA damage caused by UV radiation. People with XP are extremely sensitive to sunlight and have a significantly higher risk of developing SCC and other skin cancers. Other genetic factors, such as a family history of skin cancer, may also contribute to an elevated risk of SCC. Genetic variations associated with decreased DNA repair capacity or altered immune response can influence an individual's susceptibility to SCC development.

1.5 Clinical Presentation and Diagnosis

- **Description of SCC's Typical Appearance, Including Raised, Scaly, or Crusty Skin Lesions:** Squamous cell carcinoma (SCC) typically presents as a variety of skin lesions, which can help in identifying and diagnosing the condition. The appearance of SCC lesions can vary, but they often share certain characteristics. Common manifestations of SCC include:
- **Raised or Elevated Growths:** SCC lesions often appear as firm, raised, or elevated growths on the skin. These growths can range in size from small nodules to larger masses.
- **Scaly or Crusted Surface:** SCC lesions frequently exhibit a scaly or crusty surface. The affected area may appear rough, scaly, or flaky. As the lesion grows, the outer layer may become thicker and form a crust.
- **Redness and Inflammation:** SCC lesions may display varying degrees of redness and inflammation. The affected skin area can appear red, irritated, or inflamed, and it may be sensitive to touch.
- **Ulceration or Open Sores:** Advanced SCC lesions may develop ulcers or open sores. These sores can be painful and may bleed easily. Persistent non-healing sores that do not improve over time should raise suspicion for SCC.
- **Tender or Itchy Lesions:** Some SCC lesions can cause discomfort, tenderness, or itching. This may be due to inflammation or irritation of the surrounding tissues. It is important to note that while SCC typically arises on sun-exposed areas, it can also occur in non-sun-exposed regions, such as the genital area, inside the mouth, or on the mucous membranes. These lesions may have different appearances compared to those on sun-exposed skin, but they share the potential for invasive growth and metastasis.

1.6 Overview of Diagnostic Methods, Such as Biopsy, Dermatoscopy, and Imaging Techniques like Ultrasound or CT Scans

- **Biopsy:** A biopsy is the gold standard diagnostic procedure for SCC. It involves the removal of a small sample of tissue from the suspicious lesion for examination under a microscope. The biopsy can be performed as a shave biopsy, punch biopsy, or excisional biopsy, depending on the characteristics and location of the lesion.
- **Dermatoscopy:** Dermatoscopy, also known as dermoscopy or dermatoscopy, is a non-invasive technique that allows dermatologists to examine skin lesions with a specialized handheld instrument called a dermatoscope. Dermatoscopy enables the visualization of specific structures within the skin, aiding in the diagnosis and differentiation of SCC from other skin conditions.
- **Imaging Techniques:** In certain cases, imaging techniques may be used to evaluate the extent of SCC and detect possible metastasis. Ultrasound can be employed to assess lymph nodes near the lesion and

evaluate the depth of invasion. For SCCs in specific locations, such as the head and neck region, computed tomography (CT) scans may be performed to assess regional lymph nodes and adjacent structures. These diagnostic methods help dermatologists and healthcare professionals accurately diagnose SCC and determine the appropriate treatment strategy based on the characteristics and stage of the lesion.

1.7 Prognosis and Prevention

- **Analysis of SCC prognosis, taking into Account Factors like Tumor Stage, Metastasis, and Patient's Overall Health:** The prognosis of squamous cell carcinoma (SCC) depends on several factors, including the stage of the tumor, the presence of metastasis, and the overall health of the patient.
- **Tumor Stage:** SCC is staged based on the size of the tumor, depth of invasion, involvement of nearby lymph nodes, and presence of distant metastasis. The most commonly used staging system is the American Joint Committee on Cancer (AJCC) TNM system. Generally, SCCs diagnosed at an early stage (localized disease) have a better prognosis compared to those that have advanced locally or metastasized.
- **Metastasis:** The presence of metastasis significantly affects the prognosis of SCC. If SCC has spread to regional lymph nodes or distant organs, the disease is considered advanced and carries a poorer prognosis. Early detection and treatment of SCC are crucial to minimize the risk of metastasis.
- **Patient's Overall Health:** The overall health and immune status of the patient play a role in SCC prognosis. Patients with compromised immune systems, such as those with organ transplantation, HIV/AIDS, or certain autoimmune diseases, may have a higher risk of SCC recurrence or progression. Emphasis on the importance of prevention, including sun protection measures, regular skin screenings, and self-examination techniques Prevention is essential in reducing the risk of developing squamous cell carcinoma (SCC) and improving prognosis. Key preventive measures include:
- **Sun Protection Measures:** Limiting exposure to harmful UV radiation from the sun is crucial in preventing SCC. This includes seeking shade during peak sun hours, wearing protective clothing (long sleeves, wide-brimmed hats, sunglasses), and applying broad-spectrum sunscreen with a high sun protection factor (SPF) regularly to exposed skin.
- **Regular Skin Screenings:** Regular skin screenings performed by a dermatologist can help detect SCC at an early stage when it is most treatable. Dermatologists can identify suspicious lesions, perform biopsies if necessary, and provide appropriate management.
- **Self-Examination Techniques:** Individuals should perform regular self-examinations of their skin to identify any changes or new lesions. This includes observing the skin for any new growths, changes in color, size, or texture of existing lesions, and any non-healing sores. Promptly reporting any concerning changes to a healthcare professional is important for timely evaluation and intervention.
- **Avoidance of Tanning Beds:** It is crucial to avoid the use of tanning beds, as they emit harmful UVA and UVB radiation, increasing the risk of developing SCC and other types of skin cancer.

By adopting these preventive measures, individuals can significantly reduce their risk of developing SCC and promote early detection for better prognosis.

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Author Contributions Statement

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Sonal GP Pillai	✓	✓	✓	✓		✓		✓	✓	✓		✓		

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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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