Squamous Cell Carcinoma in a Psoriasis Patient Possibly Due to Long-term Methotrexate

Guneet Awal, Manpreet Kaur, Ravika Kanish Budhiraja
Department of Dermatology, Venereology and Leprosy, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India

Abstract

Squamous cell carcinoma (SCC) in a patient of psoriasis is a rare occurrence with paramount clinical significance for selecting the appropriate management options. We report a case of SCC in a 45-year-old male patient of psoriasis on unsupervised methotrexate for over 10 years. This case report highlights the importance of early diagnosis of SCC, carcinogenic potential of methotrexate, and role of acitretin in the management of such patients.

Keywords: Acitretin, methotrexate, psoriasis, squamous cell carcinoma

INTRODUCTION

Psoriasis is a chronic inflammatory process characterized by multiple remissions and relapses, thereby necessitating a long-term treatment and follow-up.\(^1\) The relationship between psoriasis and increased cancer risk is being increasingly debated. Squamous cell carcinoma (SCC) has been reported in association with long-term psoralen and ultraviolet A therapy, cyclosporine, and methotrexate. Appropriate patient counseling and clinical follow-up are deemed necessary to maximize safety and minimize adverse effects with these agents.\(^2\)

CASE REPORT

A 45-year-old male belonging to Fitzpatrick skin Type IV was referred from the surgery inpatient department to the dermatology outpatient department with a nonhealing ulcer with graft failure on the extensor aspect of left forearm. A detailed history of the patient was taken which unraveled a 15-year-old history of chronic plaque psoriasis manifesting as multiple erythematous scaly papules and plaques over the scalp, chest, abdomen, upper limbs, and lower limbs. They were associated with mild pruritus. The chief complaint of the patient was an asymptomatic nonhealing ulcer over the left forearm for 3 months. It started as a hyperpigmented nodule over the preexisting plaque of psoriasis which slowly progressed in size to form an ulcer. On further probing, he revealed an unsupervised intake of oral methotrexate for 10 years with a cumulative dose amounting to 4240 mg along with topical treatments in the form of salicylic acid and corticosteroids. The patient denied any history of phototherapy, topical coal tar application or of any other oral antipsoriatic treatment. He was nonalcoholic and nonsmoker. There was no history of excessive exposure to sun or intake of any indigenous medication.

On examination, multiple erythematous papules and plaques covered by silvery white scales were present on the scalp, chest, abdomen, upper limbs, and lower limbs involving 20% of the body surface area. A well-defined ulcer measuring 5 cm × 5 cm covered by a graft with yellowish crusts was present on the extensor aspect of the left forearm. It also had some areas of denudation and was surrounded by an erythematous scaly plaque. A biopsy from the edge of the ulcer showed large, round-to-polygonal tumor cells with nuclear pleomorphism, vesicular chromatin, prominent nucleoli along with extracellular keratinization in the form of keratin pearls [Figure 3]. These findings were consistent with the diagnosis of SCC. Complete blood count, liver function tests, renal function tests, lipid profile, urine complete,

Address for correspondence: Dr. Guneet Awal,
469, East Mohan Nagar, Opp. DSP Park, Sultanwind Road, Amritsar, Punjab, India.
E-mail: guneetawal@gmail.com

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and random blood sugar were normal. The viral markers (HBV, HCV, and HIV) were nonreactive. Ultrasonography of the abdomen was normal with no fibrosis or enlargement of liver. Skin swab for culture and sensitivity showed no growth. Keeping in mind the history, examination, and histopathology, we made the diagnosis of methotrexate-induced SCC with chronic plaque psoriasis. Methotrexate was stopped, and the patient was treated with acitretin 25 mg twice a day keeping in mind its antipsoriatic and anticarcinogenic role.

**Discussion**

Our patient was a known case of chronic plaque psoriasis and was on unsupervised methotrexate for over 10 years. He eventually developed SCC in the preexisting lesions of psoriasis. The patient was Fitzpatrick skin Type IV which is protected by greater amount of melanin in skin and therefore has lesser intrinsic predisposition to SCC as compared to Fitzpatrick skin Type I and II, thus attributing its development even more to long-term methotrexate administration. No other risk factors of SCC were found in our patient.

Psoriasis itself reduces the risk of development of cancer due to lower cutaneous levels of a known carcinogen, aryl-hydrocarbon hydroxylase, but certain modalities used in its treatment are carcinogenic. Methotrexate is one of the most common drugs used in the management of psoriasis. Stern and Laird reported that prolonged exposure to methotrexate is a risk factor for developing SCC with relative risk being 2.1. Methotrexate being a photosensitizer accelerates the phototoxic process leading to an increased incidence of nonmelanoma skin cancer (NMSC). Moreover, therapy-related immunosuppression can inhibit cancer-related immune surveillance. Hence, drug-induced immunosuppression is a risk factor for NMSC, particularly squamous cell tumors.

In a study done by Nyfors and Jensen, they observed 248 psoriatics taking single, weekly, oral dose of methotrexate ranging from 5 to 25 mg over a follow-up period of 5–14 years. They reported three cases of ovarian cancer, two of breast cancer, two of lymphoma, and one of esophageal carcinoma with a single case of SCC of the scrotal skin.

Anishchenko also observed five cases of cutaneous SCC in psoriasis and emphasized the need of early diagnosis which carries an immense prognostic importance. A poor prognosis is most frequently explained by late diagnosis of the tumor process. Jensen et al. stated in their study that when a localized SCC is diagnosed, the patient should be referred for radical treatment. In addition, once a patient is diagnosed with one nonmelanoma skin cancer, they are at increased risk for additional cutaneous malignancies. Systemic retinoids are extremely useful in these cases because of their dual action, i.e., chemoprevention of nonmelanoma skin cancers and desired antipsoriatic action. Therefore, they are a preferred modality of management in such patients.

We report this case because of the rarity of association as well as for highlighting the need for regular surveillance in all patients on long-term immunosuppressant antipsoriatic treatment.

**Conclusion**

Cutaneous toxicities with methotrexate are usually manageable and not life-threatening, but a prolonged treatment may
culminate in SCC. This devastating side effect should be borne in mind of a treating physician. However, these need to be further evaluated by prospective studies.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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