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Case Report

Inflammation of Actinic Keratoses Induced by Combination of Carboplatin and Paclitaxel: Two Case Reports

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Keywords
Actinic keratoses · Inflammation · Chemotherapy · Carboplatin · Paclitaxel

Abstract
The observations of a beneficial effect of 5-fluorouracil-induced actinic keratoses (AK) inflammation led to the development of topical fluorouracil, a product registered for the management of AK. A conscientious surveillance of AK inflammation during chemotherapy may conceivably lead to the development of further drugs for treatment of AK. A number of other chemotherapeutics have thus been linked to similar reactions without ensuing development. Here, we describe two further cases linking chemotherapy with carboplatin and paclitaxel to possible anti-AK effects, identifying them as potential treatments. Whether multidrug chemotherapy leads to stronger AK inflammation or cure AK more successfully is currently unknown.

Introduction

A conscientious surveillance of inflammation of manifested and/or subclinical actinic keratoses (AK) during chemotherapy may lead to the development of further drugs for the management of AK. The observations of a beneficial effect of 5-fluorouracil-induced AK

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inflammation have already contributed to the successful registration of topical fluorouracil in the management of AK [1, 2]. Besides pyrimidine analogs, a number of other chemotherapeutics, classified into chemotherapeutic groups of protein kinase inhibitors, taxanes, folic acid analogs, alkylating agents, platinum compounds, purine analogs, vinca alkaloids, cytotoxic antibiotics, and monoclonal antibodies, have been linked to similar reactions, suggesting potentially meaningful new pharmacodynamics mechanisms for further research [3–12]. Here, we present two interesting new cases of inflammation of AK induced by chemotherapy with carboplatin and paclitaxel to add new evidence for their anti-AK effect. Whether multidrug chemotherapy leads to stronger AK inflammation or cure AK more successfully is currently unknown.

Case Report

For the case presentation, see Table 1 and Figures 1, 2. The manuscript was prepared according to the CARE Checklist, attached as supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528128).

Discussion

Our 2 cases of inflamed AK occurred 1 month and 2 days after initiation of chemotherapy. These observations potentially link carboplatin, paclitaxel, and trastuzumab to anti-AK effect.

Selective inflammation of AK during chemotherapy is possibly a consequence of direct cytotoxicity of an active compound on atypical keratinocytes that accumulate ultraviolet-induced damage of deoxyribonucleic acid, but the exact mechanism of how different chemotherapeutics achieve this effect seems to be drug-dependent [13]. Alternative explanations of skin lesions (i.e., subacute lupus erythematosus, actinic lichen planus, cutaneous vasculitis, hypersensitivity drug reactions, drug-induced photosensitivity reactions, and photocontact dermatitis) were in both patients excluded on the basis of a history, typical clinical features of AK, and in the first case with the additional characteristic presence of atypical keratinocytes on histological examination [14–20].

Reports of partially successful curing of AK while undergoing therapy with carboplatin and/or docetaxel, a chemotherapeutic agent belonging together with paclitaxel to the pharmacological group of taxanes, already exist [21–24]. Since a co-occurrence of inflamed AK and treatment with trastuzumab has not been reported before and it targets human epidermal growth factor receptor 2-overexpressed cells, its role in AK inflammation is questionable [25]. This suggests the importance of prioritizing research into potential topical forms of paclitaxel and carboplatin in the management of AK. In conclusion, careful observations of AK inflammation in patients undergoing chemotherapy represent a starting point for the development of new topical products for the management of AK.

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Table 1. Case presentations

	Case 1	Case 2
Age, gender	68, female	78, female
Duration of lesions	1 week	2 days
Clinical features	Erythematous slightly scaly macules and flat plaques	Numerous bright erythematous maculo-papules with slight scaling and hyperkeratosis
Location of the lesions	Extensor surfaces of the hands and forearms, right cheek, and upper back	Face
Involvement of non-photoexposed areas, mucous membranes	No	No
Local/systemic symptoms	Slight pruritus/none	Pruritus, burning sensation/none
Chemotherapeutic agents	Carboplatin, paclitaxel	Carboplatin, paclitaxel, trastuzumab
Type of cancer	Ovarian	Breast carcinoma and adenocarcinoma of the lung
Interval between the initiation of chemotherapy and the onset of inflammation	1 month	2 days
Previous history of AK	None	Known history of multiple cryotherapy treatments
Other concomitant diseases	Arterial hypertension, atrial fibrillation	None
Other potential triggers of skin eruption (i.e., sun exposure, other new medications, supplements, topical products)	None	None
Family history	None	None
Diagnosis	Clinical and histopathological, which revealed AK with an intensive interface inflammatory reaction	Clinical; dermoscopy showed strawberry pattern
Treatment of inflamed AK/duration	Methylprednisolone aceponate cream once daily/1 week	Methylprednisolone aceponate cream once daily and fusidic acid twice daily/1 week
Status of treatment with chemotherapy after observing inflammation of AK	As planned	As planned
Time of follow-up	2 months	Several months later
Outcome (regression of AK)	Partial	Partial

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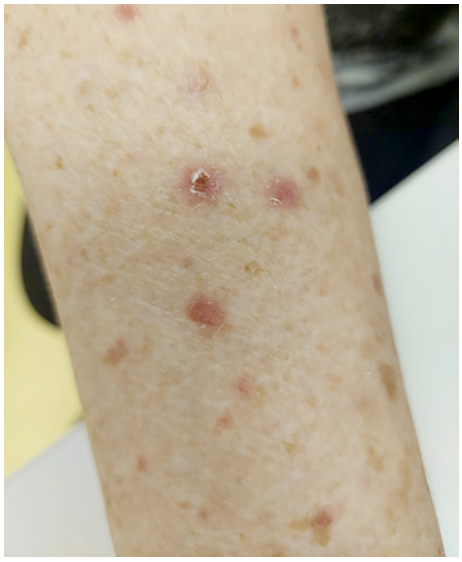

Fig. 1. Close-up photo of the first patient, showing inflamed AK on the extensor part of the right forearm.

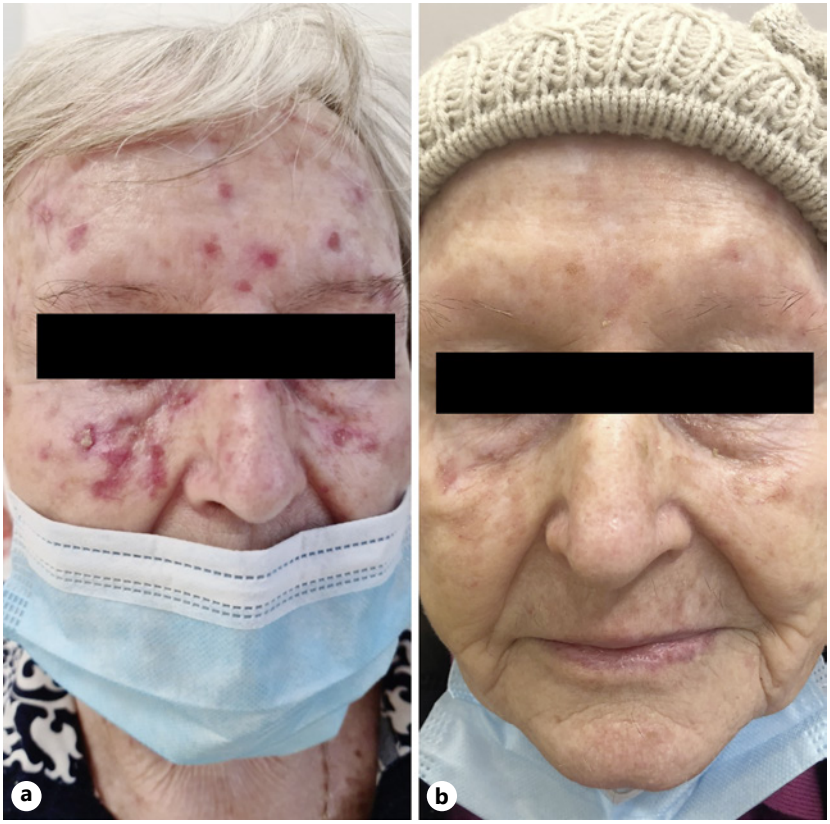

Fig. 2. Photos of the second patient, showing (**a**) inflamed AK at the referral and (**b**) regression of inflammation with few AK left at follow-up several months later.

Statement of Ethics

Although case reports present only objective data on the patients' disease and the authors did not test new methods of diagnosis and treatment, ethics approval was not required for

the publication of the study according to the rules on the membership, responsibilities, and working methods of the Republic of Slovenia National Medical Ethics Committee (EVA 2019-2711-0059; SOP 2020-01-0342). Written informed consent was obtained from both patients for publication of this case report and any accompanying images.

Conflict of Interest Statement

Gregor Borut Ernst Jemec has received honoraria from AbbVie, Chemocentryx, Coloplast, Incyte, InflaRx, Kymera, Leo Pharma, Moonlake, Novartis, UCB, Union Therapeutics, and Wella for participation on advisory boards and grants from AbbVie, AstraZeneca, CSL, InflaRx, Janssen-Cilag, Leo Pharma, Moonlake, Novartis, Regeneron, and Sanofi for participation as an investigator and received speaker honoraria from AbbVie, Boehringer Ingelheim, Galderma, and Novartis. He has also received unrestricted departmental grants from Leo Pharma and Novartis. Other authors report no conflict of interest.

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Author Contributions

Špela Šuler Baglama contributed to conception and writing; Anja Trajber Horvat and Irena Peteln contributed to writing; Gregor Borut Ernst Jemec revised the article; all the authors gave final approval of the version of the article to be published.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary materials. Further enquiries can be directed to the corresponding author.

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