

Case Report

5-FLUOROURACIL IN THE TREATMENT OF ACTINIC KERATOSIS AND PHOTOAGING: A CASE WITH SEVERE LOCAL IRRITANT REACTION DURING TREATMENT

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ABSTRACT

In the treatment of actinic keratosis, various topical agents are used for treatment of field cancerization as well as lesional destructive treatments. In this case report, it was aimed to present a photographic follow-up of a patient who developed severe local irritant reaction by usage of topical 5% fluorouracil but is very satisfied with the long-term anti-aging effect and to emphasize the place of 5-fluorouracil in photoaging treatment. Topical 5-Fluorouracil 5% cream therapy was recommended for widespread actinic keratosis lesions in a 67-year-old female patient who had previously undergone non-melanoma skin cancer surgery. On day 20 of treatment, a severe local irritant reaction developed. Severe local reactions were controlled by skin supportive therapy. It was observed that the patient does not have actinic keratosis recurrence in the second year following treatment, has significant improvement in photoaging and is satisfied with the treatment. Topical 5 fluorouracil treatment treats both actinic keratoses and field cancerization, prevents actinic keratoses from developing and simultaneously treats photoaging. Considering all this, topical 5-fluorouracil treatment, which is very economical, seems to be the treatment method that should be preferred in the treatment of actinic keratosis.

Key words: Actinic keratosis, 5-fluorouracil, photoaging, irritation, side effect

ÖZET

Aktinik keratoz tedavisinde, lezyonel destrüktif tedavilerin yanı sıra alan kanserizasyon tedavisi için çeşitli topikal ajanlar kullanılır. Bu olgu sunumunda topikal% 5 florourasil kullanımı ile şiddetli lokal iritan reaksiyon gelişen ancak tedavinin uzun süreli anti-aging etkisinden çok memnun kalan bir hastanın fotografik takibini sunmak ve fotoyaşlanma tedavisinde 5-fluorourasilin yerini vurgulamak amaçlandı. Melanom dışı deri kanseri operasyon öyküsü olan 67 yaşında kadın hastaya, yaygın aktinik keratoz lezyonları için topikal 5-Fluorourasil % 5 krem tedavisi önerildi. Tedavinin 20. gününde ciddi bir lokal iritan reaksiyon gelişti. Şiddetli lokal reaksiyonlar deri bakımı ile kontrol altına alındı. Tedaviyi takip eden ikinci yılda hastada aktinik keratoz rekürrensi olmadığı, fotoyaşlanmada belirgin düzelme olduğu ve hastanın tedaviden memnun kaldığı gözlemlendi. Topikal 5 florourasil tedavisi hem aktinik keratozları hem de alan kanserizasyonunu tedavi eder, aktinik keratozların gelişmesini engeller ve aynı anda fotoyaşlanmayı tedavi eder. Bütün bunları göz önüne alırsak, çok ekonomik olan topikal 5-fluorourasil tedavisi, aktinik keratoz tedavisinde tercih edilmesi gereken tedavi metodu gibi gözükmemektedir.

Anahtar kelimeler: Aktinik keratoz, 5-fluorouracil, fotoyaşlanma, iritasyon, yan etki

INTRODUCTION

Actinic keratoses are skin lesions that occur in light-skinned individuals due to chronic ultraviolet damage, which are common, cause serious financial culprit, and most importantly, have malignant transformation potential. There are different views that suggest actinic keratoses are precancerous lesions or in situ squamous cell carcinoma (SHC), as well as an epiphenomenon in chronic photoaging. Although most actinic keratosis lesions may show spontaneous regression, conversion to SHC is reported to be 0,025-20% per year. In the treatment of actinic keratosis, destructive treatments such as cryotherapy, curettage & electrocautery, laser skin resurfacing are used for the lesional treatment as well as topical agents such as 5-fluorouracil, imiquimod and diclofenac are used for field cancerization. In an American study, it was found that actinic keratosis treatment costs 1-2 billion USD annually, destructive treatments such as cryotherapy were performed 10 times more in actinic

keratosis treatment, and topical prescription products were used less. In a meta-analysis, it was found that topical 5-fluorouracil 5% cream was highest and cryotherapy followed by topical diclofenac sodium had the lowest clearance rate in actinic keratoses. However, another meta-analysis and 2012 Cochrane review did not reveal such clear ordering of efficacy. It was reported that patient satisfaction in actinic keratosis treatment is not only dependent on treatment efficacy, but also on severity of and the ability to control side effects, pain associated with topical treatments, development of exudative ulcers and other factors affect treatment compliance.¹

In this case report, it was aimed to present a photographic follow-up of a patient who had a severe local irritation reaction with topical 5-fluorouracil 5%, but was also very satisfied with the antiaging effect in the long term and to emphasize the place of 5-fluorouracil in photoaging treatment.

CASE REPORT

A 67-year-old female patient was admitted to the dermatology outpatient clinic because of swelling in the operation scar that she had previously had. Dermatologic

examination revealed postoperative scar of flap reconstruction in the right ala nasi and widespread erythematous and some brownish macules and papules with

desquamation over the cheeks, nose and forehead. Her personal medical history revealed previous operation for nasal basal cell carcinoma, heart rhythm disturbance, coronary arterial disease, hypertension, type II diabetes, and chronic hepatitis associated with hepatitis B infection. Topical 5-fluorouracil 5% cream was recommended for applying at night to all regions for field cancerization treatment

and *Triticum vulgare* extract (Fito®) cream was recommended for use in the daytime against irritation. On the 20th day of the treatment, the patient reapplied with the complaints of widespread exudative wounds and swelling, inability to speak and inability to wash her face. There was diffuse facial erythema, edema, rhagades and crusts on the dermatologic examination (Figure 1).



Figure 1. Severe local irritant reaction in the case presenting on day 20 of topical 5-fluorouracil treatment.

Topical 5 fluorouracil therapy was discontinued, frequent use of *triticum vulgare* cream was recommended, and oral non-steroid anti-inflammatory therapy with oral antibiotherapy was

recommended. Desquamation started on the fourth day (Figure 2) and widespread erythema and mild desquamation remained on the 7th day (Figure 3).



Figure 2. The appearance at the fourth day following the development of the irritant reaction.



Figure 3. At the seventh day, all the irritation findings seem to have disappeared.

The case indicated that she was told to be rejuvenated by the people around her at the fourth (Figure 4) and 13th (Figure 5)

month controls and expressed her satisfaction with the treatment.



Figure 4. The appearance at the fourth month after the completion of treatment of the case.



Figure 5. 13th month appearance of the case following the completion of the treatment

Patient's informed consent was taken. Meanwhile, complete clearing of actinic

keratotic lesions was achieved. The case is still under follow-up and there is no

recurrent actinic keratosis or newly developing non-melanoma skin cancer at the second year following treatment.

DISCUSSION

5 fluorouracil was first introduced in 1957 and has been shown to be effective in the treatment of many benign, precancerous and cancerous dermatologic diseases and photoaging. It is a topical nucleotide analogue antitumor agent. 5-fluorouracil shows its therapeutic efficacy by affecting synthesis and functions of DNA and RNA in rapidly proliferating cells and by increasing p53 expression. After completion of the complete treatment period with topical 5-fluorouracil, it was observed that the total number of actinic keratoses were reduced by 90% and complete clearing was observed in approximately half of the patients.² In another published study, it was reported that topical 5-fluorouracil reduced the number of newly formed actinic keratoses and the need of additional local treatment for longer than 2 years following a one-month single cure application, in short it prevents the development of new actinic keratoses.³ Treatment compliance with 5-fluorouracil 0.5% cream was found to be higher than expected in patients and the treatment compliance being 86% in a study designed

to explore treatment compliance. Despite the high incidence of side effects, the authors concluded that the high adherence to treatment may be related to adverse events being mild and moderate in severity, the sense of adverse drug reactions meaning that the drug is being effective, patients being older and treatment compliance is higher in elderly patients, increased anxiety due to precancerous character of lesions and that the duration of the treatment being fixed may result in a psychological feeling of "the appearance of light at the end of the tunnel" at the end of the treatment.⁴ Our case continued to the treatment until the 20th day of treatment despite the severe local irritant reaction that developed and reapplied while still using the treatment in the most severe period of adverse reaction. Our case also shows that contrary to what is thought, side effects following topical 5-fluorouracil usage are common, but patient compliance is high due to the factors just mentioned.

5-fluorouracil topical therapy has been shown to produce its efficacy in photoaging

by stimulating epidermal injury (increasing keratin 16 expression), pro-inflammatory cytokines (IL-1 β) and increasing mRNA and protein synthesis of basic molecules (matrix metalloproteinases 1 and 3, procollagen I and III) in wound healing response. It was reported that topical 5-

fluorouracil significantly reduced overall fine wrinkling, tactile roughness, mottled hyperpigmentation, lentigines, sallowness and photoaging overall severity scores, and the patients were satisfied with the treatment.⁵

CONCLUSION

Currently, even there is no definitive treatment method for actinic keratosis that is approved by consensus in the efficacy, topical 5-fluorouracil treats both actinic keratoses and field cancerization, prevents actinic keratoses from developing and simultaneously treats photoaging.¹

Considering all this and the fact that it is able to treat field cancerization and very economical, topical 5-fluorouracil treatment seems to be the treatment method that should be preferred in the treatment of actinic keratoses.

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