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CASE REPORT

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A case of vitiligo developed after isotretinoin therapy

Correspondence
Mehmet Semih Celik, Fırat University Medical School, Department of Dermatology, Elazig, Turkey.

e-mail
drmsemihcelik@gmail.com

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ORCID ID of the author(s):
MSC: 0000-0002-3378-0619
DC: 0000-0001-8405-7730

Mehmet Semih Celik[1] - Demet Cicek[1]

1. *Firat University Medical School, Department of Dermatology, Elazig, Turkey.*

Abstract

Oral isotretinoin, a 13-cis retinoic acid and a derivative of the retinoids, is very effective for severe nodulocystic acne and papulopustular acne, which at times turns scar-forming and resistant. Common mucocutaneous and ocular dryness are the side effects. Also, musculoskeletal symptoms such as back pain, arthralgia, and myalgia may be seen in about 16% of adults post-isotretinoin therapy, usually resolving after treatment discontinuation. Depressive side effects and suicidal thoughts are concerns voiced against its use. Vitiligo is an autoimmune disorder characterized by the selective loss of melanocytes and depigmented patches on the skin. Recently, it has been classified to include metabolic, oxidative stress, genetic, and environmental factors. We present a very rare case of vitiligo developing after systemic isotretinoin therapy in a 24-year-old female patient with severe nodulocystic acne. The patient responded well to topical treatment, and her lesions improved significantly during the five months of follow-up. This case points out that, when prescribing isotretinoin, dermatologists should consider all possible dermatological adverse effects, including vitiligo, and conduct timely intervention and monitoring.

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Introduction

Oral isotretinoin is a synthetic derivative of retinoid, 13-cis retinoic acid, indicated for severe nodulocystic acne and severe papulopustular acne, including scar-forming and resistant types (1). Mucocutaneous and ocular dryness occur, as the most common side effect after oral isotretinoin use (2). The musculoskeletal side effects include, after oral isotretinoin therapy, back pain, arthralgia and/or myalgia in about 16% of patients in adults (3). These symptoms are usually mild in degree and fully resolve after withdrawal of treatment (4). Depression and suicidal thoughts are also well-recognized complications of isotretinoin treatment (5).

Vitiligo is a depigmenting skin disease caused by selective loss of melanocytes, leading to pigment loss in the affected areas of skin. The lesions are completely amelanotic, so scaling will not appear when examined, and it appears like chalk-like white in color. Recent developments have classified the pathogenesis of vitiligo as an autoimmune disease associated with metabolic, oxidative stress, genetic, and environmental factors (6,7). The present study reports a rare case of vitiligo developing after systemic isotretinoin therapy.

Case description

A 24-year-old female patient presented to our dermatology clinic with complaints of severe acne on her body. She had previously used topical antibiotic treatment for two months without improvement. The patient had no chronic illnesses and was not on any systemic medication. Dermatological examination revealed widespread papulopustular and nodular lesions with occasional atrophic scars extending from both scapular areas to the lumbar region on the posterior aspect of her body. She was diagnosed with nodulocystic acne, graded as severity 4 on the IGA scale

Figure 1: A few depigmented macular lesions approximately 0.5x0.5 cm in size, more clearly observed under Wood's light examination, located on the patient's forehead and temporal region.

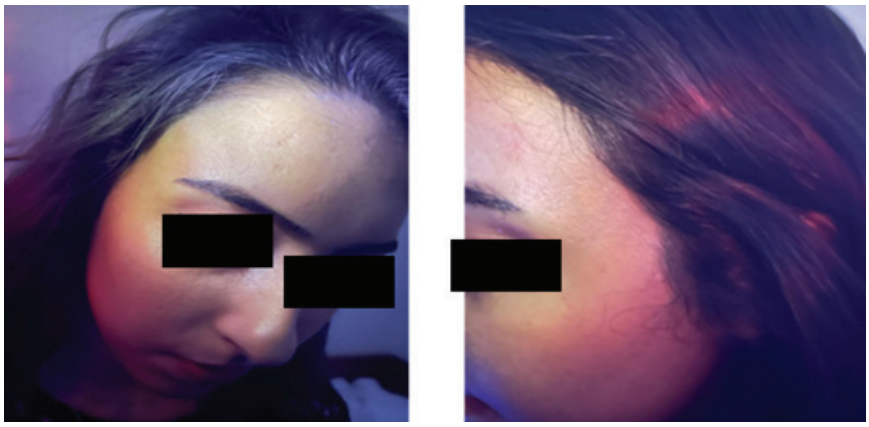

Figure 1: Complete resolution of the lesions after treatment

accepted by the American FDA. Systemic isotretinoin treatment was planned. Laboratory tests were within normal limits, including lipid panels (cholesterol, LDL cholesterol, VLDL cholesterol, triglycerides), AST, ALT, and kidney function.

Systemic isotretinoin treatment started with 20 mg/day in the first month, increased to 30 mg/day in the second month, and continued with 40 mg/day in the third and fourth months. The patient reported only mild skin dryness during treatment. In the fourth month, she returned to the clinic with complaints of whitening on her face. Examination under Wood's light revealed a few depigmented macular lesions approximately 0.5x0.5 cm in size on her forehead and temporal area (**Figure 1**). The patient had no personal or family history of autoimmune disease or vitiligo. Thyroid function tests, vitamin B12 levels, and autoantibody results were normal.

The patient's oral isotretinoin treatment was discontinued upon diagnosis of vitiligo, and she was treated with topical corticosteroid ointment during weekdays and 0.03% tacrolimus ointment on weekends for one month. After the first month, treatment continued with 0.03% tacrolimus ointment once daily, and the patient was advised to use sunscreen regularly. Monthly follow-ups showed complete regression of lesions by the end of the fifth month, with no depigmented macules observed under Wood's light examination (**Figure 2**). The topical tacrolimus ointment was discontinued, and the patient was recommended to use sunscreen only.

Discussion

In this study, we present a case of vitiligo that developed after systemic isotretinoin treatment in a patient with nodulocystic and scar-forming acne on the body. Such cases are limited in the literature. In a study involving 50 participants investigating the efficacy and safety of low-dose isotretinoin treatment (20 mg/day, approximately 0.3-0.4 mg/kg/day) for moderate to severe acne vulgaris, the most common side effect observed was cheilitis (98%), while one case developed vitiligo (8). This study highlighted that the development of vitiligo associated with systemic isotretinoin use was a new observation that had not been previously reported, but no explanation was provided regarding the possible pathogenesis.

In another study, a 17-year-old male patient with resistant acne, who was started on isotretinoin, developed segmental vitiligo lesions surrounded by erythematous areas in the malar and perioral regions, not crossing the midline (9). This case was presented as the first ever reported case of segmental vitiligo with systemic isotretinoin use. In this case, similar to our patient, the vitiligo lesions began in the fifth month of treatment. In our patient, vitiligo lesions were frontotemporal and bilateral in distribution. This patient was prescribed 0.1% tacrolimus ointment applied twice a day for two months with the logic of having minimal perilesional erythema, but there was no considerable improvement in achromia. Further, this patient was prescribed a course of 20 sessions of UVB-NB phototherapy, which resulted in minimal perifollicular pigmentation. In our case, after the diagnosis of vitiligo, oral isotretinoin treatment of the patient was stopped, and topical corticosteroid cream was applied twice daily during weekdays but 0.03% tacrolimus ointment was applied twice daily during weekends for one month. At the end of the first month, 0.03% tacrolimus ointment was continued once daily, and the patient was recommended to use sunscreen regularly. By the fifth month, his lesions completely regressed.

In another study, a case of vitiligo that developed secondary to isotretinoin treatment for facial scarred acne was presented. The vitiligo lesions started on the nose and later spread to the perioral area, cheeks, and ankle. In this case, an eight-week treatment with 0.1% tacrolimus was ineffective, and the patient switched to homeopathic treatment (10).

The relationship between vitiligo and systemic isotretinoin was inversely investigated in another study, which examined the use of systemic isotretinoin in patients with vitiligo. In this study, it was found that 1.4% of the 1301 vitiligo patients used isotretinoin before the onset of vitiligo, and 2.2% used it after the onset, totaling 3.6%. When comparing the group that used isotretinoin before the onset of vitiligo to their age-matched peers who did not use isotretinoin, the use of isotretinoin before the onset of vitiligo was associated with decreased disease body surface area and reduced accompanying autoimmunity (11)

The mechanism of action for this assumed relationship with isotretinoin is not yet fully explained, but the

drug is seen to play a role in triggering autoimmunity in genetically susceptible individuals. Various autoimmune diseases such as diabetes, autoimmune hepatitis, Guillain-Barré syndrome, and thyroiditis have been reported in association with isotretinoin therapy. Additionally, in vitro studies have shown that retinoids may have a proapoptotic effect on melanocytes (12,13).

Conclusions

Although a cause-and-effect relationship for this association has not yet been proven, the increasing number of new cases reported in the literature serves as a warning sign for dermatologists to be aware of this potential new side effect. Due to the limited number of studies and available literature, it is unclear whether vitiligo is a side effect of isotretinoin or if its occurrence is coincidental. More cases are needed to determine this.

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Contributions

Research concept and design: MSC, DC

Data analysis and interpretation: MSC, DC

Collection and/or assembly of data: MSC, DC

Writing the article: MSC, DC

Critical revision of the article: MSC, DC

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