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CASE REPORT

Isotretinoin Treatment Results in Demodex-positive Discoid Lupus Erythematosus Variant Cases

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ABSTRACT

Discoid lupus erythematosus (DLE) is the most common form of chronic cutaneous lupus erythematosus, characterized by hardened discoid lesions with scaling, primarily on the face and scalp. The efficacy of isotretinoin in treating rosacea has been attributed to its capacity to reduce cutaneous blood flow and the number of sebaceous glands. In addition, isotretinoin has comparable efficacy to other commonly used treatment modalities, such as hydroxychloroquine, in the treatment of refractory subacute cutaneous lupus erythematosus (SCLE), DLE, and chronic cutaneous lupus erythematosus (CCLE). Nine Demodex-positive patients with a diagnosis of DLE who were treated at the tertiary Dermatology Clinic between December 2022 and July 2023, with a mean age of 48.78, were included in the study. The lesions responded positively to isotretinoin treatment, and the patients showed partial and complete remission. Isotretinoin's anti-inflammatory properties make it a potential treatment option, especially for Demodex-positive DLE cases.

Keywords: Demodex, discoid lupus erythematosus, isotretinoin, lupus, oxidative stress

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INTRODUCTION

Discoid lupus erythematosus (DLE) is the most typical chronic cutaneous lupus erythematosus type. It predominantly affects the face and scalp, presenting with characteristic hardened discoid lesions covered in scale.[1] Rosacea is a chronic skin condition that mainly affects the face. It is characterized by inflammatory lesions such as transient or permanent erythema, telangiectasia, papulopustules, and swelling. Persistent erythema of the facial skin has an essential place in the course of the disease.[2] Demodex mites have been frequently identified in patients with rosacea and DLE. These two conditions can occur together, mimic each other clinically, and have similar potential etiological factors.[3] Although isotretinoin is the gold standard in treating severe acne, its anti-inflammatory properties make it a potentially applicable treatment for a wider range of dermatological conditions in the near future.[4] The effectiveness of isotretinoin in treating rosacea has been attributed to its capacity to reduce cutaneous blood flow and the number of sebaceous glands.[4] Chu et al.[4] reviewed 15 studies on isotretinoin treatment, reporting positive outcomes with varying doses and modalities in a total of 991 rosacea patients. Moreover, according to recent studies, isotretinoin has comparable efficacy to other commonly used treatment modalities, such as hydroxychloroquine, in the treatment of refractory subacute cutaneous lupus erythematosus (SCLE), DLE, and chronic cutaneous lupus erythematosus (CCLE).[5,6] This case series presents the results of cases diagnosed with Demodex-positive discoid lupus erythematosus variant and treated with isotretinoin.

MATERIALS AND METHODS

Nine Demodex-positive patients diagnosed with DLE, with an average age of 48.78, whose treatments were planned between December 2022 and July 2023 at Necmettin Er-

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bakan University Faculty of Medicine Dermatology Clinic, were included in the study. The patients were treated with isotretinoin, and their recovery processes were followed. The isotretinoin dose used in the patients was standard. All patients were started on 0.3–0.5 mg/kg isotretinoin, and the total dose (120 mg/kg) was completed according to the patient's kilogram. Patients were also prescribed topical mometasone furoate cream (once daily, five days a week) for two months. The histopathological diagnosis of discoid lupus erythematosus in all patients was confirmed by the dermatopathologist.

Sampling Method: Standardized Skin Surface Biopsy (SSSB)

The SSSB is used to measure Demodex density as a quantitative method. A standard area of 1 cm^2 was drawn on a microscope slide. A drop of cyanoacrylate adhesive was placed on the other side of the slide, and the sticky surface was applied to the cheek skin. After allowing the adhesive to dry (about 1 min), the slide was removed gently with surface skin. After removal from the skin, the slide was clarified with one drop of immersion oil (=cedar oil). The samples were studied microscopically at ×40 magnification. A positive Demodex level of 5/cm^2 and above was considered Demodex-positive. All evaluations were conducted from the same region of the face (cheek), by the same dermatologist, to reduce any mistakes in the techniques and microscopic inspections.

Treatment success was evaluated by a single dermatologist with standardized digital photography at baseline and after isotretinoin treatment, in addition to clinical examination. Patients with 100% remission were recorded as complete remission, and patients with 0–99% remission were recorded as partial remission (according to visual analog scoring, 0–100).

RESULTS

Patients diagnosed with Demodex-positive DLE, with an average age of 48.78, were treated with isotretinoin for several months. These patients presented with various symptoms, including facial spots, itching, hyperpigmentation, crusted lesions, and facial erythema. Facial photos of patients with partial response after treatment (Figs. 1, 2). The face of the patient whose active lesions had almost completely regressed after treatment and only postinflammatory changes remained (Fig. 3).

Four patients (44.44%) were male, and five (55.56%) were female. All patients were started on 0.3–0.5 mg/kg isotretinoin, and the total dose (120 mg/kg) was completed according to the patient's kilogram. Five patients (55.56%) were treated with isotretinoin for six months, and the other four were treated with isotretinoin for 8, 9, 10, and 12 months, respectively. While three of the patients (33.3%) showed complete remission, six of them (66.6%) showed partial remission.

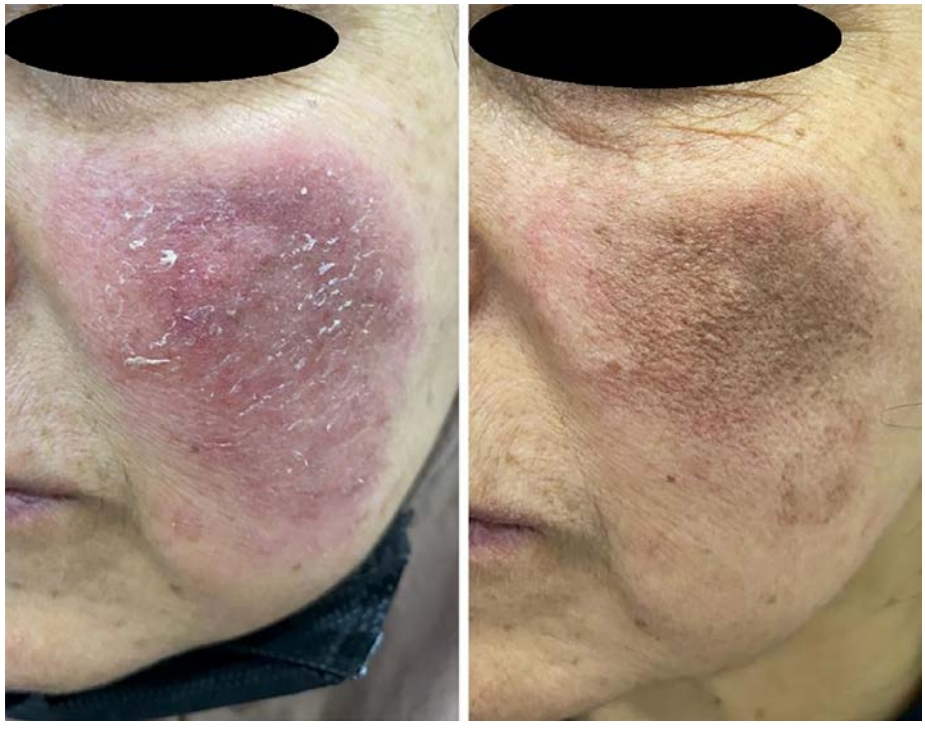

Figure 1. Photographs of patients with partial response

Figure 2. Photographs of patients with partial response

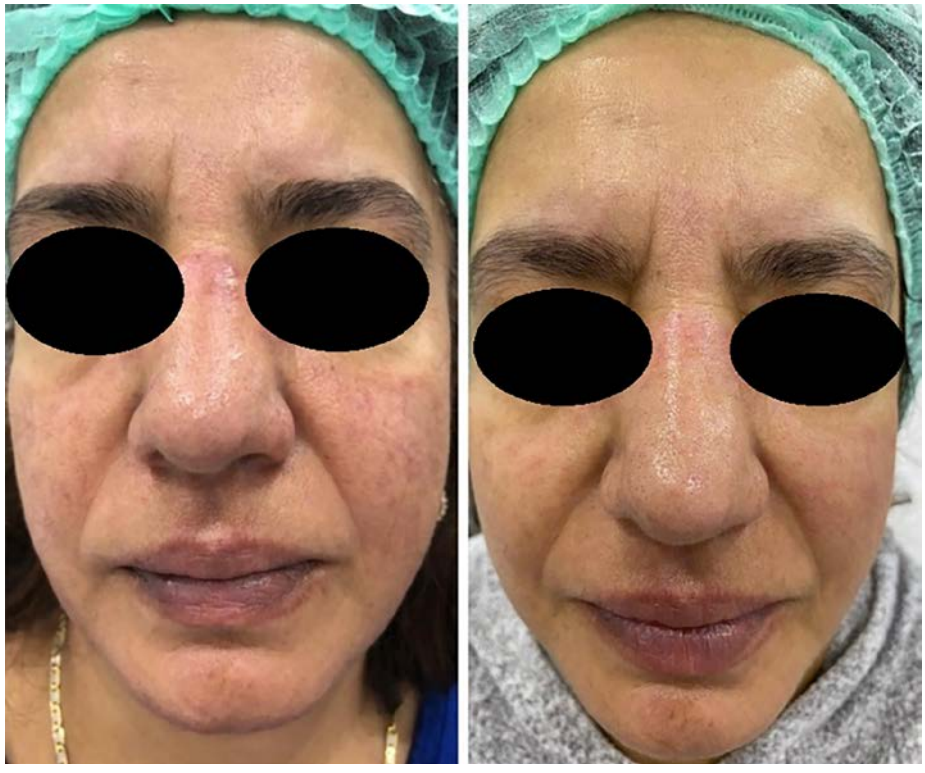

Figure 3. Photographs of patient with complete response

Table 1. Clinical response to isotretinoin treatment

Case	Age	Gender	Diagnosis	Demodex	Treatment	Remission
1	58	F	DLE	Positive	6 months of isotretinoin treatment	Partial remission
2	53	F	DLE	Positive	6 months of isotretinoin treatment	Partial remission
3	41	F	DLE	Positive	6 months of isotretinoin treatment	Partial remission
4	59	F	DLE	Positive	6 months of isotretinoin treatment	Partial remission
5	55	M	DLE	Positive	6 months of isotretinoin treatment	Complete remission
6	42	M	DLE	Positive	8 months of isotretinoin treatment	Partial remission
7	49	M	DLE	Positive	9 months of isotretinoin treatment	Partial remission
8	47	M	DLE	Positive	10 months of isotretinoin treatment	Complete remission
9	35	F	DLE	Positive	12 months of isotretinoin treatment	Complete remission

F: Female; M: Male; DLE: Discoid lupus erythemathosus

Clinical conditions such as age, gender, treatment duration, and treatment response of all patients are given in Table 1.

DISCUSSION

The most common form of chronic cutaneous lupus erythematosus is called discoid lupus erythematosus (DLE). On the face and scalp, it typically manifests as hard discoid lesions with an overlying scale. LE is caused by dysfunction of the adaptive and innate immune systems. There is a loss of tolerance to self in the adaptive immune system caused by the production of autoantibodies. Inappropriate responses of these antibodies to self-antigens present in cellular debris after apoptosis result in T and B cell recruitment, activation, and the creation of immune complexes that directly harm the tissue. Patients with LE have upregulated proinflammatory signaling pathways that increase cytokine activity. The complement and innate immune systems are essential to eliminate pathogens, recognize foreign antigens, and eliminate apoptotic cells. Dysfunction of these two systems also contributes to increased symptoms of LE.[1]

CLE and cancer are sporadically linked. Scar carcinomas and discoid LE (DLE) may be linked. It has the potential to be a paraneoplastic phenomenon in solid and non-solid organ tumors, especially subacute LE (SCLE).[7] SCLE, chronic cutaneous LE (CCLE), acute cutaneous LE (ACLE), and bullous LE are different types of cutaneous lupus. CCLE has subtypes such as chilblain lupus, lupus profundus, lupus tumidus, and DLE. ACLE, SCLE, and CCLE have similar histological findings; it is impossible to differentiate between the types using histology alone. A combination of clinical evaluations, serological tests, and histopathological findings is used for diagnosis. Since these findings are also frequently seen in dermatomyositis, a comprehensive clinical examination is required to determine the diagnosis.[1] Autoantibody tests are helpful for both follow-up and diagnosis of CLE. The majority of CLE patients (60–80%) and SLE patients (medium to high titers) have positive ANA results.[7] Compared to other CLE subtypes, antibodies such as ANA, dsDNA, Sm, U1RNP, and Ro/SSA were found to have a lower positivity rate in DLE patients.[8]

In histological examination of DLE, the inflammatory infiltrate becomes less noticeable over time, and scarring often occurs on DLE biopsies. As the epidermis thins and the upper dermis undergoes sclerotic changes, the basement membrane thickens, and periodic acid–Schiff is positive. Mucin deposits form in the reticular dermis.[9] DLE lesions appear as polymorphic mild eruptions, granuloma faciale, sarcoidosis, SCLE, lymphomacutis, and pseudolymphoma in the early stages of the disease. As the condition worsens, DLE's discoid lesions can mimic actinic damage or non-melanoma skin cancers like keratoacanthomas and squamous cell carcinoma. The fully mature lesion may be confused with hypertrophic lichen planus. It is useful to evaluate long-standing asymmetric discoid lesions with biopsy to exclude the diagnosis of non-melanoma skin cancer presenting as CLE.[1]

In mild cases of CLE, preventive measures such as using sunscreen or quitting smoking and topical treatment alone may be sufficient. The standard first-line treatment for CLE is topical corticosteroids. Alternatively, topical calcineurin inhibitors such as pimecrolimus and tacrolimus can be used. When used together, these two medications have been shown to be efficient at healing lesions.[10,11] Intralesional steroid injection is another treatment option for localized disease, especially in DLE lesions.[12] Antimalarials are the first choice of systemic treatment for more severe cases. Alternative treatments for patients who are resistant or unable to tolerate antimalarial therapy include treatment with immunosuppressive, immunomodulatory, or biologic

agents. If topical treatments and antimalarial therapy fail, various immunosuppressive drugs such as, methotrexate, oral corticosteroids, mycophenolate mofetil (MMF), azathioprine, cyclophosphamide, and cyclosporine can be administered as monotherapy or combination therapy for the treatment of CLE. Due to their side effect profiles, current European treatment guidelines advise against treatments like cyclosporine, cyclophosphamide, and azathioprine in patients with CLE without systemic involvement and only suggest methotrexate and MMF.[7]

Rosacea is a chronic skin condition characterized by inflammatory lesions such as transient or permanent erythema, telangiectasia, papulopustules, and swelling. Additionally, it affects the sebaceous glands in the eye, and phymatous lesions occur due to collagen stimulation. Rosacea affects approximately 10% of the world's population and is most common in fair-skinned women between the ages of 35 and 50.[2] Although the exact cause of rosacea's etiopathogenesis is still unknown, genetic and environmental factors are known to be crucial contributors. It is suggested that the disease has many causes and triggers. It is thought that rosacea occurs and its prognosis worsens due to several causative elements such as ultraviolet (UV) radiation, microbial stimuli, Demodex colonization, heat, and stress.[13] Possible causes of TLR2 activation and increased protease activity observed in rosacea include chitin released from Demodex mites.[14] In the study by Casas et al.,[15] skin samples taken from Demodex-infected areas showed higher levels of interleukin (IL)-8, IL-1, tumor necrosis factor (TNF), cyclooxygenase-1, and inflammasome.

Various treatment modalities, including topical and systemic medications, lasers, and light-based treatments, have been used to treat rosacea with varying degrees of success. The mainstay of treatment is oral antibiotics such as metronidazole, tetracyclines, and topical medications such as oral retinoids. These medications are used alone and are commonly used in combination. Light therapies such as intense pulsed light and pulsed dye laser are more effective for the erythematous–telangiectatic type. In recent years, topical brimonidine, oxymetazoline, ivermectin, tacrolimus, pimecrolimus, low-dose modified-release tetracyclines, and botulinum toxin have been added to the treatment options.[2]

In recent years, the literature has suggested that Demodex-positive DLE is a separate variant.[3] According to our study, the effectiveness of isotretinoin treatment in Demodex-positive DLE variant cases resulted positively in complete remission in three patients (33.3%) and partial remission in six patients (66.6%). However, the effectiveness of the treatment should be investigated on a larger number of patients.

Disclosures

Ethics Committee Approval: This is a case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Dursun R, Temiz SA, Fındık S, Durmaz K, Oltulu P. Immunohistochemical evaluation of TNF-α, IL-1, IL-12, IL-17, IL-23 expression and ınvestigation of the effect of demodex in patients with discoid lupus erythematosus. Turk J Immunol 2023;11:23–8. [CrossRef]
2. Temiz SA, Durmaz K, Işık B, Ataseven A, Dursun R. The effect of 577-nm pro-yellow laser on demodex density in patients with rosacea. J Cosmet Dermatol 2022;21(1):242–6. [CrossRef]
3. Dursun R, Durmaz K, Oltulu P, Ataseven A. Demodex positive discoid lupus erythematosus: Is it a separate entity or an overlap syndrome? Dermatol Ther 2020;33:e13394. [CrossRef]
4. Chu S, Michelle L, Ekelem C, Sung CT, Rojek N, Mesinkovska NA. Oral isotretinoin for the treatment of dermatologic conditions other than acne: a systematic review and discussion of future directions. Arch Dermatol Res 2021;313:391–430. [CrossRef]
5. D'Erme AM, Milanesi N, Difonzo EM, et al. Treatment of refractory subacute cutaneous lupus erythematosus with oral isotretinoin: a valid therapeutic option. Dermatol Ther 2012;25:281–2. [CrossRef]
6. Vena GA, Coviello C, Angelini G. Impiego dell'isotretinoina orale nel trattamento del lupus eritematoso cutaneo [Use of oral isotretinoin in the treatment of cutaneous lupus erythematosus]. G Ital Dermatol Venereol 1989;124:311–5. [Italian]
7. Shornick JK, Formica N, Parke AL. Isotretinoin for refractory lupus erythematosus. J Am Acad Dermatol 1991;24:49–52. [CrossRef]
8. Okon LG, Werth VP. Cutaneous lupus erythematosus: diagnosis and treatment. Best Pract Res Clin Rheumatol 2013;27:391–404. [CrossRef]
9. Obermoser G, Sontheimer R, Zelger B. Overview of common, rare and atypical manifestations of cutaneous lupus erythematosus and histopathological correlates. Lupus 2010;19:1050–70. [CrossRef]
10. Sigges J, Biazar C, Landmann A, Ruland V, Patsinakidis N, Amler S, et al; EUSCLE Co-Authors. Therapeutic strategies evaluated by the European

Society of Cutaneous Lupus Erythematosus (EUSCLE) Core Set Questionnaire in more than 1000 patients with cutaneous lupus erythematosus. Autoimmun Rev 2013;12:694–702. [CrossRef]

11. Wons A, Reitmeir P, Ruland V, Luger TA, Ruzicka T. Efficacy of tacrolimus 0.1% ointment in cutaneous lupus erythematosus: a multicenter, randomized, double-blind, vehicle-controlled trial. J Am Acad Dermatol 2011;65:54–64, 64.e1–2. [CrossRef]
12. Gunasekera V, Jayaram H,Kashani S, Toma NM, Olver JM. Refractory discoid lupus erythematosis of the eyelid successfully treated with intra-lesional triamcinolone. Eye 2008;22:1205–6. [CrossRef]
13. Woo YR, Lim JH, Cho DH, Park HJ. Rosacea: Molecular mechanisms and management of a chronic cutaneous inflammatory condition. Int J Mol Sci 2016;17:1562. [CrossRef]
14. Steinhoff M, Schauber J, Leyden JJ. New insights into rosacea pathophysiology: A review of recent findings. J Am Acad Dermatol 2013;69:15–26. [CrossRef]
15. Casas C, Paul C, Lahfa M, Livideanu B, Lejeune O, Alvarez-Georges S, et al. Quantification of Demodex folliculorum by PCR in rosacea and its relationship to skin innate immune activation. Exp Dermatol 2012;21:906–10. [CrossRef]