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SUCCESSFUL TREATMENT OF SEVERE DISCOID LUPUS ERYTHEMATOSUS WITH AZATHIOPRINE: A CASE REPORT

Esra ADIŞEN, Meltem ÖNDER, Pınar ÖZTAŞ, Mehmet Ali GÜRER

Discoid lupus erythematosus (DLE) is a chronic, indolent skin disease characterized by sharply marginated, scaly, atrophic, red, discoid plaques. Although there are many treatment modalities for DLE, such as systemic steroids, hydroxychloroquine, dapson, mycophenolate mofetil and retinoids, the therapy for resistant and severe cases is still a problem. In this report, we present a severe, resistant DLE case treated successfully with azathioprine.

Key Words: Discoid Lupus Erythematosus, Systemic Therapy, Azathioprine.

TEDAVİYE DİRENÇLİ DİSKOİD LUPUS ERİTEMATOZUSUN AZOTİYOPRİNLE BAŞARILI TEDAVİSİ: BİR VAKA SUNUMU

Diskoid Lupus Eritematozus (DLE), keskin sınırlı, eritemli skuamlı atrofik, diskoid plaklarla seyreden kronik bir hastalıktır. DLE tedavisinde sistemik steroidler, hidroksiklorokin, dapson, mikofenolat mofetil ve retinoidler kullanılmaktadır. Tedaviye dirençli ve şiddetli olguların tedavisi ise halen sorun olmaktadır. Bu yayında tedaviye dirençli ve şiddetli bir DLE olgusu ve azotiyoprinle başarılı tedavisi sunulmaktadır.

Anahtar Kelimeler: Diskoid Lupus Eritematozus, Sistemik Tedavi, Azotiyoprin.

Gazi University Faculty of Medicine, Department of Dermatology, Ankara- Turkey.

Discoid lupus erythematosus (DLE) is a chronic, indolent skin disease characterized by inflammatory, scarring lesions mainly involving the head or neck, but also on photoexposed areas. Typical lesions in DLE appear as round or oval erythematous plaques with scales and follicular plugging. These plaques are well demarcated and spread peripherally. On the face, they can form a butterfly-like rash involving the cheeks and nose (1-3). Patients with DLE generally have a favorable prognosis and can be managed with safe yet effective therapy (3). On the other hand, DLE cases principally involving the palms and soles are generally resistant to standard medications (4,5). In these conditions, therapy with azathioprine, retinoids, or occasionally dapsone can be used (6). We present a DLE patient who was successfully treated with azathioprine.

CASE REPORT:

A 30-year-old woman attended our out-patient clinic with erythema and desquamation on her face and extremities. She had been suffering from these lesions for five years. On her dermatological examination, old scars with hypo- and hyperpigmentation, new and active erythema and scaling were seen on the entire face, and the dorsa of the hands and feet. On her palmar and plantar areas, highly macerated desquamation was observed (Fig. 1). A histopathological examination indicated a diagnosis of DLE. The systemic investigation was negative according to the American Rheumatism Association (ARA) criteria except for antinuclear antibodies (ANA) and anti-dsDNA positivity. In 1999, during the postpartum period, her condition exacerbated with new cutaneous lesions not only on the head but also on the extensor aspects of the forearms, arms, palms and soles as well. She was treated with hydroxychloroquine 400 mg/day for 16 weeks and 600 mg/day for 6 weeks; however, the skin lesions remained unchanged and new lesions developed. Systemic steroid therapy with 60 mg/day fluocortolon was started. The lesions on the face improved but the hand and feet lesions were resistant to therapy. Azathioprine at a dosage of 100 mg daily was started, and a dramatic improvement in the lesions was obtained, while steroid dose was being tapered slowly. Total improvement was achieved after six months of treatment (Fig. 2).

DISCUSSION

The diagnosis of cutaneous LE is based upon the presence of clinical lesions that on biopsy demonstrate a characteristic pathological picture. An immunofluorescence examination and serological testing are also useful. Once a diagnosis of cutaneous LE has been established, the patient should be evaluated to assess the presence of systemic disease associated with LE. In the absence of severe systemic disease, the focus of therapy may then be upon the cutaneous lesions (3). DLE lesions can heal with permanent scar-

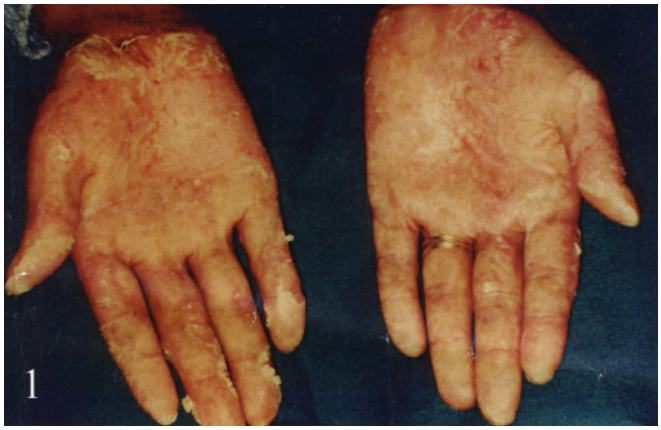

Figure 1: DLE lesions on the palmar area, maceration and desquamation.

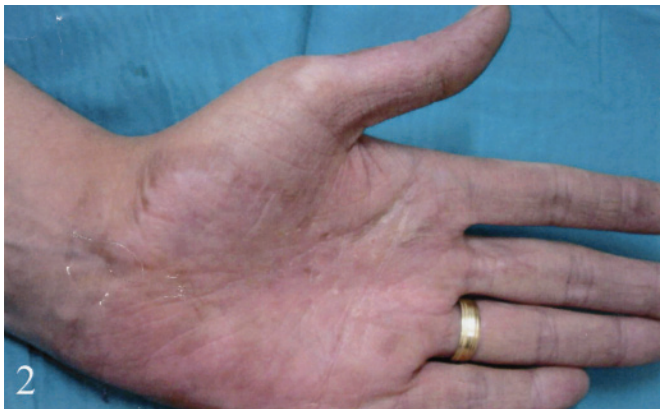

Figure 2: Satisfactory results with an azathioprine and steroid combination.

ring, causing cosmetic problems, or occasionally squamous cell carcinoma may develop on these scars (7). Scarred lesions may be excised if they are inactive; however, this should be performed with caution as the Koebner phenomenon has been reported to occur in some patients with LE (8). Spontaneous remissions are rarely seen. There are several local and systemic modalities for DLE treatment. For localized DLE, topical application of steroids in combination with sunscreens and intralesional steroids is recommended (7). Topical retinoids are effective in some patients with DLE and hypertrophic LE (3).

When discoid lesions are not controlled by topical agents or intralesional corticosteroids, systemic therapy is indicated. The first-line therapy is an antimalarial drug. Systemic therapy with antimalarials, either alone or in combination, is usually effective for controlling the lesions but when patients do not respond after at least a 2-month trial other therapeutic agents should be tried (9-12). When these standard treatment modalities fail, azathioprine, retinoids, or occasionally dapson may be effective. Immunosuppressive agents have been used especially in severe organ involvement (renal) with their steroid-sparing effects. DLE cases principally involving the palms and soles that were difficult to treat with standard medications have been described in the literature. Most of these cases were successfully treated with azathioprine (5,10,11).

Azathioprine is a cytotoxic immunosuppressive agent that was originally developed for the control of graft rejection in transplant surgery (13). It is used in the treatment of several cutaneous diseases. Pemphigus, dermatomyositis, systemic lupus erythematosus and DLE are well established clinical indications for azathioprine (13,14). It is used for these conditions either alone or, more commonly, in combination with corticosteroids. The therapeutic effect is delayed for weeks. Azathioprine has a steroid-sparing effect that reduces the long-term toxicity of corticosteroids (13). Its mode of action is not well known. Azathioprine interferes with purine base production, and DNA and RNA synthesis, and thus cell division. It has inhibitory effects on some functions of T cell and B cell proliferation (14). The recommended dosage is 1.5-2.5 mg/kg/day (13).

A recent case, reported by Tsokos et al., showed a rapid response to azathioprine 100 mg/day in extensive discoid skin lesions of SLE that were resistant to treatment with steroids, both topical and systemic, and high doses of hydroxychloroquine (9). Shehade has also reported successful results with azathioprine 150 mg/day in discoid skin lesions (10). In the literature, new agents like mycophenolate mofetil (4,15), high-dose intravenous immune globulin (16) and tacrolimus (17) are being more widely used in the treatment of resistant DLE. Finally, oral retinoids are found effective in some patients with lesions on the palms and/or soles (18).

Our patient failed to respond to treatment with hydroxychoroquine sulfate in combination with oral steroids. Finally we treated her with azathioprine 100 mg daily with success. Our result indicates that azathioprine can be recommended for resistant, severe generalized DLE patients as an alternative treatment with minimal side effects.

Correspondence Address:
Esra ADIŞEN, MD.
Gazi Üniversitesi Tıp Fakültesi Dermatoloji Anabilim Dalı
06500 Ankara-Turkey.
Phone: 312 202 61 05
Fax: 312 212 90 18
E-mail: eozsoy@gazi.edu.tr

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