Rapid Improvement of Subacute Cutaneous Lupus erythematosus with Low-Dose Methotrexate

I. Böhm  
M. Uerlich  
R. Bauer

Department of Dermatology, University of Bonn, Germany

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When standard regimens fail in controlling cutaneous lupus erythematosus (LE), a variety of other therapeutics including azathioprine, isotretinoin, interferon α2a, cyclophosphamide, dapsone, cyclo-sporin A or thalidomide have been used. Recently it has been shown that methotrexate (MTX) is able to control rheumatoid arthritis with a low rate of adverse effects [1, 2]. Therefore, we treated with low-dose MTX once a week a female patient with subacute cutaneous LE who was refractory to systemic glucocorticosteroids; we could document an excellent clinical outcome without any side-effects.

A 36-year-old female patient presented with a 10-year history of cutaneous LE with arthralgias. Erythematousquamous and papulosqua-mous lesions were seen mainly on the trunk, the arms and upper legs (fig. 1).

Skin biopsy revealed hyperkeratosis, focal thinning of the epidermis and some scattered colloid bodies. The basal cells showed minimal hydropic degeneration and the basement membrane was slightly thickened. Lymphocytic infiltration was seen in the upper dermis with a perivascular pattern and showed particular invasion into the epidermis. Focal extravasation of erythrocytes was present. Direct immuno-fluorescence showed only perivascular deposits of the complement component C3. Routine laboratory findings were normal except for the erythrocyte sedimentation rate (62/72 mm), dsDNA antibodies (ELISA) 534.0 U/ml (normal 9-40) and antinuclear antibodies (Hep2 cells) 1:2,560 (normal < 1:80) with a homogeneous fluorescence pattern.

Antibodies against Ro (SSA), La (SSB), U1-snRNP and RNP-SM complex were detected. Anti-cardiolipin antibodies were 34.8 U/ml (normal 0-12.0). Other systemic LE symptoms could be excluded. Based on these findings, the diagnosis of subacute cutaneous LE with systemic involvement was made.

Before admission she had been treated for 10 years with systemic glucocorticosteroids with a daily dose of up to 20 mg. Initially, she noticed improvement, but later the skin lesions were refractory to steroid therapy and she had developed Cushing’s symptoms. We started MTX therapy with 25 mg/week i.v. (first injection with 12.5 mg/week). Two weeks after starting
MTX, the inflammatory subacute cutaneous LE lesions had completely cleared. Only postinflammatory hyperpigmentation and skin scaling could be seen (fig. 2). Additionally the arthralgias disappeared after 6 weeks of treatment. After 13 weeks, MTX treatment was discontinued. A mild relapse occurred 10 weeks later with few small erythematousquamous and papulosqua-mous macules on the upper arms and the upper trunk. Fifteen weeks after the last MTX injection, LE skin lesions recurred and she received again low-dose MTX. After clearing of the cutaneous LE, we stopped MTX administration. Now she remains free of LE signs without continuation of MTX treatment. During MTX treatment, routine laboratory and lymphocyte subsets (by using FACS analysis and monoclonal antibodies against CD3, CD4, CD8 and HLA-DR) were measured. We neither found an immnosuppressant effect nor pathological changes of other parameters. MTX therapy was well tolerated without any objective or subjective side-effects.

Fig. 1. Clinical picture of subacute cutaneous LE in a 36-year-old female patient before MTX therapy.

Fig. 2. The same patient after 2 injections and a total dose of 37.5 mg 2 weeks after starting MTX treatment.

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Reports about MTX therapy in LE patients are rare in the literature [3-5]. Recently, 2 patients with discoid LE have been published [6,7]. But the mode of action of MTX in LE is unknown. MTX is a folic acid antagonist which blocks the dihydrofolate reductase and in this way inhibits nucleotide metabolism. This effect is dose dependent. But in our case it is rather unlikely that the improvement could result from an antiproliferative effect, because the cumulative MTX dose after 2 weeks was only 37.5 mg. So other pharmacological mechanisms should be responsible for the anti-inflammatory action of MTX. There are indications that MTX is able to influence the immune system at the cytokine level. MTX treatment does not cause any inhibition of interleukin-1 (IL-1) synthesis or secretion but has an inhibitory effect on IL-1 activity [8] and interferes with IL-1 which leads to the inhibition of IL-1 receptor binding [9]. Furthermore,
peripheral blood mono-cytes from patients with rheumatoid arthritis receiving MTX showed a reduced in vitro production of IL-1 that was accompanied by a beneficial clinical response [10]. If standard treatment with antimalarials and/or systemic glucocorticosteroids fails in controlling LE or causes adverse effects, MTX is an interesting therapeutic alternative for patients with cutaneous LE. We think that low-dose MTX is safe and effective and shows less side-effects than other immunosuppressants. Nevertheless, investigations in larger patient groups are warranted.

References
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Intraepidermal IgA Pustulosis Associated with Monoclonal IgA Gammopathy in an HIV-Infected Patient
M.A. Barnadas”, C. Nadal, G. Vergerb, C. Geipíc,
J.L. Rodriguez, JM. de Moragas’A
Departments of “Dermatology, infectious Diseases and “Immunology,
Hospital de la Sta. Creu i St. Pau, Barcelona, Spain
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Intraepidermal IgA pustulosis (IEAP) is a term coined by Wallach [1] characterized by a pustular eruption similar to the subcorneal pustulosis of Sneddon and Wilkinson, but it differs from this entity in that the direct immunofluorescence test shows deposits of IgA in the epidermis, at the intercellular level in most of the cases. Clinicopathologically there seem to be two distinct types: (1) resembling subcorneal pustular dermatosis (SPD type) and (2) intraepidermal neutrophilic IgA dermatosis (IEN type) [2]. As this entity has recently been associated with HIV
infection [2], we would like to report another case of an HIV-infected patient who developed an IEAP and who presented an associated IgA \( \lambda \) paraprotein.

In November 1994, a 35-year-old male came to our Department because of a generalized vesiculopustular eruption of 1 month of duration. The patient had a history of HIV antibody positivity diagnosed in April 1993 in a routine blood test and had been following therapy with zidovudine since July 1993.

Physical examination revealed the presence of papules, vesicles and pustules arranged in a circinate pattern that were spreading centrifugally. They involved the trunk and, upper limbs, with a predominant involvement of the axillae and groins (fig. 1).

A bacteriological culture revealed the presence of Staphylococcus aureus and Streptococcus group A, both sensitive to ciprofloxacin. Systemic therapy with ciprofloxacin (500 mg b.i.d.) was initiated and topical antibiotics (neomycin, bacitracin and polymyxin B) were applied. Although some improvement was observed, control of the disorder 1.5 months later was only partial.

Topical betamethasone dipropionate 0.05% associated with topical gentamycin 0.1% was then given, and the disorder completely resolved in 3 weeks.

The histopathological study showed a subcorneal pustule containing some isolated acantholytic cells. A direct immunofluorescence test using perilesional skin revealed intercellular IgA in the upper layers of the epidermis. An indirect immunofluorescence test did not reveal circulating anti-intercellular-substance of epidermis antibodies.

Routine laboratory investigations showed the following abnormalities: total proteins 83.4 g/l, albumin 36.9 g/l and gammaglobulins 29.15 g/l without any homogeneous component. An immunoelectrophoresis test revealed the presence of a monoclonal gammopathy with IgA \( \lambda \).

We report the case of a patient presenting the clinical, histopathological and direct immunofluorescence features reported in IEAP [1]. The fact that the pustules were not sterile raised the question whether the patient suffered from bullous impetigo or not. We consider it a superinfection of the previous vesiculopustular eruption for several reasons: firstly, the lesions only disappeared when topical cortico-