Treatment of Cutaneous Lupus erythematosus with Etretinate

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Nineteen patients with different clinical subsets of cutaneous lupus erythematosus (LE) were treated with the aromatic retinoid etretinate. In 11 of them excellent or good treatment results were obtained within two to six weeks. Best response to etretinate therapy was seen in male patients with discoid lupus erythematosus. Etretinate should prove a valuable drug in LE therapy. (Received January 23, 1985.)

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Antimalarials and glucocorticosteroids are the mainstays of systemic therapy in cutaneous lupus erythematosus (LE). In certain forms of LE such as urticarial vasculitis and vesiculobullous LE, dapsone proved to be highly effective (1, 2). In otherwise intractable cases, thalidomide showed excellent efficiency (3, 4). The usefulness of all these agents is limited by sometimes serious toxicity. Thus, alternative pharmacologic principles are needed to complement the therapeutic armamentary in LE treatment. Recently, Grupper & Berretti (5) reported the use of the aromatic retinoid etretinate alone or in combination with antimalarials in the treatment of discoid LE (DLE). Good responses were obtained particularly in hyperkeratotic DLE. Bauer et al. (6) observed a favourable response to etretinate alone or in combination with prednisolone in five patients with disseminated cutaneous LE. One case of subacute cutaneous LE (SCLE) was successfully treated with etretinate by Lubach & Wagner (7).

We wish to report favourable treatment results obtained with the aromatic retinoid etretinate in 19 cases with different forms of cutaneous LE.

PATIENTS AND TREATMENT

Nineteen patients attending the Lupus Erythematosus Clinic at the Department of Dermatology of the University of Munich were enrolled in this open trial. They had been off treatment for at least four weeks before starting etretinate therapy. Female patients in reproductive age were informed about the teratogenic potential of the drug and accepted for etretinate treatment only if strict contraception over a period of at least two years was guaranteed. Other reasons for exclusion from retinoid therapy included hepatopathy and hyperlipidemia. The diagnosis of LE in these patients was based on the typical clinical picture and histological, direct immunofluorescence as well as serological findings.

Thirteen patients were female, six male, age range 21 to 67 years. Nine patients suffered from discoid LE (DLE) localized to the face, two patients had disseminated discoid LE involving the chest and back, seven patients presented with the clinical and serological characteristics of the subacute cutaneous LE (SCLE) variant (8) and one patient suffered from systemic LE (SLE) with cutaneous manifestations. The pertinent clinical and laboratory features of the patients are given in Table I.

Initial dosage of etretinate was 50 mg daily given in two divided oral doses. Response to therapy was assessed at 2-week intervals. Regular laboratory controls included ESR, RBC, WBC as well as measurements of serum transaminases, lipids, complement, antinuclear, anti-DNA and anti-Ro antibodies. If any clinical response was observed, the dosage of etretinate was reduced to 25 mg, and an attempt to reduce the dosage to as low as 10 mg daily was made if further improvement was noted. No other treatment except for topical sunscreens was allowed during the initial evaluation phase

which extended to six weeks. In cases showing unsatisfactory response at this point, treatment was switched to topical high potency glucocorticosteroids, systemic glucocorticosteroids or chloroquine. In cases showing partial response, additional treatment with a 1% hydrocortisone acetate cream or low dose 6-methylprednisolone was instituted.

RESULTS

Table II shows the results of etretinate therapy. Eight patients showed an excellent response, i.e. complete clearing of all cutaneous lesions leaving sometimes minimal residual erythema, which could be suppressed by a short treatment with a hydrocortisone cream (Fig. 1 A, B, 2 A, B, C, D, 3 A, B). In three patients, a good, however incomplete response was noted necessitating a short course of systemic 6-methylprednisolone treatment at a dosage of 8 mg daily. Thus, satisfactory results were obtained in a total of 11 patients.

Table I. *Clinical and laboratory features of patients*

Patient						Pathological serological findings
No.	Initials	Age	Sex	Diagnosis	Clinical features	
1	CF	21	f	DLE	Non-scarring, non scaling malar erythema	∅
2	EL	43	f	SCLE	Slightly scaling polycyclic erythemas on face, chest, upper arms, vitiligo	ANA 640, anti-Ro+, $C_4\downarrow$
3	DN	52	m	SCLE	Scaling polycyclic erythemas on face, chest, back, upper arms	∅
4	KB	22	m	DLE	Non-scarring, non scaling malar erythema	∅
5	CH	37	m	Diss.DLE	Scaling discoid lesions on face, neck, chest	∅
6	HO	25	m	DLE	Slightly scaling malar rash	∅
7	LR	67	f	DLE	Massive, confluent, widespread scaling plaques, rheumatoid arthritis	CRP+, RF+
8	IS	27	f	SLE	Malar rash, faint, scaling erythema on chest, livid papules on fingers	ANA 40, anti-DNA+ C_3, $C_4\downarrow$
9	MM	29	f	DLE	Discoid, scarring, malar erythema livid papules on fingers	$C_4\downarrow$
10	EH	54	f	SCLE	Scaling erythemas on scalp, face, chest, back	∅
11	GK	28	f	DLE	Scarring discoid lesions	∅
12	GH	42	f	SCLE	Anular scaling lesions, scarring alopecia	Anti-Ro+
13	DT	35	f	SCLE	Non-scaling erythema on face, arms, chest, arthralgias, Raynaud-Syndrom	∅
14	MF	49	f	DLE	Scarring, discoid lesions on ears	∅
15	JW	42	m	DLE	Non-scarring discoid facial lesions	∅
16	HI	51	f	Diss.DLE	Scarring discoid lesions on face and back, scarring alopecia	$C_4\downarrow$
17	GG	16	f	SCLE	Malar rash, anular scaling superficial lesions on chest, and back, photosensitivity	Anti-Ro+
18	BH	42	f	SCLE	Anular scaling lesions on chest and back, malar rash, photosensitivity	anti-Ro+
19	WS	46	m	DLE	Hypertrophic facial discoid lesions	ANA 80

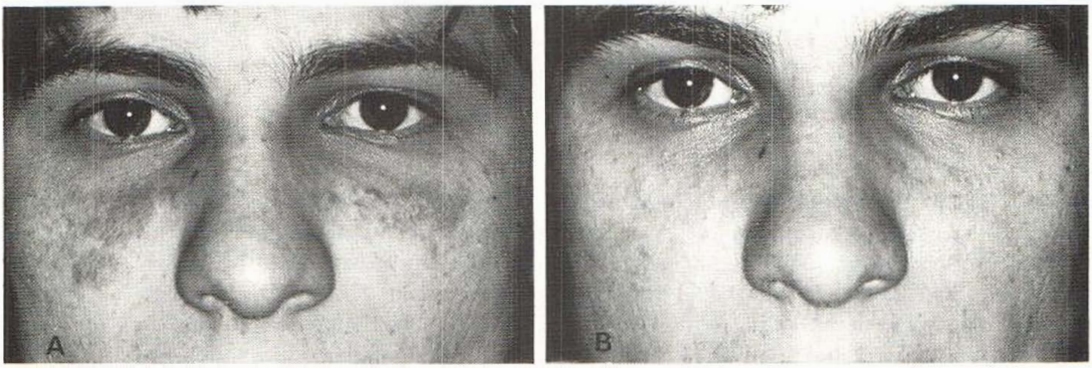

Fig. 1. (A) Patient 4, discoid LE, initial superficial lesions, before treatment. (B) Patient 4, complete clearing of lesions after four weeks of etretinate treatment.

In three patients, unequivocal reduction of infiltration, hyperkeratosis and scaling were observed. The result was, however, considered unsatisfactory. One of these patients (no. 9 in Table I) failed to respond to a subsequent course of chloroguine and is currently being treated with a combination of 10 mg etretinate and 10 mg 6-methylprednisolone daily with partial clearing of the lesion only. The other two patients (nos. 11 and 16) displayed hypertrophic and scarring lesions which slowly resolved under topical application of high potency glucocorticosteroids.

Five patients (1 SLE, 1 DLE and 3 SCLE) showed virtually no response to 6-week etretinate therapy. Patient 1 responded to subsequent chloroquine therapy. Patient 10 suffering from chloroquine retinopathy responded to topical and systemic glucocorticosteroids. Patient 12 was resistant to all forms of therapy except thalidomide, and patient 13 had to be kept on long term intermittent systemic glucocorticosteroid treatment.

In all responders, partial or complete clearing occurred rapidly and was seen after two to four weeks of treatment. If no effect was seen at this point, further therapy usually proved ineffective. Conspicuously, out of six male patients, five showed an excellent and one a good response to etretinate. Thus, no therapeutic failure was observed among male patients. Overall, the best results were obtained in male patients with localized or disseminated discoid LE. In the SCLE group, four patients responded favourably and three not at all. The four responders showed disseminated psoriasiform, superficial scaling lesions without systemic symptoms, while the nonresponders displayed non-scaling, infiltrated, faint erythematous lesions associated with arthralgias.

Table II. *Response to etretinate treatment*

	Response to treatment (no. of cases, sex)			
Diagnosis	Excellent	Good	Moderate	None
DLE	6 (5 male, 1 female)	1 (female)	3 (all female)	1 (female)
SCLE	2 (both female)	2 (1 male, 1 female)		3 ((all female)
SLE				1 (female)
Total	8	3	3	5

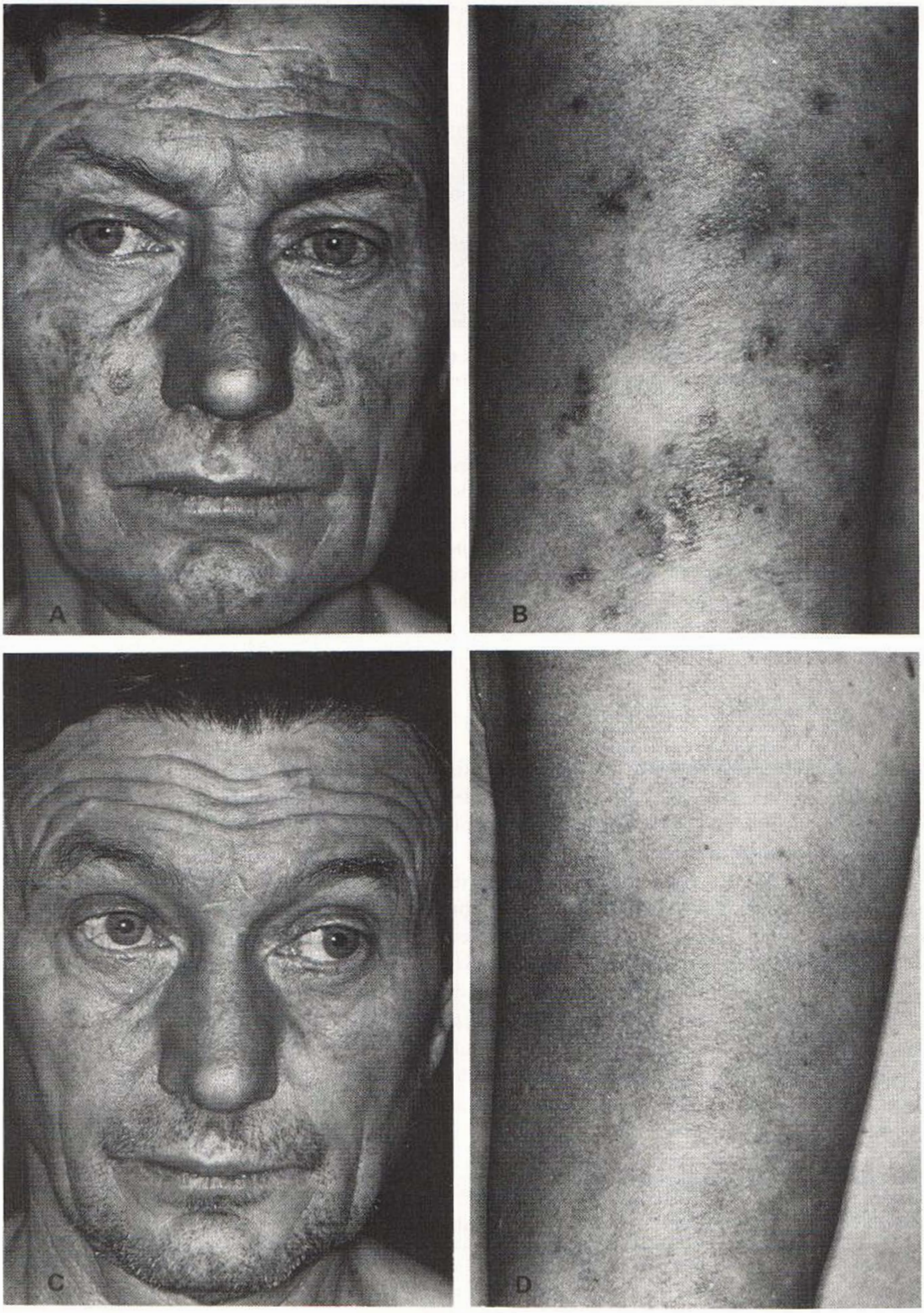

Fig. 2. (A, B) Patient 3, SCLE, face and upper arm before treatment. (C, D) Patient 3, complete clearing of lesions after four weeks of etretinate treatment and one week of topical hydrocortisone cream therapy.

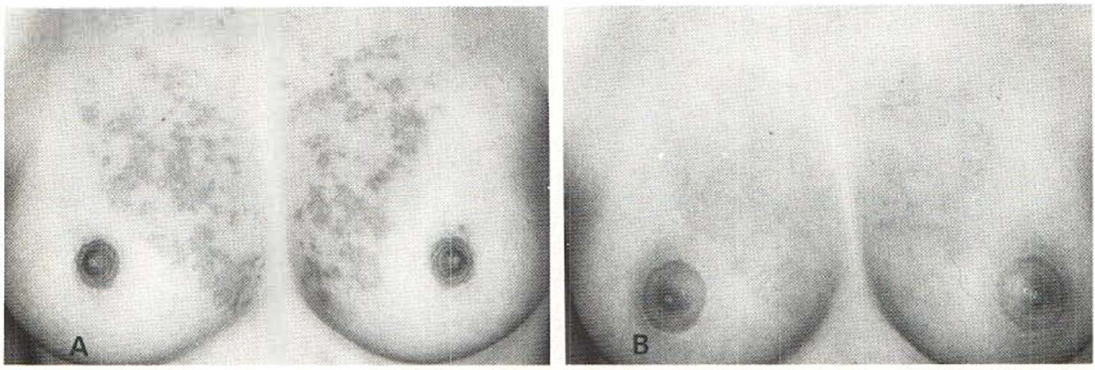

Fig. 3. (A) Patient 17, SCLE-lesions developing after sun exposure. (B) Patient 17, complete clearing of lesions leaving residual hyperpigmentation after two weeks of etretinate treatment.

Side-effects did not differ from those observed in psoriasis patients treated with etretinate but were usually milder due to the lower initial dosage. Only in one case side-effects led to interruption of therapy. In this patient (no. 19), a male alcoholic with hypertrophic DLE, an excellent response to therapy was compounded by a massive increase in serum triglyceride levels exceeding 800 mg/100 ml. Slight increase in serum lipid levels under the initial higher dosage of etretinate was observed in three further patients. Other side effects are listed in Table III. All side effects were well tolerated by the patients and reversible upon dosage reduction.

DISCUSSION

We report favourable results with the aromatic retinoid etretinate in the treatment of cutaneous lupus erythematosus. Eleven of 19 patients showed a complete or almost complete clearing within two to six weeks of treatment. Initial etretinate dosage was 50 mg daily, which could be further reduced to 25 or even 10 mg daily. In some cases, topical treatment with a 1% hydrocortisone acetate cream further improved the cosmetic result by suppressing residual erythema. In partial responders, combination with low dose systemic glucocorticosteroids proved efficient. Moderate responses or treatment failures were observed in eight patients, some of whom proved previously or subsequently to be resistant to other treatment modalities as well. Side effects of etretinate were minor with the exception of one case showing massive hypertriglyceridemia. Best treatment results were obtained in male patients suffering from discoid LE. In some patients with SCLE, dramatic responses similar to the patients of Lubach & Wagner (7) were observed (Fig. 3 A, B), but others were responsive to systemic glucocorticosteroid therapy only.

Table III. *Side effects of etretinate therapy*

Side effects	No. of patients
Cheilitis	11
Hyperlipidemia	4
Hair loss	4
Pruritus	2
Painful desquamation of soles	1

In our hands, etretinate proved to be approximately equipotent with chloroquine and its indications should comprise localized and disseminated discoid LE as well as erythematosquamous SCLE without signs of systemic disease. Furthermore, when antimalarial or glucocorticosteroids are contraindicated, etretinate should prove particularly useful. Combinations of etretinate with antimalarials (5) or prednisolone (6, present report) might yield drug regimens with enhanced clinical effectiveness and reduced side effects.

In our experience gained from the treatment of 19 patients with different forms of cutaneous LE, etretinate proved to be a valuable drug highly effective in over 50% of cases, and thus should enlarge the therapeutic arsenal of the dermatologist treating this disorder. The major drawback of etretinate is its teratogenicity requiring contraception for prolonged periods in view of the cumulative pharmakokinetics of the drug and thus limiting its usefulness in women in reproductive age. Therefore, the development of retinoids displaying more favourable pharmakokinetic profiles should yield drugs with even greater therapeutic potential in LE.

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