

Treatment of Erythrodermic Psoriasis with Etretinate

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We have investigated the clinical response of 12 patients with erythrodermic psoriasis to therapy with etretinate. Initial dosage of etretinate was 20–60mg/day. The time for complete disappearance of scales averaged 19.9 days. In 10 of 12 patients (83.3%) satisfactory results were obtained after 2 to 11 months of treatment. Cheilitis was the most common side effect. Three patients had mild elevation of blood lipids, which was corrected by dose reduction. Remission period, of ten patients who showed good result, averaged 4.2 months.

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Psoriatic erythroderma represents the generalized form of the disease which affects all body sites including the face, hands, feet, nails, trunk, and extremities. Although all of the symptoms of psoriasis are present, erythema is the most prominent feature and scaling is usually less severe as compared to chronic psoriasis. The treatment of psoriasis, particularly the erythrodermic variety, is not easy. Etretinate, a synthetic derivative of retinoic acid, has been shown to be more efficacious in the treatment of pustular and erythrodermic psoriasis than in the chronic plaque type.^{1,2} Recently, etretinate therapy has been considered for initial treatment of patients with pustular psoriasis or with erythrodermic psoriasis.^{3–5} In

these patients etretinate clearly provides a therapeutic advantage over other treatments. Therefore we undertook this open study to investigate the efficacy of etretinate in the treatment of erythrodermic psoriasis.

MATERIALS & METHODS

Twelve patients with erythrodermic psoriasis, nine males and three females, were included in this study. Patient profiles at the beginning of treatment are shown in Table 1. Ten patients were hospitalized due to severe systemic symptoms (e.g., fever, chills, malaise, and leukocytosis). Age distribution was 10 to 62 years (mean age : 27.3 years). Two patients (case 6 and 8) had history of pustular psoriasis for 11 and 5 years, respectively, which later developed into erythrodermic form. In the other patients, previous lesions were all plaque form psoriasis. In eight patients a few pustules remained at the beginning of treatment. Alopecia was shown in case 6. Nail involvement (nail pitting and/or

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Table 1. Patient profiles at the beginning of the treatment

Case	Age/Sex	Duration of psoriasis(Years)	Previous lesion	Pustule	Associated lesion
1	29/M	6	plaque	+	nail pitting
2	20/F	16	plaque	—	—
3	34/M	5	plaque	—	—
4	54/M	7	plaque	+	—
5	19/F	4	plaque	—	nail pitting
6	12/M	11	pustule	+	nail pitting, onycholysis
7	34/F	18	plaque	+	alopecia
8	10/M	5	pustule	+	nail pitting, onycholysis
9	43/M	4	plaque	+	nail pitting
10	30/M	15	plaque	+	nail pitting
11	10/M	1 ¹ / ₂	plaque	+	nail pitting
12	62/M	1	plaque	—	—

onycholysis) was shown in seven patients. Initially etretinate was orally administered in doses of 20–60 mg/day (0.3–1.0 mg/kg/day) for two or three weeks. Thereafter the dosage was gradually reduced or increased according to the response to therapy or side effects. The duration of treatment ranged from two to eleven months.

Treatment efficacy was assessed with respect to erythema and scale. The time of initial response and complete clearing was recorded. Laboratory tests, which included complete blood cell count, urinalysis, liver function test, and blood lipid level, were performed before treatment and repeated at weeks 2, 4, 8, 12 and 16. Each patient was followed up for at least three months, and one patient (case 7) was followed up for eight months.

RESULTS

Ten out of 12 patients (83.3%) were successfully treated with etretinate but two patients (case 9 and 10) did not respond to etretinate therapy alone. As for the response to the treatment, the period when scale reduction began averaged 8.6 (5 to 14) days and the time to

complete disappearance of scale averaged 19.9 (15 to 28) days. The systemic symptoms resolved during this time. Erythema, however, did not completely disappear and remained at a moderate degree even when scale disappeared completely. The duration of treatment for clearing of erythema ranged from 2 to 11 months (average 4.3 months). The disease-free remission period ranged from two weeks (case 1) to eight months (case 7) in the 10 successfully treated patients. Mean remission period for the ten patients showing good result was 4.2 months. At follow-up three months after discontinuation of etretinate, four patients showed complete clearing and another four patients showed faint erythema, but the other two patients reavealed plaque type psoriasis (Table 2).

Mild to moderate cheilitis was noticed in all patients and thinning of the skin, hair loss, and pruritus were also observed. The results of laboratory tests were evaluated in comparison with baseline for significant changes in hematologic values, urinalysis, and blood chemistry. There were, however, no significant changes. Mild to moderate increase of triglyceride and cholesterol values was observed in three patients (case 1, 4, and 5) but it normalized with

Table 2. Follow-up of 12 patients treated with etretinate

Case	Treatment period (months)	Initial dosage (*/***)	Remission period	Follow-up at e months after discontinuation of etretinate
1	5	60/0.9	2 weeks	plaque
2	4	30/0.6	3 months	faint erythema
3	2	40/0.7	5 months	faint erythema
4	4	30/0.5	3 months	palque
5	4	45/1.0	3 months	clearing
6	4	50/0.9	3 months	clearing
7	4	20/0.5	8 months	clearing
8	5	30/0.5	4 months	clearing
9	9	30/0.5	—	erythema
10	6	30/0.6	—	erythema
11	4	20/0.5	6 months	faint erythema
12	11	20/0.4	6 months	faint erythema

* mg/day **mg/kg/day

dose reduction.

DISCUSSION

Two forms of erythrodermic psoriasis exist.⁶ Chronic psoriasis may evolve gradually or suddenly into an exfoliative phase. It can be regarded as an extensive psoriasis involving all, or almost all, the cutaneous surface. The second form is part of the spectrum of unstable psoriasis. It may occur at any time, either presenting suddenly and unexpectedly, or ushered in by a period of increasing intolerance to local applications, light, etc. and of loss of control over the disease. Generalized pustular psoriasis may revert to an erythrodermic state. In our cases, presumptive provocative factors included sudden withdrawal of steroid (in case 1, 5, and 10), upper respiratory tract infection (in case 2 and 4), and irritation due to phototherapy (in case 9 and 12). In case 6 and 8, previous generalized pustular psoriasis reverted to an erythrodermic state. In the others (case 3, 7, and 11) we could not find apparent provocative factors.

Before etretinate was introduced, the treatment of erythrodermic psoriasis was mainly dependent on systemic corticosteroid or methotrexate, but the benefits of their use and potentially life-threatening side effects had to be carefully weighed. Windhorst⁷ said that etretinate was the drug of need for patients with pustular and erythrodermic psoriasis as a single mode of therapy. In order to control pustular psoriasis, an initial high dosage (75mg/day; 0.8–1.0mg/kg/day) is generally required and should be maintained for a minimum of 3 to 4 weeks before decreasing the dose.^{2,8} A rapid response is seen in generalized pustular psoriasis.⁵ In erythrodermic psoriasis, due to the risk of exacerbation, rather low doses (25–35 mg/day; 0.3–0.4mg/kg/day) are preferable, increasing after 3–5 weeks up to 50–60mg/day (0.7–0.8mg/kg/day).^{2,8} But Lowe⁷ said that this dosage schedule is inadequate for some patients with erythrodermic psoriasis and the dosage should be increased to 1.2mg/kg/day for 4 week period. We used 20–60mg/day (0.3–1.0 mg/kg/day) as an initial dosage and increased or decreased the dosage according to the

response to the therapy and the side effects. We obtained good results in 10 patients, including the patients(case 1 and 5) who recieved a dosage of 1.0mg/kg/ day initially. This result suggest that not only a low initial dose, but also a moderate to high initial dose of etretinate may be used for the treatment of erythrodermic psoriasis. However, the risk of exacerbation due to an excessive dose must always be considered.^{2,8} In the treatment of psoriasis, Ehmann and Voorhees⁹ analysed etretinate efficacy on the basis of erythema, scaling, infiltration, and pruritus. In erythrodermic psoriasis, erythema and scale are the most characteristic clinical findings. Therefore, we used them as the criteria for treatment efficacy. With exfoliative erythrodermic psoriasis, the time to improvement takes usually four to six weeks from the start of the etretinate therapy.⁸ In our study the time to complete disappearance of scales took two to four weeks. In all cases, erythema decreased more slowly than scale did. The time of disappearance of erythema averaged 4.3 months(2 to 11 months).

The side effects under the therapy with etretinate are of the same nature as the typical hypervitaminosis A symptoms. For example, mucocutaneous changes are observed in virtually all patients, which commonly consist of cheilitis, thinning of skin, loss of hair, desquamation, and nail fragility. Systemic effects on lipid metaboilsms and liver function are additionally observed in some patients. Additionally etretinate has a high teratogenic potential and therefore constitutes a particular risk in clinical use for women of child bearing potential. Except for teratogenicity, these side effects are dose related and reversible in most cases.¹⁰ Most of these findings were observed in our study, but they were mild to moderate. Continuation of treatment was usually possible by lowering the daily dosage.

In this study four patients showed complete clearing, and another four patients showed only

faint erythema at 3 month follow-up period⁴ after discontinuation of etretinate. Two patients(case 1 and 4) demonstrated an initial remission, but relapsed with mild plaque type psoriasis. The remaining two patients(case 9 and 10) did not respond to etretinate alone. Namely 10 of 12 patients(83.3%) showed remission or near remission. This result is comparable to the reported experience with etretinate therapy to erythrodermic psoriasis.³⁻⁵ In view of the result of this study, etretinate seems to be a good systemic drug for the acute and active phase of erythrodermic psoriasis. When the illness stabilized to its previous psoriatic lesion status, however, topical treatment or phototherapy can be considered as maintenance therapy.

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