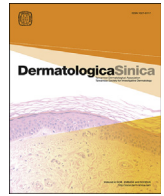




Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: <http://www.derm-sinica.com>

CORRESPONDENCE

Effect of pulse corticosteroids and low dose methotrexate in cases of treatment-resistant lichen sclerosis



Dear Editor,

Lichen sclerosis (LS) is a skin disease primarily located in the anogenital area that may affect other areas of the body as well as mucosal surfaces.¹ The use of pulse corticosteroids and methotrexate (PCM) to treat dermatological diseases has recently increased.^{2,3} However, data regarding the efficacy of PCM treatment for LS is limited.⁴ In this case series, we investigated the efficacy of PCM treatment in LS patients who had been unresponsive and refractory to previous treatments.

Six female patients who had been clinically and histopathologically diagnosed with LS were included in this case study. Written informed consent was obtained from each patient. Intravenous methylprednisolone (1000 mg) was given to each patient once a month for three consecutive days. In addition, subcutaneous methotrexate (7.5 mg) was administered once a week. This treatment protocol was applied for at least three months, and the patients were evaluated monthly. Clinical scoring performed according to Kreuter et al.⁴ was used for the pre- and post-treatment evaluations. For scoring of patients with extra-genital LS, seven anatomical regions were considered: arms, shoulders, chest (including the submammary region), trunk, back, inguinal area and legs. LS severity was assessed according to a four-point scale (0 indicating normal skin; 1, mild sclerosis/induration, atrophy and/or depigmentation; 2, moderate sclerosis/induration, atrophy and/or depigmentation with or without blister formation; and 3, severe sclerosis/induration, atrophy and/or depigmentation with or without superficial erosions). The severity of the involvement of each body region was also evaluated according to a four-point scale (0 indicates no involvement; 1, <33%; 2, 33–67%; and 3, >67%). Clinical severity and the sum of the involvement scores of the affected anatomical regions represented the total clinical score.

The mean ages and duration of disease of the six female patients were 53 (46–63) and 5 (1–9) years, respectively. Three of the patients had generalized lesions in the trunk with genital involvement, two had only genital involvement, and one had only generalized lesions in the trunk. Laboratory analyses were unremarkable for all patients. All patients had previously received topical corticosteroids; however, no response had been achieved. Additional therapies had also failed. The two patients with only genital involvement had not responded to acitretin treatment.

Two of the patients with trunk and genital involvement had not responded to ultraviolet A-1 treatment. The patient with only trunk involvement had not responded to narrow-band ultraviolet B. Finally, three patients (the two patients with only genital involvement and one of the patients with trunk and genital involvement) had not responded to colchicine.

The pulse corticosteroid treatment lasted 3–6 months. However, patients continued to receive methotrexate. The mean duration of the methotrexate treatment was 12.6 (3–18) months. All patients responded well to the studied regimen. The median total clinical scores decreased from 14 (0–28) in the pre-treatment period to 2.5 (0–11) in the post-treatment period (Table 1). The mean pre-treatment Dermatology Quality of Life Index score was 15 (4–29), whereas these scores decreased to 1.5 (0–10) after PCM treatment (Table 1). Clinical images of the patients before and after PCM treatment are shown in Fig. 1 (1a–h). The follow-up period was at least 10.6 (6–17) months. No side effects were observed during the treatment.

Pulse corticosteroid therapy has been used to treat many dermatological diseases.⁵ In a study by Kreuter et al.,³ 15 patients with severe localized scleroderma were successfully treated intravenously with methotrexate (15 mg/week) and methylprednisolone (1000 mg) for at least six months. Uziel et al.⁶ reported that 9 of 10 paediatric patients with localized scleroderma responded well to PCM treatment. Kreuter et al.⁴ also used PCM for LS treatment. Their study reported that seven patients with generalized, extra-genital, resistant LS were successfully treated with PCM for at least six months. We found similar results in our study, as reflected in the significant decrease in the patients' clinical scores. In addition, we showed a significant decrease in the quality of life index. However, two patients had a recurrence of LS after 18 months.

Recent data on the use of methotrexate in sclerotic skin diseases has considerably increased. Seyger et al.⁷ successfully used methotrexate at 15 mg/week in nine patients with generalized morphea. Nayeemuddin et al.⁸ also reported that all LS lesions were regressed in a 49-year-old female patient after methotrexate treatment at 10 mg/week for eight months.

In conclusion, we suggest that PCM may be an appropriate therapy in treatment-refractory LS patients. There is a need for further comprehensive studies to identify the optimal dose and duration of the treatment regimen and to evaluate the side effect profile.

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

<https://doi.org/10.1016/j.dsi.2018.05.005>

1027-8117/Copyright © 2018, Taiwanese Dermatological Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1 Clinical and DLQI scores before and after PCM treatment in patients with LS.

Patient No/Age	Arms		Shoulders		Chest		Abdomen		Back		Inguinal		Legs		Total score		DLQI scores		Only genital involvement
	PT	PST	PT	PST	PT	PST	PT	PST	PT	PST	PT	PST	PT	PST	PT	PST	PT	PST	
1/53	0	0	0	0	4	0	5	2	4	1	4	0	2	0	19	3	5	0	–
2/63	2	1	2	1	4	2	6	1	6	2	4	2	4	2	28	11	20	2	–
3/59	0	0	0	0	0	0	2	0	2	0	0	0	5	2	9	2	4	0	–
4/46	2	1	0	0	4	2	4	2	2	0	5	2	2	0	19	7	10	1	–
5/52	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	29	10	+
6/49	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	21	9	+

DLQI: Dermatology Life Quality Index, PT: Pre-treatment, PST: Post-treatment.

Clinical score; 0–3 points for body area involvement and 0–3 points for clinical severity of LS.

**Fig. 1** a,b,c,d: Back and lower extremities before(a,b), after(c,d) treatment, e,f: femoral and gluteal region before(e), after(f) treatment, g,h: genital area before(g), after(h) treatment.**Appendix A. Supplementary data**

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.dsi.2018.05.005>.

Ayşe S. Karadag, Necmettin Akdeniz

Department of Dermatology, Istanbul Medeniyet University, Istanbul, Turkey

Emin Ozlu*

Department of Dermatology, Duzce University, Duzce, Turkey

Hulya Suslu, Tugba K. Uzuncakmak

Department of Dermatology, Istanbul Medeniyet University, Istanbul, Turkey

Halenur Bozdog

Department of Obstetrics and Gynecology, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey

Ebru Zemheri

Department of Pathology, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey

Mukaddes Kavala

Department of Dermatology, Kafkas University, Kars, Turkey

E-mail addresses: karadagaserap@gmail.com (A.S. Karadag), drnakdeniz@gmail.com (N. Akdeniz).

* Corresponding author.

E-mail address: halenurbogzdog@hotmail.com.

E-mail address: dermatolog@gmail.com (E. Ozlu).

References

1. Karadag AS, Kavala M, Ozlu E, et al. The co-occurrence of lichen sclerosus et atrophicus and celiac disease. *Indian Dermatol Online J* 2014;**5**:S106–8.
2. Droitcourt C, Milpied B, Ezzedine K, et al. Interest of high-dose pulse corticosteroid therapy combined with methotrexate for severe alopecia areata: a retrospective case series. *Dermatology* 2012;**224**:369–73.
3. Kreuter A, Gambichler T, Breuckmann F, et al. Pulsed high-dose corticosteroids combined with low-dose methotrexate in severe localized scleroderma. *Arch Dermatol* 2005;**141**:847–52.
4. Kreuter A, Tigges C, Gaifullina R, et al. Pulsed high-dose corticosteroids combined with low-dose methotrexate treatment in patients with refractory generalized extragenital lichen sclerosus. *Arch Dermatol* 2009;**145**:1303–8.
5. Adisen E, Gurer MA. Pulse steroid therapy in dermatology. *TurkiyeKlinikleri J Dermatol* 2006;**16**:102–7.
6. Uziel Y, Feldman BM, Krafchik BR, Yeung RS, Laxer RM. Methotrexate and corticosteroid therapy for pediatric localized scleroderma. *J Pediatr* 2000;**136**:91–5.
7. Seyger MM, van den Hoogen FH, de Boo T, de Jong EM. Low-dose methotrexate in the treatment of widespread morphea. *J Am Acad Dermatol* 1998;**39**:220–5.
8. Nayeemuddin F, Yates VM. Lichen sclerosus et atrophicus responding to methotrexate. *Clin Exp Dermatol* 2008;**33**:651–2.

Received: Mar 6, 2018

Revised: May 2, 2018

Accepted: May 25, 2018