

Rapid response to cyclosporine in patients with *Parthenium* dermatitis: A preliminary study

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Parthenium hysterophorus, a weed of the Compositae family, is the most common cause of airborne contact dermatitis in India.¹ It is a chronic debilitating illness resulting in high morbidity. Corticosteroids have been the mainstay of treatment.² However, the long-term use of corticosteroids is known to cause severe and sometimes irreversible side effects. Azathioprine has emerged as an effective alternative,³ albeit with a slow therapeutic response adversely affecting patient compliance. Furthermore, its potential bone marrow and hepatic side effects limit its use. Cyclosporine, an anti-inflammatory and immunosuppressant, has been shown to be effective in two patients with *Parthenium* dermatitis.⁴ In this case series, we evaluated clinical efficacy and safety of cyclosporine in patients with parthenium dermatitis.

METHODS

Twenty clinically suspected patients of parthenium dermatitis were screened and patch tested with *Parthenium* extract⁵ and the Indian baseline series, following written informed consent and institutional ethics board approval of the study. Nine patients were patch-test positive to *Parthenium*, of whom eight were included in the study and one was excluded due to hepatitis C virus infection. Five patients were men and three women, between 32 and 80 years of age (mean $\pm$ SD: 55.6 ± 16.2 years), having the disease from 2 to 22 years (mean $\pm$ SD: 11 ± 7.8 years). Three male patients were farmers and two were retired government servants, whereas all three female patients were housewives. The patients had received oral ($n = 1$) and topical ($n = 8$)

TABLE 1 Clinical characteristics of the patients and response to cyclosporine

S. N.	Age (y)/sex	Disease duration (y)	Sites of involvement	Pre-treatment CSS ^a	Post-treatment CSS	Time to complete remission (mo)	Relapse (mo)
1	75/M	15	Face, neck, feet	38.3	0	2.0	3.0
2	32/M	3	Face, hands, back, feet	44.7	0	3.0	0.5
3	50/F	22	Face, neck, feet, back	47.1	0	1.5	0.5
4	80/M	6	Face, neck, scalp, hands, feet	35.4	0	2.0	-
5	47/M	6	Hands, abdomen, face	33.2	0	1.5	-
6	65/F	14	Face, abdomen, back, neck, hand	56.1	-	Lost to follow-up	-
7	47/F	20	Hands, face, back, chest, neck	26.6	0	2.0	1.0
8	49/M	2	Neck, face, flexures, back	51.9	0	2.0	-

^aCSS, clinical severity score.



FIGURE 1 (A) Pre-treatment lichenified inflammatory lesions on face. (B) Complete remission of lesions after 2 months of cyclosporine therapy

corticosteroids, azathioprine ($n = 3$), and methotrexate ($n = 1$) with oral antihistamines in the past with remitting and relapsing courses of the disease. All presented with itchy erythematous papules and lichenified plaques on the face and neck, dorsa of hands, feet, abdomen, and back. The disease severity in all the patients was assessed by determining the clinical severity score (CSS),⁶ which ranged from 26.6 to 56.1 (mean $\pm$ SD: 41.6 ± 10.0).

After a routine baseline laboratory evaluation consisting of complete blood count, liver and kidney function tests, and urine and stool examination, all patients were treated with oral cyclosporine 2.5 mg/kg/d (along with oral levocetirizine 5 mg and topical clobetasol propionate cream 0.05% w/w, once daily for symptomatic relief) for 3 months or until complete clinical remission, whichever was observed earlier. The patients were followed-up every month and a complete clinical evaluation as well as laboratory investigations were repeated every month to determine response to therapy and adverse effects.

RESULTS

Seven patients completed the treatment and one patient was lost to follow-up. There was significant improvement in the dermatitis after 2 to 4 weeks of therapy and all patients achieved complete clinical remission after 1.5 to 3 months (mean $\pm$ SD: 2 ± 0.5 months), with a post-treatment clinical severity score of "0" (Table 1, Figure 1, $P = .001$). None of the patients developed any clinical or laboratory side effects. Three patients had a mild relapse of the disease after a

period of 2 weeks to 3 months of stopping their treatment (mean $\pm$ SD: 1.3 ± 1.2 months).

DISCUSSION

Parthenium dermatitis is a cell-mediated hypersensitivity immune reaction in response to airborne allergen contact with the skin. Following presentation of the allergen by cutaneous dendritic cells to the immune system, there is activation and proliferation of T cells and production of inflammatory cytokines. The serum levels of pro-inflammatory cytokines, that is, tumor necrosis factor α (TNF- α), interleukin 6 (IL-6), IL-8, and IL-17, have been found to be significantly increased in these patients, whereas levels of anti-inflammatory cytokines such as IL-4 and IL-10 are reduced.⁷ These inflammatory cytokines are important mediators of disease in *Parthenium* dermatitis. Cyclosporine is a calcineurin inhibitor that exerts its immunomodulatory action by inhibiting T-cell proliferation and differentiation by suppressing calcineurin phosphatase required for IL-2 synthesis.⁸ It also inhibits the release of other inflammatory cytokines, including the ones secreted by various antigen-presenting cells, mast cells, and cells involved in the inflammatory cascade.⁹ Therefore, it has been shown to be beneficial in patients of *Parthenium* dermatitis. In our study, a rapid response to dermatitis with disease remission was achieved in all the patients with cyclosporine and there were no clinical or biochemical adverse effects. Thus, cyclosporine appears to be an effective drug in treatment of patients with *Parthenium* dermatitis, particularly when corticosteroids and azathioprine are contraindicated. However,

further controlled trials with a larger sample size are required to establish its effectiveness and safety in these patients.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Kaushal Verma: Conceptualization; funding acquisition; supervision; writing-review and editing. **Neetu Bhari:** Conceptualization; funding acquisition; writing-original draft; writing-review and editing. **Braj Mohan Kutar:** Data curation; writing-original draft; writing-review and editing.

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