Parthenium dermatitis treated with azathioprine weekly pulse doses

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ABSTRACT

Background: Parthenium dermatitis is a serious problem in India. Corticosteroids are the mainstay of treatment but the prolonged use of corticosteroids can cause serious side effects. Azathioprine used in daily doses has been shown to be effective. **Aim:** We have evaluated the effectiveness of azathioprine weekly pulse doses for the treatment of parthenium dermatitis. **Methods:** Twelve patients, ten males and two females, aged between 39 and 65 years (mean ± SD = 53.5 ± 8.7) having air-borne contact dermatitis to *Parthenium hysterophorus* for 3–19 years (mean = 6.33) were included in the study. The diagnosis in each patient was confirmed by patch-testing. The severity of the disease was determined by clinical severity score (CSS) on the basis of erythema, itching, type of lesions, and areas of body involved. **Results:** The pretreatment CSS in these patients varied from 29.7 to 55.5 (mean ± SD: 40.40 ± 7.95). After clinical and laboratory evaluation, the patients were treated with 300-mg azathioprine once-weekly doses for 6 months. Clinical and laboratory evaluations were repeated at weeks 1, 2, and then every 4 weeks until the end of therapy to evaluate the therapeutic response and side effects. The response was excellent (80–100% clearance of disease) in seven (58.33%) patients and good (60% clearance) in five (41.66%) patients. The post-treatment CSS decreased from the mean ± SD of 40.4 ± 7.95 to 10.9 ± 8.43 (P = 0.002). There were no significant side effects of the therapy. **Conclusions:** In this preliminary open study, azathioprine in weekly pulse doses has been found to be effective without any serious adverse effects in the treatment of parthenium dermatitis. The cost of therapy with this regimen is reduced by 60%.

Key Words: Azathioprine pulse, Parthenium dermatitis, Side effects, Treatment

INTRODUCTION

Parthenium dermatitis is the commonest type of air-borne contact dermatitis in India. It is caused by the compositae weed *Parthenium hysterophorus*. The disease occurs in sensitized individuals and usually manifests as itchy, erythematous papules and plaques on exposed areas of the body, such as the face (including the upper eyelids), neck, "V" area of the upper chest, flexures of the forearms, and the antecubital and popliteal fossae.[1,2] The type of lesions and pattern of dermatitis may vary in some individuals.[3]

P. hysterophorus grows profusely during the rainy season almost throughout the country. However, the plant is present perennially and so is the antigen in the atmosphere; therefore the patients suffer from dermatitis throughout the year with exacerbation during

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rainy seasons. Parthenium dermatitis is a very distressing and intractable problem in India. Attempts to eradicate the weed have been unsuccessful. Efforts to desensitize the patients with plant material have given inconsistent and unreliable results.[4] Corticosteroids, therefore, have been the mainstay of treatment. However, the long-term use of corticosteroids has often caused serious and sometimes irreversible side effects.[5,6] In our previous studies, we have been able to achieve remissions in patients of parthenium dermatitis with azathioprine, used as daily doses as well as monthly bolus doses, with negligible side effects.[7–9] In this study we evaluated the therapeutic response and side effects of azathioprine pulse, 300 mg, given once weekly in patients of parthenium dermatitis.

METHODS

Twelve patients with a clinical diagnosis of air-borne contact dermatitis by *P. hysterophorus* were included in the study. The patients were patch-tested with aqueous extract of *Parthenium* and the titer of contact hypersensitivity (TCH) was determined by the technique standardized by Pasricha *et al*.[10,11] Patients with active liver disease, renal or hematological disorders, and pregnant and lactating females were excluded from the study.

A detailed clinical examination was undertaken after written consent. The severity of the disease was assessed by determining the clinical severity score (CSS), a scoring system developed by us for determining the severity of the dermatitis in parthenium dermatitis based on erythema, itching, type of lesions, and area of involvement. To determine the CSS, (a) erythema and (b) itching were graded as mild, moderate, and severe, (c) type(s) of lesions as papules, plaques, lichenified papules, and plaques and exudative lesions, and (d) areas of the body involved were assessed. Each of these parameters was assigned a number (score) depending on the severity of the symptom or the approximate area of the body involved (score of 1 was given to an approximate area of 9% involvement). The details appear in Table 1. The CSS was calculated by adding (a), (b), (c), and (d) and multiplying it by 3 to get a maximum score of 99.

Table 1: Clinical Severity Score (CSS) Assessment

		Severity score
A.	**Itching:**	
	Nil	0
	Mild	1
	Moderate	2
	Severe	3
B.	**Type of lesions:**	
	Papules	1
	Plaques	2
	Lichenifed papules	3
	Lichenifed plaques	4
	Exudative lesions	5
C.	**Erythema:**	
	Nil	0
	Mild	1
	Moderate	2
	Severe	3
D.	**Areas of involvement:**	
	Face; Forehead	0.2
	Cheeks R & L	0.2 each
	Nose, chin	0.1 each
	Periorbital areas R & L	0.05 each
	Ears and retroauricular areas R & L	0.1 each
	Neck; Anterior & Posterior	0.2 each
	Scalp;	0.7
	Upper Limbs; Dorsae of hands R & L	0.2 each
	Flexors of forearms R & L	0.4 each
	Extensors of forearms R & L	0.4 each
	Flexors of arms R & L	0.4 each
	Extensors of arms R & L	0.4 each
	Shoulders R & L	0.2 each
	Chest;	2
	Abdomen;	2
	Back; Upper & Lower	2 each
	Lower Limbs; Dorsae of feet R & L	0.2 each
	Anterior aspects of leg R & L	0.8 each
	Posterior aspect of leg R & L	0.8 each
	Popliteal fossae R & L	0.1 each
	Anterior aspects of thigh R & L	1 each
	Posterior aspects of thigh R & L	1 each
Total Score = (A + B + C + D) X 3		(Maximum CSS - 99)

Baseline investigations, consisting of complete blood count, hepatic and renal function tests, serum electrolytes, routine and microscopic examination of urine and stool, chest X-ray, and electrocardiography, were done. Estimation of thiopurine methyl transferase (TPMT) activity could not be done in these patients because this facility was not available.

Patients with a positive patch test to *P. hysterophorus* and normal investigations were given one tablet of azathioprine (50 mg) as a test dose and observed for a period of 48 hours. Thereafter, they were given azathioprine 300 mg (six tablets of 50 mg each,

together) orally after a meal once every week for 6 months. Patients already on some form of treatment were given a wash-off period of 2 weeks before starting the therapy; 10-mg cetirizine hydrochloride orally once daily and clobetasol propionate cream (0.05%) applied twice daily was also given to patients for symptomatic relief.

Clinical and laboratory evaluation (complete blood counts and hepatic and renal function tests) were repeated at 1, 2, and 4 weeks after the initiation of therapy to determine any side effects. Thereafter, clinical and laboratory evaluations were done at 4-week intervals to assess the therapeutic response and side effects. The therapeutic response was determined by assessing the overall post-treatment improvement in dermatitis and itching. It was considered to be excellent if the improvement was more than 75%, good if it was 50–75%, and poor if the improvement was <50%. The post-treatment CSS was also determined to evaluate the response to therapy.

RESULTS

Of the 12 patients included, there were 10 males and 2 females, between 39 and 65 years (mean ± SD = 53.5 ± 8.7 years) of age having dermatitis on face, neck, upper chest, dorsae of hands and feet since 3–19 years (mean 6.33 years). The pretreatment CSS varied from 29.7 to 55.5 (mean ± SD: 40.40 ± 7.95). The pretreatment TCH values ranged from undiluted positive to 1:1000. All the 12 patients received the treatment for 6 months.

At the end of 6 months of therapy, there was an excellent response in seven (58.33%) patients and a good response in five (41.66%). No patient had a poor or no response. The post-treatment CSS became zero in all four patients who had 100% improvement, whereas it reduced significantly in all other patients with substantial reduction of CSS (from a pretreatment mean ± SD of 40.40 ± 7.95 to a post-treatment mean ± SD CSS of 10.9 ± 8.43; $P = 0.002$] (Table 2). Concomitant oral betamethasone (2 mg daily) had to be given to two patients with severe disease for 4 weeks in the initial phase of the therapy, whereas in one patient with thick lichenified plaques it had to be used for 16 weeks to control the disease. The post-treatment patch test became negative in two patients, decreased by one dilution in two patients, increased by one dilution in one patient, and remained unchanged in the remaining patients.

Table 2: Response to therapy with azathioprine weekly pulse doses

S. No.	Age & Sex	Clinical Severity Score (CSS)		Overall Improvement (%)
		Pre-treatment	Post-treatment	
1.	65/M	31.2	0	100
2.	54/M	43.2	16.8	80
3.	60/M	29.7	12.9	60
4.	50/F	46.2	0	100
5.	48/M	31.5	10.8	80
6.	39/F	39	16.2	60
7.	53/M	37.2	16.8	80
8.	56/M	44.7	0	100
9.	40/M	42.6	20.1	60
10.	62/M	34.2	18	60
11.	50/M	49.8	0	100
12.	65/M	55.2	19.2	60
Mean	53.5 ± 8.7 years	40.40 ± 7.95	10.9 ± 8.43 (P=0.002)	78.33 ± 18

Most patients tolerated the therapy well but two patients had vomiting after the initial doses of azathioprine; this was managed by administration of the antiemetic domperidone (10 mg orally) half an hour before the azathioprine dose. In these patients, while on therapy, the vomiting subsided after two and four doses of the drug, respectively, and they continued the therapy further without antiemetics. Two patients complained of anorexia and experienced weight loss of 2 and 3 kg each, whereas one patient had paresthesia of the hands. The treatment did not have to be discontinued owing to side effects in any of these patients. The laboratory parameters also remained within the normal range in all these patients while on treatment.

DISCUSSION

Parthenium dermatitis is a T-cell-mediated immune injury to the skin caused by activated lymphocytes in *P. hysterophorus*-sensitized individuals. Because the plant grows perennially almost throughout the country, these patients require regular treatment almost throughout the year. Long-term use of systemic corticosteroids

induces several serious, and sometimes irreversible, side effects.[5,6] Hence, azathioprine has been used as a corticosteroid-sparing agent in these patients.[7,8] Azathioprine is a 6-mercaptopurine derivative, which inhibits purine synthesis and acts as a potent immunosuppressive and a powerful anti-inflammatory agent.[12,13] Its immunosuppressive effect is owing to inhibition of the activated T-lymphocytes,[14] the cells primarily responsible for the dermatitis. In our previous studies, we have demonstrated that azathioprine given in a dose of 100 mg daily with or without a 300 mg monthly bolus dose could induce clinical remissions in these patients.[7,8] The drug has been found to be safe even on long-term use without any significant clinical or biochemical side effects.[9,15,16]

In this study all patients responded to azathioprine in a 300 mg bolus dose every week. Seven (58.33%) out of 12 patients had 80–100% improvement whereas five (41.66%) patients had 60% improvement. The response was noticed after 4–6 weeks of therapy. Five of the 12 patients had side effects, which were managed conservatively; in none of the patients, however, did the therapy need to be discontinued. The laboratory parameters also remained within normal limits during the course of therapy. Before starting azathioprine it is recommended that the TPMT activity should be measured in patients if the facilities are available.

The other advantages of this regimen were that the patients had to take only four doses of azathioprine in a month, which improved the compliance, and the cost of therapy was reduced by 60% compared with daily azathioprine therapy. Our study shows that weekly pulse doses of azathioprine are effective and safe in the treatment of parthenium dermatitis. However, larger controlled studies are required before it can be recommended as a substitute for daily treatment with azathioprine or corticosteroids for the treatment of parthenium dermatitis.

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