

Azathioprine as a Corticosteroid Sparing Agent for the Treatment of Dermatitis Caused by the Weed *Parthenium*

KAUSHAL K. VERMA, YASHPAL MANCHANDA and J. S. PASRICHA

Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, India

Air-borne contact dermatitis caused by *Parthenium hysterophorus* is a serious problem in India. Patients with this condition have to use corticosteroids regularly in order to maintain clinical remissions, but prolonged usage causes serious side-effects. The weed cannot be eradicated. We have used 3 therapeutic regimens with azathioprine, which led to an effective control with minimal side-effects even when used for long periods. A total of 22 patients (group I) were given 50 mg azathioprine twice a day; 11 patients (group II) received 50 mg azathioprine per day and 300 mg azathioprine every 28 days, and 10 patients (group III) were given 50 mg azathioprine twice a day along with 300 mg azathioprine every 28 days. The duration of treatment varied from 6 months to 3 years. Twenty patients in group I and 9 patients each in groups II and III had complete remission. Nine, 7 and 6 patients in the respective groups needed additional oral betamethasone 1–2 mg per day for brief periods only during the peak season in order to maintain complete remission. One patient in each group had only partial relief. The need for oral betamethasone during the second and the third year was further reduced. One patient each in group I and group II could not continue azathioprine due to the side-effects of the drug. **Key words:** contact dermatitis; *Parthenium*; therapy; azathioprine.

(Accepted August 10, 1999.)

Acta Derm Venereol 2000; 80: 31–32.

K. K. Verma, Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, 110029, India.

Air-borne contact dermatitis (ABCD) caused by the Compositae weed *Parthenium hysterophorus* is a distressing disease. This weed was accidentally introduced into India with imported food grains (1), and was first noticed in Pune in 1956. Subsequently, it has spread all over the country except for the high-altitude hills and the desert region (2). The first cases of contact dermatitis due to this plant were detected by Lonkar & Jog in 1968 (1), and later from other regions too. At present this is the most common cause of contact dermatitis due to the plants in India (2, 3).

The dermatitis primarily affects the areas of the skin which are not protected by the clothes or other items of apparel, but in severe cases the entire skin may be involved. The plant grows more profusely during the rainy season, but the antigen is present in the atmosphere almost throughout the year. The patient therefore suffers from severe itching and dermatitis throughout the year, though most patients experience exacerbations during the monsoons. Attempts at eradication of the weed have failed, protection of the skin with clothes and barrier creams have been largely ineffective, and desensitization procedures (4) have given inconsistent and

undependable results. The mainstay of the treatment therefore has been topical and systemic corticosteroids, which invariably produce serious and often irreversible side-effects because these have to be used for long periods. We recently achieved reasonable success using azathioprine as a substitute for corticosteroids (5) and another recent report (6) has also reported similar results. The present study was therefore planned to use azathioprine on a long-term basis and observe if (i) dependence on corticosteroids can be avoided/reduced, and (ii) the side-effects can be minimized.

MATERIAL AND METHODS

All adult patients having air-borne contact dermatitis, who were willing to take this treatment and were not suffering from any other major concomitant disease were included in the study. Pregnant or lactating mothers were excluded. The diagnosis of ABCD was confirmed in each case with a patch test using standardized antigen-impregnated discs, as described previously (2). On the basis of these criteria, a total of 43 patients (age range 31–75 years; duration of disease 0.5–20 years) who have received the treatment for at least 6 months were used for analysis.

Pre-treatment laboratory evaluation included estimation of haemoglobin, total and differential leukocyte counts, platelet count, serum bilirubin, hepatic transaminases, blood urea, serum creatinine, examination of the urine for sugar, proteins and cells, and stools for occult blood, chest X-ray and an electrocardiogram. Clinical examination and the blood chemistry evaluation were repeated every month during the treatment.

The first group of patients were treated with 50 mg azathioprine twice a day, but subsequently 2 more regimens were also added. Thus, group I included 20 women and 2 men who received 50 mg azathioprine twice a day, group II included 6 women and 5 men who received 50 mg azathioprine once a day and 300 mg once every 28 days, while group III included 10 patients, all men, who received 50 mg azathioprine twice a day with 300 mg once every 28 days. Systemic betamethasone 1–2 mg/day was used during the first 2–4 weeks to induce a quicker regression of the existing lesions. It was used again during the first year for 2–38 weeks for 9 patients of group I, for 4–20 weeks for 4 patients of group II, and for 8–28 weeks for 5 patients of group III. During the second year betamethasone was needed for 14 and 20 weeks by 2 patients of group I, 8–24 weeks in 3 patients of group II and for 10 and 16 weeks for 2 patients of group III. During the third year no patient has required corticosteroids so far.

RESULTS

Complete relief from dermatitis was obtained in 38 (88%) patients, but 22 (58%) of these required oral corticosteroids in order to maintain complete clinical remission (Table I). The differences between the three regimens were not significant.

Three patients, 1 in each group, could obtain only partial relief in spite of the treatment, but the relief was clinically significant and more than 50% in each case.

Table I. Effect of treatment with azathioprine in the 3 groups of patients

Group	Number of patients who:				Total
	Obtained complete remission		Obtained incomplete remission in spite of corticosteroids	Could not continue treatment	
	without corticosteroids	with corticosteroids			
I	11	9	1	1	22
II	2	7	1	1	11
III	3	6	1	–	10
Total	16	22	3	2	43

Side-effects

One patient in group I developed drug-induced hepatitis 7 months after the start of treatment and therefore had to discontinue the azathioprine. Another patient in group II developed severe nausea, vomiting, malaise, fever and palpitation and stopped the treatment.

In addition, 8 patients developed bacterial infections, and 1 patient each developed pulmonary tuberculosis, dermatophytosis, scabies, oral ulcers, nausea, herpes labialis, herpes zoster and acne, all of which were considered to be unrelated to the treatment. The laboratory parameters continued to remain within the normal range in all the patients, except in 2 patients who showed a temporary rise in the levels of serum transaminases, which, however, returned to normal levels without interrupting the treatment with azathioprine.

DISCUSSION

We believe that the clinical severity of contact dermatitis depends on: (i) the degree of contact hypersensitivity in the patient; (ii) the amount of the antigen to which the patient is exposed; and (iii) the proportion of the antigen which penetrates the skin barrier. Thus, the dose of corticosteroid or immunosuppressive drug required to maintain a complete clinical remission is expected to vary, not only in different patients, but also in the same patient at different times. This means that if all the patients are treated with a fixed dose schedule, all the patients are not expected to obtain complete relief, and some patients may develop a recurrence whenever the quantity of the antigen in the environment is high. Patients having more severe disease are likely to need additional treatment with corticosteroids, but as the contact hypersensitivity reduces the need for corticosteroids would

also be reduced. Ninety-five percent of the patients tolerated azathioprine without any side-effects, even when given for long periods. The few patients who could not tolerate azathioprine were treated with alternative drugs.

Concomitant use of the high (pulse) doses of azathioprine at 28-day cycles was aimed at reproducing the results we achieved previously with dexamethasone cyclophosphamide pulse therapy regimen in pemphigus (7) and collagen vascular diseases, with which we were able to obtain complete clinical remission without recurrence with no any maintenance treatment. The data obtained so far in *Parthenium* dermatitis is insufficient.

REFERENCES

- Lonkar A, Jog MK. Dermatitis caused by a plant *Parthenium hysterophorus*. A preliminary report. *Indian J Dermatol Venereol* 1968; 34: 194–196.
- Pasricha JS. Contact dermatitis in India. 2nd edn. New Delhi: Department of Science and Technology, 1988.
- Nandkishore TH, Pasricha JS. Pattern of cross-sensitivity between four Compositae plants *Parthenium hysterophorus*, *Xanthium strumarium*, *Helianthus annuus* and *Chrysanthemum coronarium* in Indian patients. *Contact Derm* 1994; 30: 162–167.
- Srinivas CR, Krupashankar DS, Singh KK. Oral hyposensitization in *Parthenium* dermatitis. *Contact Derm* 1988; 18: 242.
- Verma KK, Pasricha JS. Azathioprine as a corticosteroid-sparing agent in air-borne contact dermatitis. *Indian J Dermatol Venereol Leprol* 1996; 62: 30–32.
- Sharma VK, Chakrabarti A, Mahajan V. Azathioprine in the treatment of *Parthenium* dermatitis. *Int J Dermatol* 1998; 37: 299–302.
- Pasricha JS, Khaitan BK. Curative treatment for pemphigus. *Arch Dermatol* 1996; 132: 1518–1519.