AZATHIOPRINE AS A CORTICOSTEROID-SPARING AGENT IN AIR-BORNE CONTACT DERMATITIS

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Two patients having air-borne contact dermatitis (ABCD) caused by *Parthenium hysterophorus* for 10 and 15 years respectively and without having had complete remissions in spite of oral betamethasone in a dose of 2-3 mg per day, experienced complete relief while taking 50-100 mg azathioprine for 5 and 12 weeks without having to take systemic corticosteroids. There were no side effects of azathioprine. With further experience and standardization of the treatment schedule, it may be possible to use azathioprine as a corticosteroid-sparing agent to reduce the side effects of corticosteroids in patients having ABCD.

Key Words: Air-borne contact dermatitis, Azathioprine, Treatment, *Parthenium hysterophorus*

Introduction

Air-borne contact dermatitis (ABCD) caused by *Parthenium hysterophorus* and less commonly by other plants is one of the most intractable problems in dermatology in India.[1] The dermatitis can be controlled with topical/ systemic corticosteroids but continued use of corticosteroids over a prolonged period of time often leads to several complications some of which can be very serious.[2,3] The only other alternative for the patient is to shift to another different place where *Parthenium* (or the other causative plant) is not found. Unfortunately *Parthenium* has already spread to almost all parts of the country (except for the high altitude hills)[1] and therefore there are hardly any places in India where the patient can shift to, and often the economic, social and other difficulties make this option also not available to the patient. Thus the unfortunate patient is left with no other choice except to either suffer from the dermatitis or bear the side effects of prolonged corticosteroid therapy. Attempts at eradication of the weed have so far been unsuccessful and claims of desensitization with the antigen have never been substantiated. Our own attempts to desensitize the patients with *Parthenium* extract,[1] or a trial with the dexamethasone-cyclophosphamide pulse therapy regimen had proved unsuccessful.[4]

Recently however, we treated two patients with oral azathioprine as a corticosteroid-sparing agent and obtained encouraging results which are being reported. We could obtain a fair control of the dermatitis without having to use systemic corticosteroids and there were no side effects of azathioprine.

Case Reports

Case 1: A 34-year-old man had been having severe dermatitis involving the face, neck, forearms, hands and legs for the last 10 years. The lesions had started as erythematous papular lesions on the eyelids which had gradually increased to involve the other areas in 2½ years time. The lesions were present throughout the year but there was usually about 50% improvement between December and February every year. Cutaneous examination revealed a severe dermatitis with lichenification on the forehead, cheeks, eyelids, chin, nose, dorsa of hands, forearms, neck, upper chest and legs. There was no other abnormality. Patch tests using standardised antigen extracts prepared from the plants in our laboratory[1,5,6] showed positive patch test reactions to *Parthenium*

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hysterophorus and Xanthium strumarium. The titre of contact hypersensitivity (TCH)[7] with *Parthenium hysterophorus* was $1:10^2$ while with *Xanthium strumarium* it was UD (undiluted antigen extract). Patch tests with *Chrysanthemum, Eucalyptus, Lantana camara, Helianthus annuus* and *Dahlia* were negative. In July 1995, we started treatment with 50 mg azathioprine twice a day orally but no oral corticosteroids. In 5 weeks time, the patient experienced an almost complete remission which he had never achieved before even with 20-30 mg prednisolone a day. There were no side effects and laboratory investigations to look for the toxicity of azathioprine before starting the treatment and subsequently at two week intervals during the treatment showed no abnormality. After 5 weeks the treatment with azathioprine was stopped, but the patient remained completely asymptomatic for another 2 months. Subsequently however, the lesions reappeared on the face and neck showing approximately 50% of the severity of the original disease, and these were controlled with 50 mg azathioprine daily.

Case 2: The second patient was a 41-year-old male clerk, with dermatitic lesions on the face, neck, hands and forearms for the last 15 years. The lesions had started on the hands and gradually spread to involve the other areas. There was approximately 25% improvement in the lesions between November and February each year but he had never had a complete remission even with 2-3 mg betamethasone orally per day. Cutaneous examination revealed erythematous papules and plaques on the forehead, eyelids, cheeks, earlobes, chin, neck, upper chest, dorsa of both hands and extensor aspects of the forearms, with crusting and lichenification. There were no other abnormalities. Patch tests with the plant antigens showed positive reactions to *Parthenium hysterophorus, Xanthium strumarium* and *Chrysanthemum* with a TCH of 1:10 for both *Parthenium hysterophorus* and *Xanthium strumarium* while the patch tests with *Lantana camara, Eucalyptus, Helianthus annuus* (Sunflower) and *Dahlia* were negative. He was treated with 50 mg azathioprine twice a day orally along with topical clobetasol propionate, and experienced almost complete relief without systemic corticosteroids. The routine investigations which included haematological parameters, liver and renal function tests, urine analysis and stools done before starting azathioprine and subsequently at 4 week intervals revealed no abnormality. There were no side effects even when the drug was continued for 12 weeks. After 12 weeks the dose of azathioprine was reduced to 50 mg per day and in about a week's time there was recurrence of the lesions on the face and the neck with about 30% of the intensity of the original disease. The TCH done with *Parthenium hysterophorus* and *Xanthium strumarium* after 12 weeks of treatment showed a reduction by one grade (UD), the undiluted antigens only.

Discussion

A patient having contact hypersensitivity to an agent is expected to develop the dermatitis whenever he is exposed to the causative agent, the severity of the dermatitis would depend upon, (1) the degree of contact hypersensitivity in the patient at that time, and (2) the quantity of the antigen to which the patient gets exposed. For an effective control of the dermatitis therefore, we should either reduce the degree of contact hypersensitivity in the patient, or make an attempt to reduce the quantity of the antigen to which the patient is exposed. So far we have no means by which we can reduce the degree of contact hypersensitivity. Therefore, the only option

available is to try to reduce the quantity of the antigen to which the patient is exposed. We had recently adopted a four point approach namely, (1) to remove as much of the causative plant as possible from the immediate environment of the patient especially the residence and the place of work, to reduce the quantity of the antigen in the patient's environment, (2) to cover as much of the skin of the patient as possible by wearing full-sleeve, high-neck shirts, long pants, socks, shoes and cap/turban etc, to protect a major part of the skin, (3) to wash the uncovered areas with soap and water as frequently as possible (preferably every 2-3 hours), to wash off the antigen from the skin before it is able to penetrate the skin, and (4) to use a barrier cream on the exposed areas after every wash, to slow down the penetration of the antigen into the skin.

This effort was to be supplemented with topical corticosteroids because some amount of the antigen was still likely to cross all these barriers. Systemic corticosteroids were to be used only when required and the practice of step-wise reduction of the dose of corticosteroids was considered unnecessary, because the dose requirement would depend upon the amount of the antigen to which the patient is exposed and this would vary from one day to the other. The patient was advised to decide the dose on a day to day basis depending upon the severity of the dermatitis, and encouraged to omit the dose on the days when there was no dermatitis. This was found to lead to a significant reduction in the cumulative dose of corticosteroids, but still this did not lead to complete freedom from the long-term side effects.

Complete relief obtained with azathioprine in the two cases is a very encouraging observation because azathioprine is a relatively safe drug especially when used judiciously,[8,9] the side effects caused by this drug when used in smaller doses are fewer and reversible, and it does not lead to long-term toxicity.[9] If the patient can be maintained on a relatively small dose and monitored for the side effects at periodic intervals, the therapy can be made fairly safe and effective. Further studies however, on a much larger number of patients will be required to establish the dosage schedules, the duration of treatment and the pattern of laboratory investigations required to evolve a safe and effective mode of treatment for these patients.

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