A LOCALISED SKIN ERUPTION DUE TO AZATHIOPRINE

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Summary

An Afghan national having bullous pemphigoid, developed itching and erythema on the medial side of his both feet 3 days after institution of treatment with azathioprine. The lesions subsided on withdrawing azathioprine but recurred at the same sites within 14 hours of provocation with 25 mg azathioprine.

KEY WORDS : Azathioprine; drug eruption.

Introduction

Azathioprine is a widely used immunosuppressive agent all over the world. The toxic effects reported so far include bone-marrow depression leading to anemia, leukopenia, thrombocytopenia, pancytopenia and macrocytosis; gastro-intestinal disturbances leading to nausea, vomiting, diarrhoea, oral ulcerations, esophagitis and steatorrhoea; pancreatitis, liver enzyme changes, cholestasis, reversible portal fibrosis, disseminated viral infections, cutaneous malignancies, acute leukaemia, myopathy, aseptic meningitis, drug fever, arthralgia and myalgia[1,2]. Skin eruptions due to azathioprine are infrequent. Adams et al[3] reported a mild maculo-papular skin rash in two out of 19 patients being treated with azathioprine for various immunological renal diseases. The skin rash, however, was observed to disappear spontaneously in spite of continuation of treatment with azathioprine. King et al[4] described two patients with skin eruption due to azathioprine. One of these patients developed a diffuse erythematous rash on four occasions each time following administration of azathioprine. The rash would disappear spontaneously within 36-48 hours after discontinuation of the drug. The second patient developed an erythematous rash which was localized to the neck and the face only. The rash disappeared on withdrawing the drug, but reappeared on provocation. We are reporting another case who developed a localised itchy erythematous eruption on the medial sides of both feet. Association of this eruption with azathioprine was confirmed by the provocation test.

Case Report

Since August, 1981, a 42-year-old male from Afghanistan was having recurrent episodes of asymptomatic, tense vesiculo-bullous lesions all over the body including the oral mucosa. Histopathology of the skin lesion confirmed the diagnosis of bullous pemphigoid. Treatment with 60 mg prednisolone a day orally led to clearance of the lesions in about a month's time. As prednisolone was being tapered slowly he again started getting new lesions while he was taking 20 mg a day. On January 30, 1982, prednisolone was increased to 60 mg daily but the response to treatment was not adequate. On February 11, 1982, therefore,

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azathioprine 100 mg orally daily was added. The next day in the afternoon he noticed severe pain in both his lower limbs down the entire length. There was no evidence of any arterial occlusion, thrombophlebitis or neuropathy. On February 13, 1982, the patient stopped taking azathioprine on his own; and the pain disappeared completely within the next 24 hours. Prednisolone 60 mg orally per day was continued. On February 19, 1982, 100 mg azathioprine a day was started again. The skin lesions showed improvement, but on February 22, 1982, he noticed itching and erythema in an area of 3 × 4 cm on the medial side of his right foot. During the next 2 days he developed similar lesions on his left foot and dorsal aspects of both hands. On February 24, 1982, azathioprine was stopped. Itching and erythema disappeared during the next 2 days. Vesiculo-bullous lesions on the skin subsided during the next 10 days. As prednisolone was slowly reduced to 20 mg daily, he again started getting new vesicles. On March 1, 1982, cyclophosphamide 100 mg daily orally was added and the activity of the disease was controlled during the next 7 days. On April 5, 1982, cyclophosphamide was stopped due to a fall in the platelet count, prednisolone 20 mg daily being continued.

Provocation with azathioprine was started on April 7, 1982, by giving 25 mg azathioprine orally. After 14 hours patient noticed itching and erythema on the medial sides of both the feet. Next day, 25 mg azathioprine was given and this led to an exacerbation of the symptoms. There was a well-defined area of scaling and erythema on the medial sides of both feet. Scrapings for dermatophyte were negative. Biopsy from the scaly erythematous area showed a band-like infiltrate closely apposed to the basal layer of epidermis consisting predominently of polymorphs. The epidermis showed focal spongiosis and extension of the polymorphonuclear infiltrate into the lower epidermis in some areas. Further administration of azathioprine was stopped and he was given an extra dose of 20 mg prednisolone and 25 mg chlorpheniramine maleate orally which led to disappearance of itching during the next 2 hours. Scaling and erythema subsided during the next 7 days.

Discussion

Causal association of the eruption in our case with azathioprine was confirmed by provocation, but the nature of this eruption could not be clarified. Allergic eruptions due to drugs are as a rule generalized with the exception of fixed drug eruptions (FDE). The eruption in the present case however, showed no clinical resemblance to FDE even though it recurred at the same skin areas and the time interval between ingestion of the drug and exacerbation of the eruption corresponded to that usually seen in FDE. Whatever the mechanism, it is important to bear in mind that azathioprine can lead to a localised eruption on skin, though such eruptions are extremely infrequent.

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