LICHEN PLANUS LIKE LESIONS CAUSED BY THIACETAZONE

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Summary

Thiacetazone has been used as a standard antituberculous drug in several countries. Side effects which include various types of skin eruptions have been observed in about 10 % of patients taking thiacetazone. We are reporting two cases of lichen planus-like lesions presumably due to thiacetazone. Of these, one case had pre-existing lichen planus hypertrophicus but the other one did not have any past history of lichen planus.

Thiacetazone (Thiosemicarbazone) and isoniazid have been extensively used in several countries, including India, as the standard treatment for tuberculosis. Approximately 10% of the patients have to discontinue thiacetazone on account of side effects[1]. The side effects include gastro-intestinal disorders, skin eruptions and vertigo[1,2]. Other less common side effects are hepatitis, jaundice, anaemia, and blood dyscrasias[3].

The skin eruptions include haemorrhagic lesions and exfoliative dermatitis[4]. Cases of toxic epidermal necrolysis presumably due to thiacetazone have also been reported[5-7]. Ravindran and Joshi[8] reported 19 cases of drug eruption due to thiacetazone which included Stevens-Johnson syndrome, hyperpigmentation and exfoliation, and pruritic papules on the trunk.

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Lichenoid eruptions have been seen with streptomycin, PAS and isoniazid[9]. However, no case of lichenoid eruption due to thiacetazone has been published so far.

The present report describes two cases which developed lichen planus-like lesions when taking thiacetazone.

Case Report

Case No. 1

On 23rd June 1977 a 51 year old male presented to the Dermatology clinic of our Hospital with the complaint of two mildly pruritic hyperkeratotic plaques on the right leg. (Fig. 1) The first plaque had developed 6 years previously whereas the second one which was located near the first plaque, had started only 8 months previously. On a mistaken diagnosis of tuberculosis verrucosa cutis, he was treated with streptomycin 1g, isoniazid 300 mg and thiacetazone 150 mg daily. Within two and a half months he developed whitish papules in the oral mucosa and on the lips (Fig 2.) There were no lesions elsewhere on the skin. The biopsy from one of the lesions on the leg suggested lichen planus hypertrophicus. The

antituberculous drugs were stopped and the oral lesions disappeared in 10 days.

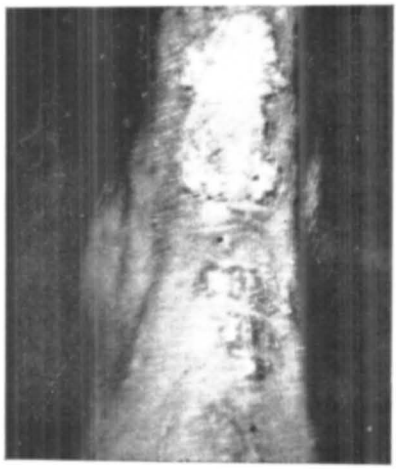

Fig 1 2 hyperkeratotic plaques are seen on the leg near the ankle (Case No. 1).

On 5th October 1977 thiacetazone was restarted in a dose of 150 mg daily. Within 3 days the lesions reappeared and they subsided within seven days of stopping thiacetazone.

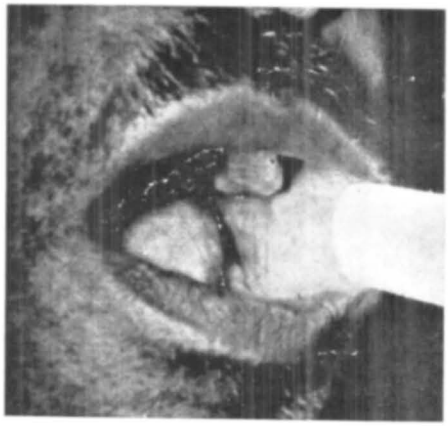

Fig. 2 A lacy network of whitish papules is seen on the buccal mucosa (Case No. 1).

Case No. 2

On 5th July 1978 a 70 year old male was admitted to our hospital with urinary retention. He was a known diabetic for 2 years and was taking $1\frac{1}{2}$ tablets of glybenclamide every day.

Three months prior to admission he had been diagnosed outside as a case of pulmonary tuberculosis and was started on an oral combination containing isoniazid and thiacetazone, of which he received 300 mg and 150 mg respectively every day. 15 days later he developed itchy papular lesions all over the body, but continued to take the antituberculous therapy till 3 days prior to admission.

Cutaneous examination revealed violaceous flat-topped papules and plaques on the extremities and diffuse dusky erythema and scaling on the trunk. The involvement on the trunk resembled an exfoliative dermatitis-like picture. The buccal mucosa showed a lacy network of whitish papules. In addition there was exfoliation on palms and soles and mild scaling on the eyelids. The nails were not affected.

A provisional diagnosis of lichen planus like eruption due to antituberculous drugs was made. Skin biopsies from the leg and trunk showed features consistent with lichen planus (Fig 3 & 4).

Fig. 3 Biopsy from upper back from area of diffuse scaling (Case No. 2).

Chest X-ray showed bilateral infiltrative lesions suggestive of pulmonary

tuberculosis. ECG revealed complete left bundle branch block. Later on prostatectomy was performed and the biopsy showed adenofibromatous hyperplasia of the prostate.

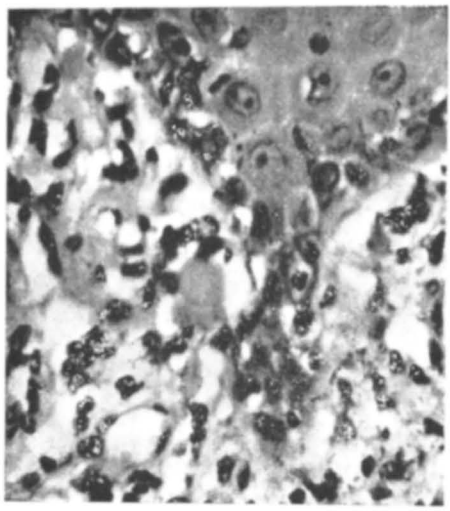

Fig. 4 Same slide (400 x) In addition to the other features of lichen planus, this section also shows 2 overlapping colloid bodies. They are in the subepidermal zone, a little to the left of centre.

Progress of the Lichen Planus Like Eruption

On admission, the patient remained off antituberculous drugs for 9 days. During this period he was on ampicillin, glybenclamide, pheniramine maleate and vitamins orally. Betamethasone cream diluted in an equal quantity of cold cream with phenol and menthol was applied three times a day. This was continued during the entire period of his hospitalization. There was marked relief of itching and the plaques begun to flatten out.

On 15th July the patient was given thiacetazone in a dose of 50 mg thrice daily for 4 days. Within 24 hours there was marked aggravation of the itching but there was no obvious change in the skin lesions. On 19th July thiacetazone was stopped and isoniazid was given orally in a dose of 100 mg thrice daily. While on isoniazid, the itching became much less. On 2 th July the patient was also given para aminosalicylic acid and ethambutol in a dose of 12 g a day and 800 mg a day respectively. These were added to provide adequate antituberculous cover. On 4th August isoniazid was stopped and the patient was given an oral combination containing 300 mg of isoniazid and 150 mg of thiacetazone in one dose. Within 9 hours the patient developed excruciating itching and swelling of the lower eyelids and he became very restless. This exacerbation was treated with 100 mg hydrocortisone injection and 50 mg promethazine injection for only one dose. The isoniazid and thiacetazone combination was stopped and the patient was continued on isoniazid, para aminosalicylic acid and ethambutol. Within 48 hours the itching markedly diminished.

Discussion :

Case No. 1

Developed lichen planus-like lesions in the oral mucosa while he was on thiacetazone. As the patient had pre-existing lichen planus hypertrophicus it would appear that in this case thiacetazone precipitated lichen planus-like lesions. This patient possibly had a constitutional predisposition to lichen planus.

Case No. 2

Also developed lichen planus like lesions presumably due to thiacetazone. However, in contrast to case No. 1, in this patient the lesions were generalised and there was no preceding history of lichen planus.

Thiacetazone was incriminated as the cause of the lichen planus like eruption by observing the response to withdrawal and provocation with this drug. It was observed that even though the patient developed severe itching on provocation with thiacetazone there was however no appreciable change in the existing lichen planus - like lesions. This was

probably because the patient continued to be on a local corticosteroid application. The corticosteroid application was started initially in order to control the eruption and was continued in order to maintain standard conditions during the remainder of the study.

Another point for comment was that when thiacetazone was administered in divided dosage the itching though aggravated, was not as severe as when, he subsequently received the combination of isoniazid and thiacetazone as a single dose. It may be that the daily total given as a single dose was more powerful in eliciting the response, as compared to the divided dosage of thiacetazone. On the other hand, the possibility remains that isoniazid may have potentiated the action of thiacetazone in precipitating the lichen planus-like eruption.

References

1. Miller AB, Nunn AJ, Robinson DK, et al : A second international co-operative investigation into thiacetazone side effects. 2 : Frequency and geographical distribution of side effects, Bull Wld Hlth Org, 47:211, 1972.
2. Mathur KC: Toxicity of thiacetazone (when used in combination with isoniazid) A study among 1225 patients, Indian J Tuberc, 22 : 152, 1975.
3. Dukes MNG (Ed) : A survey of unwanted effects of drugs reported in 1972-1975 : In Meyler's side effects of drugs ; Vol 8, American Elsevier Publishing Co Inc, New York, 1976, p 6 2.
4. Ferguson GC, Nunn AJ, Fox W, et al : A second international co-operative investigation into thiacetazone side effects : Rashes on two thiacetazone containing regimens, Tubercle (Lond) 52 : 166, 1971.
5. Sehgal VN, Bahadur P, Ghosh SK, et al : Toxic epidermal necrolysis as a result of antitubercular drugs, Indian J Chest Dis, 15 : 57, 1973.
6. Handa F, Kumar K and Rani R : Toxic epidermal necrolysis due to thiacetazone, Indian J Tuberc, 21 : 37, 1974.
7. Bedi TR, Singh OP and Bhutani LK : Acute epidermal necrolysis (Lyell syndrome) induced by thiacetazone, Indian J Chest Dis, 16 : 58, 1974.
8. Ravindran P, Joshi M : Dermatological hypersensitivity to thiacetazone, Indian J Chest Dis, 16 : 58, 1974.
9. Samman PD : Lichen Planus and Lichenoid Eruptions, Text book of Dermatology, vol 2, 2nd Edition by Rook A, Wilkinson DS and Ebling FJG, Blackwell Scientific Publications, Oxford, 1972, p 1351.