ETHAMBUTOL INDUCED BULLOUS AND **LICHKNOID** SKIN **E**RUPTIQNS

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Summary: Two cases of Ethamhutol induced bullous and liclenoid skin eruptions, confirmed by provocation test, are reported and the importance of including Ethambutol also in the list of anti tuberculosis drugs suspected to cause these manifestations is stressed.

Introduction

Cutaneous reactions are among the most frequently observed adverse reactions to drugs. They are observed in about 2.2% of medical in-patients (Arndt, 1976). Antituberculnsis drugs like Thiacetazone, Para-amino salicylic acid, Streptomycin and Isoniazid are notorious for producing significant cutaneous side effects (Levantine, 1972; Gupta and Pasricha, 1982) while with Ethambutol hydrochloride, the frequency of major side effects is not very high, taking into consideration its increasingly frequent consumption, although dose-related ocular toxicity to this drug is not uncommon (Leibold, 1966). Cutaneous side effects of Ethambutol reported in literature include purpura (Jesiotr, 1969), pruritic erythematous papules (Pasricha and Kanwar, 1977) and exfoliative dermatitis (Mani and Mathew, 1983). In the present communication, we report 2 cases of Ethambutol induced bullous and lichenoid skin rashes confirmed by provocation test.

Case Reports

Case 1

A 15 year old girl was put on anti-tuberculosis treatment with INH, Rifampicin and Etharmbutol for tuberculosis of the cheek. After 25 days of treatment, she reported back with complaints of fever, generalised itching and vesiculobullous eruptions She denied taking any other medication during this period and was not known to have allergy *to an*y other drug or food items.

She was febrile (102°F). No significant positive finding was detected on systemic examination Cutaneous examination revealed crusted oozing erosions on and around lips and flaccid vesicles on chest and abdominal wall on erythematous base. Similar vesicles were seen on both cubital fossae and dorsal aspects of both hands and feet extending to the ankles, including the genitalia. Lesions on the feet and ankles further showed crusting erosions (Fig. 1) and diffuse scaling, desquamation and pigmentation was seen on the palms (Eig. 2). Nikolsky und bullas pread signs were negative. Tzano. smear did not show any acantholytic cells.

Fig. 1

Bitaterally symmetrical oozing, vesiculo-bullous eruptions over the dorsum of both feet and lower legs

Fig. 2

Both palms showing diffuse desquamation and exfoliation and pigmentation with deep seated vesicles

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All anti-tuberculosis drugs were discontinued and patient was put on systemic steroids 20 mgdaily with Erythromycin 250 mg 6 hourly and topical therapy for a period of two weeks. The lesions cleared completely.

Provocation tests administered for 1NH and Rifampicin as per the schedule of Girgling (1984), were negative. Provocation test with Ethambutol at a dose of 100 mg induced within 10 hours generalised itching, erythematovesicular skin eruptions, more marked on the extremities Further administration of Ethambutol was stopped but 1NH and Rifampicin in full doses were continued.

Ethambutal induced skin eruptions cleared spontaneously in a week's time.

Cane 2

A 28 year old housewife suffering from genitourinary tuberculosis had been on INH, Rifampicin, Pyrazinamide and Ethambutol for 2 months, and subsequently on INH, Rifampicin and Elhambutol for a period of 3 months. She reported with complaints of generalised itchy rash. No other history of additional medication or allergy to any drug or food was elicited.

A thorough examination did not delect any general or systemic abnormality- Cutaneous examination revealed diffuse erythema and lichenoid papules, scattered diffusely over both anterior and posterior aspects of the trunk, ill-defined hyperpigmented macules were observed on the trunk, more on the anterior abdominal wall. All the drugs were withdrawn and challenge doses of 1NH and Rifampicin were given as in Case 1- Since no untoward effects were observed, she received full doses of both drugs for a week after which Ethambutol was administered in a dose of 100 mg. A prompt recurrence of the skin eruptions within 6 hours of administration confirmed Ethambutol to be responsible for the reaction. When the present report was prepared, she was being continued on INH and Rifampicin without any adverse effects.

Discussion

It has been observed that adverse reactions with anti-tuberculosis drugs usually occur early in the course of treatment (Levantine, 1972; Girgling, 1984) or at any time during the course of drug therapy (Levantine, 1 972) This is well exemplified in Case 2 which developed cutaneous reactions to Ethambutol several months after initiation of chemotherapy. Since INH, though innocuous, is commonly incriminated in cutaneous drug eruptions (Mani and Malhew, 1983), our first suspicion was on this agent in both patients.

Rifampicin mostly produces red coloration of urine, but skin rashes like Stevens-Johnson syndrome, pemphigus and porphyria cutanea tarda reported in literature arc very rare (Jopling, 1984) and hence it was naturally not suspected as the cause of allergy in both cases. Lthambutol too enjoyed the reputation of safety as a cutaneous allergen till Jesioter (1969) first reported Ethambutol induced purpuric rashes. Since then, a few more documented cases of Ethambutol induced cutaneous eruptions have appeared in literature

It was, therefore, surprising to observe erythema multiformae type skin lesions caused by Ethambutol in Case 1 which would be reproduced by provocation test. This type of rash resulting from administration of Ethambutol has not so far been reported in literature.

Lichenoid and lichen planus type of skin eruptions have so far been reported to be due to PAS (Wintroub, 1979; Mani and Mathew, 1983) and Thiacetazone (Mani and Mathew, 1983), but in Case 2, it was Ethambjtol which produced symptomatic lichenoid eruption whereas INK and Rifampicin could be continued in full dosage in this patient without any side effect. This further proves that the clinical manifestations of drug eruptions arc diverse in nature and may mimic almost any known dermatosis. The often used cliche "any drug may produce any rash", though an overstatement, attests to the complexity of drug induced adverse reactions (Wintroub et al, 1979).

In conclusion, the present report as well as the previous ones should alert the clinician to consider Ethambutol also as one of the possible offending agents in the causation of cutaneous eruptions and it is always preferable to confirm the cause of eruption by provocation test ensuring all safety measures, preferably in hospitals.

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REFERENCES

Arndt, K.A. and Jick, H. : Rates of cutaneous reactions **to** drugs. JAMA, 1976, 235, 918.

Girgling, D.J : Adverse effects of anti-tuberculosis drugs. Bulletin of the International Union against Tuberculosis, 1984, 59, 152-62.

Gupta. K. and Pasricha, J.S. : Drugs causing skin eruptions (An analysis of cases confirmed by provocation tests). Ind. J. DermaloL Venereal. Leprol. 1982, 48, 96-98.

Jesiotr, M. : Ethambutol in the treatment of 26 patients with chronic active pulmonary tuberculosis. Tubercle, 1969, 50, 54-55.

Jopling, W.H. : Handbook of Leprosy, 1984, 3rd Edn., William Heinemann Medical Books Ltd., London, pp. 91-92.

Leibold, J.E. : The ocular toxicily of Ethambutol and its relation to dose. Annuls of New York Academy of Sciences, 3966, 135, 904.

Levantine, A. and Almeyda, J. : Cutaneous reactions to anti-tuberculosis drugs. Br. J. Derm.1972,80, 651-53.

Muni, M.Z. and Matlicw, M. ; A study of 2 IS drug mipiioiis. Ind J, Oenn.uoi. Vencreol. Leprol.1983, 49, 109-17.

Pasricha, J.S. and Kanwar, A.J: Skin eruption caused by Ethambutol. Archives of Dermatology,1977, 113, 1122-23.

WintroLib, B.U , Shiffman, N.J. and Arndt, K,A. : Adverse cutaneous reactions to drugs. In : Dermatology in General Medicine. Edited by Fitzpatrick T.B., Eisen A.Z., Wolff K., et al, 2nd Edn., McGraw Hill Book Company, New York, 1977, pp. 555.