Balanitis due to fixed drug eruption associated with tetracycline therapy

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An eruption is called 'fixed' if it recurs at the same site after re-exposure to the drug which precipitated the previous lesion. The eruption is commonly erythematous and sharply defined but may be bullous, herpetiform, or urticarial, and can be solitary or widely scattered. The commonest target areas are the trunk and the proximal portions of the limbs and the mouth, eyes, and urethra may sometimes be involved. Many drugs have been implicated, including phenolphthalein, phenacetin, salicylates, barbiturates, dapsone, sulphonamides, and tetracycline (Peck and Feldman, 1950; Welsh, 1955; Browne, 1964; Baer and Harris, 1967).

Recently we observed five patients who developed a fixed eruption on the glans penis after oral tetracycline treatment for non-gonococcal urethritis (NGU). No similar instances have been found in the available literature and as such cases may give rise to diagnostic difficulties, the histories are reported below.

Case reports

Case 1, a single Caucasian male teacher aged 24, attended the special clinic from March 1968 to July 1969, with recurrent non-gonococcal urethritis. He gave a history of NGU in 1967; there had been no other significant illness and there were no known allergies. During the period of attendance he had six separate episodes of NGU, each of which was treated with tetracycline 250 mg. four times daily for 5 days to which the urethritis responded.

During the fourth attack he developed a circumscribed irritating herpetiform eruption on the glans penis a few hours after starting treatment. The lesion became worse over the next 5 days and then cleared rapidly. A diagnosis of NGU with probable herpes genitalis was made. A further attack of NGU occurred 4 months later and after treatment was started the same sequence of events was noted except that the lesion on the glans was erythematous. A month later another episode of NGU brought him to the clinic and this time we considered the possibility that he was subject to a fixed eruption due to tetracycline. To prove this we obtained permission from the patient to

give him tetracycline and to observe the effects; within 3 hours of the first dose of tetracycline an erythematous area developed on the glans penis at the same site as before (Figure). The urethritis cleared within 7 days and so did the eruption. During the period of attendance the patient had not taken any other drugs.

FIGURE *Case 1. Fixed drug eruption on glans penis following 250 mg. tetracycline*

Case 2, a married Caucasian policeman aged 29, attended the clinic from June to August 1969, and gave a history of gonorrhoea treated uneventfully with penicillin. NGU was diagnosed and treated with tetracycline 250 mg. four times daily for 5 days.

On the first day of treatment a raised itchy circumscribed erythematous rash appeared on the glans penis which subsided after a week. The patient then stated that an identical lesion had developed in 1967 and again early 1969, on each occasion after taking, achromycin, medically prescribed. The lesions subsided without treatment.

Case 3, a married Caucasian male sales representative aged 34, first attended in 1964 with NGU. He had previously had pulmonary tuberculosis which was treated with streptomycin and artificial pneumothorax. For the urethritis he received several courses of tetracycline without untoward reactions. In 1966 he had a further attack of NGU and was given tetracycline; the urethritis cleared but he was found to have a small erythematous area on the glans penis shortly after starting treatment. There was another episode of NGU 3 months later and he was given a course of demethylchlortetracycline which he did not take. He returned to the clinic 8 months later with a recurrence of urethritis and balanitis. The history was that he had had urethritis a few days earlier and had taken the demethylchlortetracycline which he had kept back from his previous visit.

About 24 hours after starting treatment an erythematous patch appeared on the glans with a sore in the centre. This cleared, possibly helped by local hydrocortisone cream. The urethritis had not cleared completely and a course of tetracycline was prescribed; the erythematous genital lesion recurred within a short time of starting the antibiotic, but faded as soon as the drug was stopped. There were two further episodes of NGU which were treated with erythromycin with relief of signs and symptoms and without further skin lesions.

Case 4, a single Caucasian male pilot aged 21, attended the special clinic between November 1968, and October 1969, with recurrent NGU. There was no history of genital infections or of allergies. During the period of attendance he had three episodes of NGU each of which was treated with tetracycline for 5 days.

Treatment of the first attack was uneventful but after starting tetracycline the second time he developed eruptions of the penis and the roof of the mouth. The lesions were circumscribed, raised, and erythematous and resolved rapidly after the course of tetracycline was completed. During treatment of the third attack the same type of lesions appeared on the penis and mouth and disappeared within a few days. The site of the eruption on the penis was identical in both attacks.

Case 5, a Caucasian male printer aged 34, was first seen in 1956 with his first attack of NGU. There was a history of mild allergic asthma provoked by feathers, house dust, and some pollens. The urethritis was treated with sulphatriad and then, achromycin, without side-effects. During the next 12 years he had four more episodes of NGU which were uneventfully treated with achromycin or tetracycline phosphate compound (Tetrex).

In May 1969, he had a further attack of NGU for which he was given the routine course of tetracycline.

After the first day of treatment he developed an irritating erythematous patch on the glans penis which cleared spontaneously and he did not mention it at his next attendance. In March 1970, a further attack of NGU brought him to the clinic and tetracycline was again prescribed. Within 24 hours of the first dose he developed a similar lesion on the glans. He stopped treatment and saw us next day as he thought the drug might have been responsible for the reaction. There was a fading erythematous patch with some oedema covering a large part of the glans. The lesion cleared rapidly within the next four days except for some residual pigmentation. The urethritis was eventually treated with erythromycin without ill-effects. *Candida albicans* was not found in any of the balanitic lesions.

All the patients were subsequently advised to avoid taking tetracycline or its analogues in future whenever alternatives were available.

Discussion

The nature of the fixed drug eruption is unknown as is the reason why any particular target area should be involved. Skin sensitivity tests with the offending substance give equivocal results and oral provocation is of much greater diagnostic value (Welsh, 1955). In our cases the glans penis was the target area which seems to be an unusual site judging from the literature. Browne (1964) investigated 350 cases and did not observe involvement of the glans; Haber (1950) reported one case with a fixed eruption on the penis and scrotum with simultaneous urethritis all of which were due to phenolphthalein taken in a laxative preparation and could be reproduced by further exposure to the drug. The common factor in our patients was pre-existing NGU which may have played a role in determining the target site. Four of the five patients had had tetracycline previously without any reaction; in Case 2 it was not known whether the patient had ever had the antibiotic before, but it has been found that a fixed eruption can develop even after the first dose of a drug (Browne, 1964). Persistent pigmentation often follows the eruption and this was noted in one of our patients.

Non-gonococcal urethritis and balanitis may be associated, as in Reiter's syndrome, even without arthritis (Csonka, 1958); with herpes simplex infection of the glans and urethra (Harkness, 1950); and with chemical agents affecting these sites.

Tetracycline is the treatment of choice in NGU and it is probable that the type of case which we describe is not exceptional but is liable to be misinterpreted if the association with tetracycline is not recognized.

In our cases, as with fixed drug eruptions generally, the lesions cleared promptly once the drug responsible was discontinued.

Summary

Five cases are reported of a fixed drug eruption arising on the glans penis as a result of treatment of non-gonococcal urethritis with tetracycline. One case followed the first exposure to the drug; in the other cases there had been multiple exposures. The pertinent literature is briefly reviewed.

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