

## Intertriginous Drug Eruption

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Presented are two patients who developed an unusual, and as yet unreported eruption due to amoxicillin. They exhibited an eruption confined to the intertriginous areas, which mimicked intertrigo. Although drug eruption can mimic a variety of idiopathic skin diseases, intertrigo is easily distinguished from drug eruption and has not been mentioned in the differential diagnosis of this reaction.

It is suggested that drug reactions should be considered in the differential diagnosis of intertrigo, in particular of atypical and therapy-resistant cases. Early detection of these cases has practical importance since the elimination of the causative drug is essential for therapy success. Case 2 showed a response of the toxic epidermal necrolysis (TEN) type, which could have been very severe and dangerous had the diagnosis not been made in an early stage before the development of generalized TEN.

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"Drug eruption is an age-old but always timely and fascinating subject" (1) for both clinicians and researchers. The manifestations of drug-induced side effects in dermatology are so manifold that drug reactions might be considered to have replaced syphilis as the great imitator.

Drug eruption can mimic a variety of idiopathic skin diseases, including psoriasis (2, 3), lichen planus and lichenoid eruptions (4, 5), pityriasis rosea (6), atopic dermatitis (7, 8), mycosis fungoides (9), acneiform eruptions (10), bullous eruptions like pemphigus vulgaris (11), bullous pemphigoid (12) and many others.

Intertrigo, however, is easily distinguished from drug eruptions and has not been mentioned in the differential diagnosis of this reaction.

presented are two patients with an unusual, and as yet unreported form of drug reaction. They exhibited an eruption confined to the intertriginous areas, which mimicked intertrigo.

### CASE REPORTS

#### Case 1

A 35-year-old woman was admitted to our clinic for evaluation of an erythematous pruritic rash of 10 days' duration in the inguinal and intergluteal areas. The patient's condition had been diagnosed elsewhere as candida intertrigo and although the microscopic examination with KOH and cultures on Sabouraud's agar were negative, she was being treated with a cream containing isoconazole nitrate 10 mg, and diflucortolone valerate 1/mg/G. The eruption, however, had not only failed to respond, but had in fact spread, and had appeared in the axillary folds. The patient's history revealed that she was a healthy woman, and that 2 days prior to the appearance of the rash she had

started treatment with amoxicillin for urinary tract infection. In the past she had developed a widespread eruption after taking ampicillin.

Our initial examination revealed symmetrical erythematous edematous plaques in the inguinal, intergluteal and axillar areas (Fig. 1).

Since the usual and appropriate treatment for intertrigo failed to alleviate the skin condition, and the eruption appeared in the axillar area (that had not been treated topically), the possibility of an eruption due to amoxicillin was considered and the drug was discontinued. The patient was instructed to continue topical treatment only on the left inguinal and axillar side and to leave the right inguinal and axillar areas untreated. Within 2 days of withdrawal of the amoxicillin the skin condition improved noticeably, and within 1 week it had cleared completely from both sides of her body.

#### Case 2

A 32-year-old healthy man was admitted because of an erythematous, erosive, oozing eruption in the genital and inguinal areas that had started a day earlier. Four days prior to the appearance of the eruption, he had received amoxicillin for an upper respiratory tract infection.

Our first examination revealed erythematous, edematous, well-defined plaques in the inguinal, perineal and intergluteal areas with erosions and crust formation. A biopsy specimen obtained from a lesion revealed hydropic degeneration of the basal cells, subepidermal separation, and necrotic keratinocytes in the epidermal tissue. The dermis showed a mild mononuclear infiltrate around the superficial blood vessels. The changes were consistent with toxic epidermal necrolysis (TEN). Repeated cultures for bacteria and fungi were negative.

The amoxicillin was discontinued, and following an initial period of several days during which the skin condition worsened, it started to improve rapidly, and within 10 days his eruption had cleared almost completely and he was discharged.

### DISCUSSION

The two patients reported had developed an unusual eruption due to amoxicillin. Evidence of the drug being the cause of the skin eruption is only circumstantial, yet strong. In Case 1 the rash appeared 2 days after the patient started taking amoxicillin. Microscopic examination and cultures ruled out the possibility of fungal infection. The rash did not respond to standard



Fig. 1. Case 1. Symmetrical, erythematous plaques in the inguinal areas.

treatment for intertrigo, which usually responds readily. It continued to spread and even appeared in distant areas – in the axilla. As soon as the amoxycillin was discontinued the rash rapidly disappeared. The disappearance of the rash from both sides of the patient's body, in spite of the fact that topical treatment was continued on one side, proves that the topical treatment had no effect – either beneficial or detrimental – and ruled out the possibility of contact dermatitis from the medication. The fact that the patient had developed a rash from a related drug (ampicillin) in the past further supports the diagnosis of a drug eruption in the present case.

Case 2 relates to a dramatic, rapid onset response TEN, confirmed by microscopic examination. Since TEN is almost always a drug reaction (13), and in view of the patient's history and the course of the current illness, one can assume that the rash was a reaction to amoxycillin.

It must be noted that the above cases are not the only cases of intertrigo-like drug reactions we have come across. We have, in fact, seen other similar cases in the past, but these two are the first well documented cases we have dealt with. We believe that this is by no means a rare phenomenon, and that many such cases have been overlooked and/or misdiagnosed.

The differential diagnosis of intertrigo includes many skin diseases such as seborrheic dermatitis, intertriginous psoriasis, erythrasma, contact dermatitis, fungal and bacterial infections and others. Drug reaction has never been mentioned in the differential diagnosis of intertrigo. It is true that drug reactions can imitate many types of skin conditions, but the picture is usually one of a widespread rash. That would explain why when faced with a localized rash, as in our case, the clinician is unlikely to think of a drug reaction – hence the importance of this report.

We suggest that drug reactions should be considered in the differential diagnosis of intertrigo, in particular atypical and therapy-resistant cases of intertrigo. We believe that the presentation of the cases will lead to the diagnosis of many more such cases that would otherwise have been overlooked and/or misdiagnosed. Apart from the theoretical considerations, the question of the localization of, and immunologic mechanisms involved in the development of drug reactions, detection of

these cases also has practical importance, since the elimination of the causative drug is essential for therapy success. Case 2 showed a response of the TEN type, which could have been very severe and dangerous had the lesions spread widely. The early diagnosis and appropriate treatment (with drawal of the offending drug) before the lesions spread may, therefore, be critical.

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