Drug-induced Blaschkitis

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Sir,

Inflammatory eruptions along the Blaschko lines of the integument are rare. We present here a woman with a widespread drug-induced blaschkitis. Oral rechallenge testing revealed metronidazole as a trigger for this particular unilateral exanthema. Nicotine was a possible cofactor. This is the second case of an inflammatory acquired blaschkolinear eruption triggered by an antibiotic.

CASE REPORT

A 41-year-old Caucasian woman presented with a 10-week history of periumbilical scaly red papules that started 2 days after using nicotine resin gum (Nicorette® 4 mg mint). These localized skin lesions evolved into a widespread pruritic papulovesicular exanthema 2 days after taking metronidazole (2×400 mg/day) for a bacterial vaginosis. The papules were strictly confined to the right side of her body and most prominent on the chest and abdomen (Fig. 1). Limb involvement occurred along the lines of Blaschko but was less obvious. After cessation of the oral antibiotic, topical treatment with corticosteroids (betamethasone valerate 0.1% cream) for 10 days resulted in complete resolution. Pruritus was controlled by cetirizine 2×10 mg/day. Family history was non-contributory. The patient was otherwise healthy; her regular medication included levothyroxine 100 μg/day and potassium iodide 130.8 μg/day.

Routine laboratory investigations (haematology, serum chemistry, urinalysis, stool cultures) and serum immunoelectrophoresis were within the normal limits. Thyroid function was normal but serology revealed raised thyroid peroxidase antibodies (269 U/ml). Further autoantibodies (ANA, ENA) and infection markers (TPHA, hepatitis screen) were negative. A control vaginal swab and gynaecological examination were unsuspicious. X-ray photographs of the chest, paranasal sinus and teeth as well as abdominal and thyroid ultrasonography were normal. Histology revealed a lichenoid dermatitis with a blurred dermo-epidermal junction, diffuse spongiosis, liquefaction of the basal cell layer and pigment incontinence (Fig. 2). Skin testing (prick, patch, intradermal) was performed with metronidazole and quinoline yellow (food colour E104 in Nicorette® 4 mg mint) on unaffected and previously affected skin according to published guidelines (1) and yielded negative results. Oral rechallenge with metronidazole (2×400 mg for 1 day) caused a significant relapse after 3 days (Fig. 3) which was rapidly controlled with local corticosteroids and oral antihistamines as previously. She continues with Nicorette® and shows no further recurrence to date.

Dedicated to Professor Fereydoun Vakilzadeh – devoted clinician, keen observer, valued friend.

DISCUSSION

Inflammatory acquired blaschkolinear dermatoses (2) include lichen striatus, adult blaschkitis, unilateral lichen planus, linear lichen sclerosus and several other

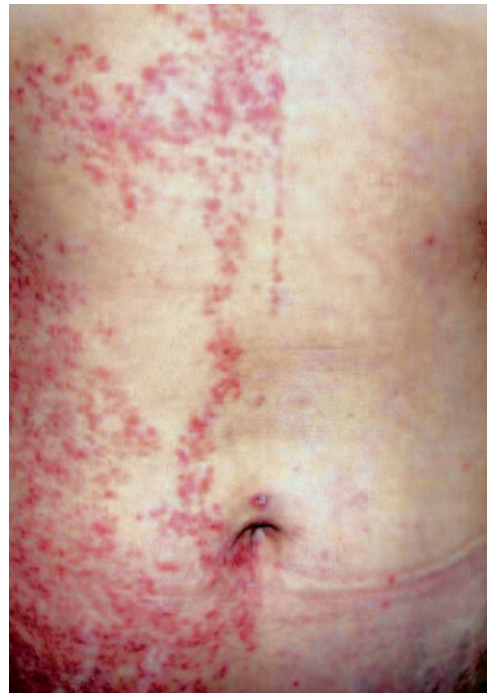

Fig. 1. Unilateral exanthema with high density of uniform, inflamed, fine-scaled papulovesicles on the trunk.

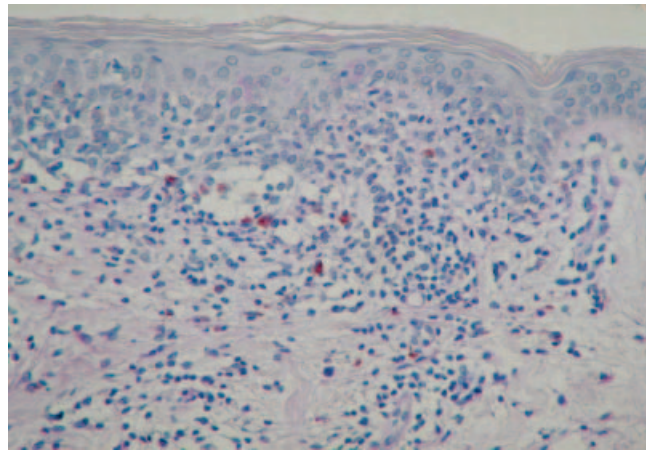

Fig. 2. Interface dermatitis with a moderately dense, band-like and perivascular lymphohistiocytic infiltrate, diffuse spongiosis with exocytosis, Max-Joseph spaces and melanophages (periodic acid-Schiff stain × 200).

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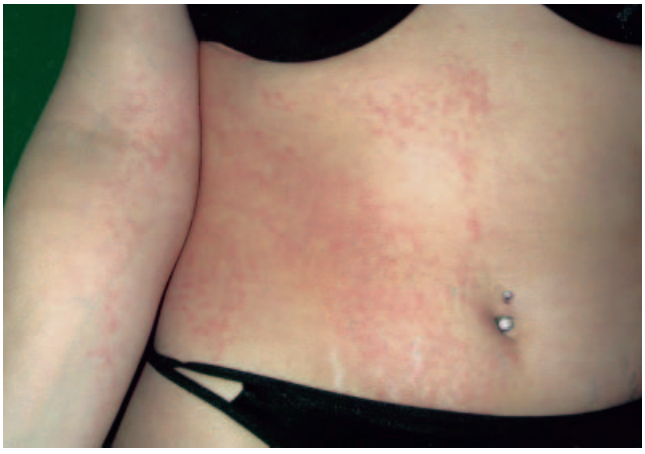

Fig. 3. Relapse of the rash after rechallenge with metronidazole. Note the blaschkolinear aspect of the skin lesions on the volar side of the upper extremities.

conditions (3). Blaschko lines are independent of nerval innervation, lymphatic flow and blood flow; they are supposed to mirror the migration of clones of cutaneous cells during embryogenesis (4). Lichen striatus has rarely been published in adults (5). Blaschkitis was proposed as a different entity to lichen striatus by Grosshans & Marot in 1990 (6). Most features of this case were consistent with adult blaschkitis according to Grosshans' criteria (2), i.e. papulovesicular pruritic skin lesions, adult onset (mean age 40 years), predominant involvement of the trunk with multiple lines, rapid resolution, no sequelae (transient pigment variation) and spongiotic histological changes. Corresponding to the more vesicular clinical aspect of the skin lesions, histology in blaschkitis shows spongiosis rather than lichenoid dermatitis. However, the microscopic changes in our patient exhibited some overlap.

The clinical picture would also be compatible with unilateral lichen planus but histology did not reveal typical acanthosis or hypergranulosis. Accordingly, we agree with previous reports, which speculate that there is a wide variety of blaschkolinear inflammatory skin diseases without clear-cut diagnostic margins (7, 8). Acknowledging this concept, the exact position of drug-induced blaschkitis within the spectrum of inflammatory acquired blaschkolinear dermatoses is ill-defined. This is the first case of adult blaschkitis triggered by metronidazole. We rechallenged with metronidazole after several weeks and provoked an acute re-inflammation of the characteristic skin lesions. A literature search revealed only one report of a linear fixed drug eruption on the left lower limb after intramuscular injection of cefazoline (9) and a case of lichen striatus associated with interferon-α and cytarabine in a patient with chronic myeloid leukaemia (10).

Adverse effects of metronidazole include chromosomal aberration (11) and immunomodulating activity (12). Several studies demonstrated that this imidazole antibiotic and its hydroxy metabolite increase the mitogenic response to phytohaemagglutinin. Based on metabolic differences, an individual susceptibility to metronidazole immunostimulation has been observed (12). Metronidazole may have induced changes in blaschkolinear distributed aberrant keratinocytes that caused them to become apoptotic. This could have happened either by direct toxicity of the drug itself (e.g. via p53 (13)) or by a T-cell-mediated immune response. In the latter case antigenic domains on the keratinocytes could have been unmasked or expressed *de novo* by metronidazole. Alternatively, metronidazole may have modified antigen-presenting cells or regulatory T cells so that pre-existing immunotolerance against those aberrant keratinocytes was temporarily broken with subsequent lymphocyte homing to the skin. Smoking cessation in our patient is interpreted as coincidental. However, nicotine is an important immunomodulator at the level of immune cell apoptosis (14) and changes of nicotine plasma levels could have influenced the manifestation or course of the skin disease.

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