

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) induced by mefenamic acid



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Key words: adverse drug reaction; drug provocation test; mefenamic acid; nonsteroidal anti-inflammatory drug; symmetrical drug-related and flexural exanthema.

INTRODUCTION

Mefenamic acid is a widely used nonsteroidal anti-inflammatory drug (NSAID) that inhibits prostaglandin synthetase by binding both isoforms of cyclooxygenase (COX). It is well known to cause urticaria, fixed drug eruptions, and maculopapular rashes as drug hypersensitivity reactions.¹⁻³ We report a case of symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) induced by mefenamic acid.

CASE REPORT

A 37-year-old woman presented to our allergy outpatient clinic with a history of a pruritic erythematous rash and localized swelling on the buttocks and the inguinal region bilaterally. The patient's medical history was significant for a dental extraction and the consecutive intake of a single dose of 500 mg mefenamic acid 2 days prior. She had already been prescribed oral methylprednisolone and nonsedating antihistamines by the referring dermatologist; thus, her symptoms had already subsided by the time of presentation. Importantly, there was no systemic involvement, and apart from the cutaneous manifestations, the patient was in a good state of health without further concomitant medication use.

After an interval of 6 weeks, skin prick, intradermal, and epicutaneous patch tests with mefenamic acid and alternative NSAIDs (ie, acetylsalicylic acid, paracetamol, diclofenac, lornoxicam) were performed according to current guidelines.^{4,5} Total serum IgE was within the normal range, and all

Abbreviations used:

COX:	cyclooxygenase
NSAID:	nonsteroidal anti-inflammatory drug
SDRIFE:	symmetrical drug-related intertriginous and flexural exanthema

drug-related skin tests yielded negative results after 20 minutes, 24 hours, and 48 hours, respectively. Subsequently, an oral drug provocation test was performed in a day clinical setting with paracetamol as an alternative compound and the potential elicitor mefenamic acid.⁶ Paracetamol was well tolerated by the patient; thus, in the following week, mefenamic acid was administered in incremental doses (125 mg, 250 mg, and 250 mg, respectively). Roughly 4 hours after the ingestion of the last tablet, the patient had similar symptoms as those previously reported: well-defined erythematous patches in the inguinal region and the gluteal area (Fig 1). The patient received a single dose of oral methylprednisolone, 60 mg, for the treatment of SDRIFE and levocetirizine for relief of the itch and was given a corresponding allergy pass.

DISCUSSION

This type of drug reaction was originally described in 1984 as *Baboon syndrome*, according to the clinical resemblance to the red buttocks of baboons, after systemic exposure to type IV allergens such as mercury and nickel, but also ampicillin.⁷ However, as the term *Baboon syndrome* is

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Fig 1. Erythema and localized swelling on the gluteal region.

considered somewhat ethically and culturally problematic, the acronym SDRIFE (symmetrical drug-related intertriginous and flexural exanthema) was introduced in 2004.⁸

The diagnostic criteria of this systemic contact dermatitis include: a) history of recent drug intake, b) sharply demarcated erythema of the gluteal/perianal region or V-shaped erythema of the inner thighs, c) involvement of at least one great flexure, d) symmetry and e) absence of systemic organ involvement. Histopathological examination is non-specific and shows a superficial perivascular mononuclear cell infiltrate with some neutrophils and eosinophils.⁸

Clinical differential diagnosis includes (multifocal) fixed drug eruption, which characteristically presents as asymmetrical round/oval patches of the skin and mucous membranes with residual hyperpigmentation and toxic erythema of chemotherapy, another intertriginous drug eruption specifically induced by chemotherapy. The skin lesions in SDRIFE resolve gradually after the withdrawal of the offending drug. Systemic/topical steroids are often prescribed to speed up the healing process, and antihistamines may be given for symptomatic management of the itch.

From our own experience, we know that SDRIFE may progress to a generalized maculopapular rash if the intake of the eliciting drug is not stopped, contrary to fixed drug eruptions, which present as localized and well-demarcated lesions. SDRIFE is most commonly associated with aminopenicillins, iodinated contrast media, heparin, allopurinol, and

terbinafine but has not yet been reported for mefenamic acid.^{8,9} Mefenamic acid, an anthranilic acid derivative, is an NSAID with worldwide availability used for various acute and chronic ailments. The mechanism of action of mefenamic acid and other related compounds (flufenamic acid, tolfe-namic acid, and meclofenamic acid) is caused by the inhibition of both COX-1 and COX-2 and consequently the prevention of prostaglandin formation.¹⁰ Previous reports show that SDRIFE can also be elicited by re-exposure to cross-reactive drugs,¹¹ which in our case was considered to be irrelevant, as mefenamic acid is the only member of its class to be commonly available in Austria.

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