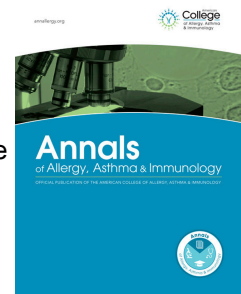


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Drug Hypersensitivity testing: Baboon Syndrome precipitated by amoxicillin challenge

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Although beta-lactam 'allergy' may be self-reported in up to 10% of individuals, only a minority of these individuals (3-5 %) will have genuine type 1 IgE-mediated hypersensitivity.¹

As there is an increasing trend amongst healthcare professionals for penicillin delabelling, potential sequelae of this approach should be considered. We report the first case of symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) following oral amoxicillin challenge.

A 19-year-old female was referred for investigation of possible penicillin allergy, based on a childhood history of rash developing after amoxicillin treatment. Details of the rash onset, distribution and resolution were not available. There were no systemic symptoms suggestive of type 1 IgE-mediated hypersensitivity. Past medical history included hypothyroidism and aplastic anaemia, for which she underwent matched unrelated donor bone marrow transplant (aged 3). Drug history comprised thyroxine and erythromycin as antibiotic prophylaxis post-transplant. Skin prick testing and blood measurement for specific IgE to the major determinants of penicillin (penicilloyl G, penicilloyl V, ampicilloyl, amoxicilloyl) and cefaclor was negative (Phadia 2500, Thermo Fisher Scientific United Kingdom). In order to exclude penicillin allergy, a low risk challenge to amoxicillin syrup was undertaken, with a final dose of 786mg tolerated with no evidence of type 1 IgE-mediated hypersensitivity. Four hours later, she developed a marked burning sensation over her back and buttocks. Examination revealed a maculopapular rash over her lower back and buttocks. Blood tests confirmed normal CRP. Seven days after the initial challenge, the rash remained persistent over the buttocks, but also

now involved the décolleté area and flexural regions over the arms (Figure). A diagnosis was made of SDRIFE, formerly known as Baboon syndrome.²

To our knowledge, this is the first case of SDRIFE to be described following amoxicillin challenge, performed to exclude immediate hypersensitivity to amoxicillin. SDRIFE is a rare dermatological disorder due to delayed type IV T cell-mediated hypersensitivity, manifesting as maculopapular rash in distinct skin areas, characteristically the buttocks. First described in 1984 by Andersen et al, Baboon syndrome was described as a well-demarcated rash over the buttocks and/or upper thighs occurring after drug administration (first three described cases after exposure to topical ampicillin, nickel, and mercury).²

In our case, SDRIFE was diagnosed based on the typical presentation after re-exposure to amoxicillin of abrupt onset symmetrical sharply demarcated rash, which involved at least one great flexure. Hausermann et al proposed criteria to diagnose SDRIFE which included exposure to systemic drug at first or repeated dose (contact allergens excluded), erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perianal area, involvement of at least one other intertriginous/flexural localization, symmetry of affected areas, and absence of systemic symptoms and signs. Small papules, pustules, abrupt vesicles, and rarely bullae may also be present in the flexural regions.^{3 4}

The mechanism underlying the propensity of SDRIFE to affect specific skin locations is unknown, but potential reasons include recall response from previous unrelated dermatitis or drug metabolites excreted from glands found within the flexural regions.^{5,6}

In 2004, Hausermann et al reviewed several cases of SDRIFE and noted half of the cases described were drug-induced and that there were two types of reaction: (1) induced by former cutaneous sensitization and (2) occurring as drug-related SDRIFE without known previous cutaneous sensitization.³ Our case is likely to represent the latter; as she had undergone a matched unrelated bone marrow transplant from a male, it is possible that the donor memory T cells may have been responsible for the rash. Transfer of donor-specific allergy to transplant recipient is rare but has been described (more commonly in solid organ transplant than bone marrow). Transfer of allergen-specific memory B (with subsequent allergen specific IgE) and allergen specific T-cells may result in immediate type hypersensitivity and delayed type hypersensitivity respectively.^{7,8}

The onset of the rash in relation to drug exposure may be from hours to 2 days.⁴ There are no specific tests to diagnose SDRIFE, so a clinical diagnosis is made following exclusion of other causes. Diagnosis may be confirmed by controlled drug provocation testing.⁴ However, our case highlights that SDRIFE may also be precipitated by routine low-risk drug provocation, performed to exclude type 1 IgE mediated hypersensitivity. Patch tests initially were described as positive in up to 50% of patients with SDRIFE but have subsequently been found to be negative in more recent reports of SDRIFE.^{3,9} Oral provocation testing is positive in almost all SDRIFE cases and is the most reliable way to confirm the diagnosis. Prick testing and lymphocyte stimulation testing are negative in the majority of cases.⁹ Histology typically demonstrates an infiltrate of CD3 T cells (mainly CD4) superficially in a perivascular distribution.^{3,4} Histological findings are non-specific and cannot be used alone to confirm diagnosis.⁹

SDRIFE has most commonly been described with penicillins used for treatment of infection but ours is the first case to develop following amoxicillin drug challenge performed to exclude immediate hypersensitivity to penicillins. The differential diagnosis of SDRIFE includes contact dermatitis due to topical treatments, irritant contact dermatitis and acute generalised exanthematous pustulosis.⁹ Systemic symptoms do not usually accompany SDRIFE. Other important differential diagnoses, especially in children, include infections such as bacterial intertrigo due to Group A beta-hemolytic *Streptococci* or *Staphylococcus aureus*, and the early stages of staphylococcal scalded skin syndrome. Fungal infection such as candidiasis may involve the major body folds with erythematous papules. Investigations which aid diagnosis include bacterial culture and fungal scrapings.⁹ In a patient with fever, necrotising fasciitis is an important differential diagnosis not to be overlooked, as this is an emergency requiring urgent debridement.¹⁰

Management of SDRIFE is primarily supportive. The rash is usually self-limiting and prognosis is good. Treatment with parenteral steroids can shorten the duration of rash, though recovery may take up to 3 weeks.¹⁰ Our patient was treated successfully with a long-acting non-sedating antihistamine and a short course of prednisolone, with her rash resolving after 10-14 days.

Given the increasing number of low-risk oral amoxicillin challenges being performed, it is important for clinicians to be aware of SDRIFE as a potential dermatological complication of drug provocation.

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- 1 **Photo 1. Well-demarcated maculo-papular rash over the buttocks, occurred after**
- 2 **amoxicillin oral challenge**

