

CORRESPONDENCE

An unusual case of non-pigmenting fixed drug eruptions in a child

DOI:10.1111/pai.12116

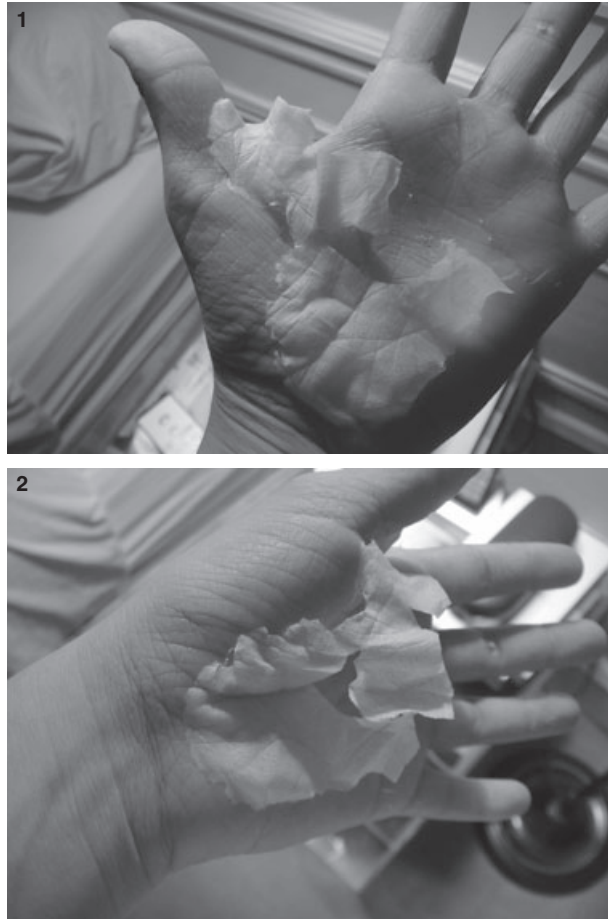
To the Editor,

Although they are probably under-recognized/underdiagnosed, fixed drug eruptions (FDE) are rare in children (1–3). Non-pigmenting FDE (NPFDE) resemble to pigmenting FDE, but leave no residual pigmentation. A few cases of NPFDE have been reported to pseudoephedrine-containing drugs, diflunisal, and furazolidone, especially in adult patients (4–7).

A 12-year-old well-being girl reported two episodes of burning bullous desquamative eruptions of the palms and soles (Figs 1–3) 24 h after the start of treatments with rifamycin (2009) and amoxicillin prescribed for the prophylaxis of Lyme's disease after a tick bite (2012). The lesions were treated with local antiseptics and oral antihistamines, and resolved within 10–12 days, without residual pigmentation. She also reported a mild unidentified eruption 48 h after the start of a first treatment with cefpodoxime (2004), resolving spontaneously within 2–3 days of the stop of the treatment. From birthdate to 2004, the child had tolerated treatments with amoxicillin alone or associated with clavulanic acid and, probably, with topical rifamycin-/rifampicin-containing eye and/or ear drops.

Allergological work-up was performed 8 months after the reaction to amoxicillin. As previously reported (8), pricks, intradermal (ID), and patch tests (on the back) were performed with the soluble forms of the suspected (or very similar) betalactams and other betalactams from the same class and other classes (penicillin G, amoxicillin, cefazoline, cefotaxime, and ceftriaxone), diluted with 0.9% sterile NaCl. The concentrations used were 250–25 000 IU/ml for penicillin G and 0.25–25 mg/ml for the other betalactams for pricks and ID tests, and 250 000 IU/ml for penicillin G and 250 mg/ml for the other betalactams for patch tests. Responses in skin tests with betalactams were negative at 15–20 min (immediate, pricks, and ID), 6–8 h (semi-late, ID), 2–3 days (late, ID, and patch tests), and 6–7 days (hyper-late, ID, and patch tests), according to EAACI/ENDA guidelines (9).

Challenge tests were performed orally with amoxicillin (2 days in the hospital) and rifamycin (2 days at home), as previously reported (8). The first day in the hospital, the child received a first dose of 10 mg of the drug, and the dose was gradually increased until the appropriate cumulative dose for age and weight was reached. At home, half the therapeutic dose was administered at 9 am and 8 pm. The second day, the child should be administered one half of the therapeutic dose at 9 am and at 12 h (in the hospital) or 8 pm (at home). However, challenge tests with the two drugs induced relapses of palm and sole burning eruptions during the night of the first day and were stopped. The lesions were treated with oral antihistamines and corticosteroids, and resolved within 7–8 days. In contrast,



Figures 1–2 Bullous desquamating lesions of the palm during treatment with amoxicillin.

challenge tests performed at home (4 consecutive days) with penicillin V and cefpodoxime were tolerated.

Thus, we diagnosed NPFDE to amoxicillin and rifamycin, with contraindication of aminopenicillins, and aminocephalosporins as a precaution, and rifamycin/rifampicin. All other betalactams and families of anti-infectious drugs were authorized.

FDE are rare in children (1–3). NPFDE have never been reported in children (4–7), and, to our knowledge, we report the first pediatric case of NPFDE due to two drugs from distinct chemical families.

Although the infectious agents (viruses, bacteria) responsible for the infections leading to treatments with rifamycin and



Figure 3 Bullous desquamating lesions of the sole during treatment with amoxicillin.

amoxicillin were unknown, the dermatologists suggested that the eruptions resulted from infectious diseases (*Streptococcus* especially). The hypothesis that the lesions resulted from primary or secondary erythromelalgia/erythralgia was highly unlikely (large size of the bullae, reactions occurring

exclusively during infectious diseases treated with antibiotics, no underlying chronic disease, and no familial history) (10).

Although skin tests gave negative responses, challenge tests with amoxicillin and rifamycin induced relapses of the initial reactions, leading to the diagnosis of NPFDE due to non-immediate hypersensitivity to two drugs from two different families. Although patch tests should have been performed on the site of lesions to diagnose FDE (11), patch tests could not be applied on palms and soles for comfort of the girl. Thus, patch tests performed on the back of the child may have led to false-negative responses.

The case of this young girl is probably exceedingly rare because of the following: (i) the reactions highly suggest an unusual type of FDE, without residual pigmentation (NPFDE), which is very rare and has not been reported with amoxicillin and rifamycin/rifampicin (4–7); (ii) FDE, NPFDE especially, are rare in children, although they are probably under-recognized/underdiagnosed (1–3); and (iii) finally, hypersensitivity to multiple drugs from several drug families is exceedingly rare, especially when sensitizations to these drugs belong to the same immunologic type and lead to similar clinical reactions (12).

C. Ponvert; P. Rufin & J. de Blic

*Department Paediatrics, Pulmonology and Allergy Service,
Necker-Enfants Malades Hospital, Paris, France.*

E-mail: claudie.ponvert@nck.aphp.fr

References

- Shin HT, Chang MW. Drug eruptions in children. *Curr Probl Pediatr* 2001; **31**: 207–34.
- Carder KR. Hypersensitivity reactions in neonates and children. *Dermatol Ther* 2005; **18**: 160–75.
- Morelli JG, Tay YK, Rogers M, Halbert A, Krafchik B, Weston WL. Fixed drug eruptions in children. *J Pediatr* 1999; **134**: 365–7.
- Tan C, Zhu WY. Furazolidone-induced nonpigmenting fixed drug eruptions affecting the palms and soles. *Allergy* 2005; **60**: 972–4.
- Shelley WB, Shelley ED. Nonpigmenting fixed drug eruption as a distinctive reaction pattern: examples caused by sensitivity to pseudoephedrine hydrochloride and tetrahydrozoline. *J Am Acad Dermatol* 1987; **17**: 403–7.
- Matsumoto K, Mikoshiba H, Saida T. Nonpigmenting solitary fixed drug eruption caused by a Chinese traditional herb medicine, ma huang (*Ephedra* *Hebra*), mainly containing pseudoephedrine and ephedrine. *J Am Acad Dermatol* 2003; **48**: 628–30.
- Roetzheim P, Herold AH, Van Durma DJ. Nonpigmenting drug eruption caused by diflunisal. *J Am Acad Dermatol* 1991; **24**: 1021–2.
- Ponvert C, Perrin Y, Le Bourgeois M, Karila C, Delacourt C, Scheinmann P, et al. Allergy to betalactams in 1865 children: results of a 20-year study based on skin and challenge tests, and clinical history. *Pediatr Allergy Immunol* 2011; **22**: 411–8.
- Brockow K, Romano A, Blanca M, Ring J, Pichler W, Demoly P. General considerations for skin test procedures in the diagnosis of drug hypersensitivity. *Allergy* 2002; **57**: 45–51.
- Heidrich H. Functional vascular diseases: Raynaud's syndrome, acrocyanosis and erythromelalgia. *Vasa* 2010; **39**: 33–41.
- Barbaud A, Gonçalo M, Bruynzeel D, Bircher A. Guidelines for performing skin tests with drugs in the investigation of cutaneous adverse reactions. *Contact Derm* 2001; **45**: 321–8.
- Studer M, Waton J, Bursztejn AC, Aimone-Gastin I, Schmutz JL, Barbaud A. Does hypersensitivity to multiple drugs really exist? *Ann Dermatol Venereol* 2012; **139**: 375–80.