

CONTACT POINT

Flare-up of previously negative patch test and intradermal test with amoxicillin after oral provocation

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KEYWORDS: amoxicillin, case report, cutaneous adverse drug reactions, delayed hypersensitivity, flare-up, intradermal test, patch test

Flare-up reactivity was first described in 1981 in patients with nickel contact eczema as a reactivation of former contact allergy and/or patch test reaction sites because of systemic metal exposure.¹ This phenomenon has been rarely reported for drugs,^{2–6} either as reactivation of formerly positive intradermal test sites^{2,3} or as activation of formerly negative patch test sites⁴ and intradermal test sites.^{5,6} Drug flare-up can follow both a patch test³ and a provocation test.^{2,4–6} We report a case of flare-up of initially negative patch test and intradermal test sites after oral provocation testing with amoxicillin.

CASE REPORT

A 46-year-old non-atopic woman was referred because of a maculopapular eruption following administration of amoxicillin for acute pharyngitis 20 years earlier. We performed skin tests with amoxicillin (Table 1). Patch tests were occluded for 2 days by the use of Haye's

Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy). Immediate and delayed readings of skin tests, according to ICDRG criteria, showed negative results (Table 1). Six months later, graded oral provocation testing with amoxicillin on 3 consecutive days was performed (Table 1). Approximately 24 hours after the last administration (1.0 g), eczematous flare-up involving the application sites of patch tests and intradermal tests with amoxicillin appeared (Figure 1A,B), and this was followed by itchy maculopapular eruptions on the neck (Figure 1C), abdomen, face, and limbs. Laboratory results, including blood count, liver enzymes, serum creatinine and C-reactive protein, were within normal limits. The flare-up reactions and the eruption resolved without therapy within 1 week.

DISCUSSION

Flare-up reactions of previous patch test sites after systemic provocation testing are mainly described in contact allergy to nickel and gold.^{1,7,8} Only a few cases of flare-up associated with drugs have been described, in particular with β -lactams, trimethoprim-sulfamethoxazole, piroxicam, heparin, and glatiramer acetate.^{2–6} Although the exact pathogenetic mechanism is not completely understood, some T cells (CD4⁺ CCR10⁺) could remain at the site of earlier allergen contact, acting as local skin memory cells, and be triggered by later contact with an allergen by a skin test or by systemic provocation.⁹ As flare-up is classified as a delayed-type hypersensitivity reaction,⁵ we could hypothesize that the maculopapular eruption presented by our patient in the past was a typical IVb-type drug reaction.¹⁰ On the other hand, a case of reactivation of a prick test site after systemic provocation testing has been reported as flare-up-like reactivity, suggesting IgE-mediated type hypersensitivity.¹¹

TABLE 1 Results of skin tests and oral provocation test with amoxicillin

Skin tests	Concentration (%)	Results (reading time)		
Patch test (pet.)	5	Neg (D2)	Neg (D4)	Neg (D7) ^a
Prick test (aq.)	2	Neg (20 min.)	Neg (D1)	
Intradermal test (aq.)	2	Neg (20 min.)	Neg (D1) ^a	
Oral provocation test	Dose (g)	Results		
D1	0.001, 0.01	Neg		
D2	0.1	Neg		
D3	1	Positive ^b		

Abbreviations: aq., saline solution; D, day; pet., petrolatum; Neg, negative.

^a Flare-up after oral provocation test.

^b Maculopapular eruption.

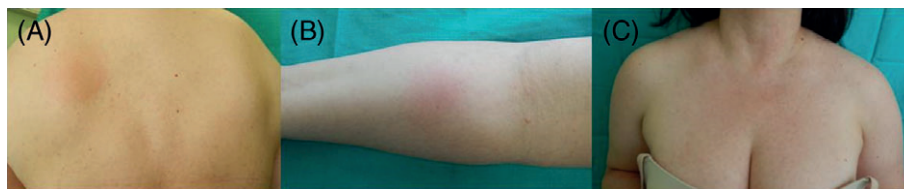


FIGURE 1 Flare-up of a previously negative patch test site (A), and an intradermal test site (B), with amoxicillin and maculopapular eruption (C), after an oral provocation test

In our patient, the negativity of the former skin tests with amoxicillin could be explained by the long interval (20 years) between the adverse drug reaction and the time of skin tests.¹² Nevertheless, the flare-up of the site of contact with amoxicillin after oral provocation testing performed 6 months later shows that patch testing apparently plays a crucial role in stimulating persisting local retention of T cells.

Conflict of interest

The authors declare no potential conflict of interests.

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REFERENCES

- Christensen OB, Lindström C, Löfberg H, Möller H. Micromorphology and specificity of orally induced flare-up reactions in nickel-sensitive patients. *Acta Derm Venereol*. 1981;61:505-510.
- Minciullo PL, Calapai G, Gangemi S. Flare up reaction during provocation test to glatiramer acetate in a patient with allergy to interferon beta1a. *Allergy Asthma Immunol Res*. 2014;6:467-469.
- Llamazares AA, Chamorro M, Robledo T, et al. Flare-up of skin tests to amoxycillin and ampicillin. *Contact Dermatitis*. 2000;42:166.
- Kardaun SH, de Waard MM, de Monchy JG. Flare-up of patch test of trimethoprim-sulfamethoxazole (co-trimoxazole) during oral desensitization. *Contact Dermatitis*. 2009;61:50-51.
- Reig Rincón de Arellano I, Villalón García AL, Cimarra Alvarez-Lovell M, Robledo Echarren T, Martínez-Cócerca MC. Flare up to betalactams. *Allergol Immunopathol*. 2005;33:282-284.
- García Robaina JC, Sánchez Machín I, Fernández-Caldas E, de la Torre Morín F. Delayed systemic reactions with flare-ups of previously negative intradermal skin tests to heparin. *Allergy*. 2003;58:685-686.
- Möller H, Ohlsson K, Linder C, Björkner B, Bruze M. The flare-up reactions after systemic provocation in contact allergy to nickel and gold. *Contact Dermatitis*. 1999;40:200-204.
- Hindsén M, Bruze M, Christensen OB. Flare-up reactions after oral challenge with nickel in relation to challenge dose and intensity and time of previous patch test reactions. *J Am Acad Dermatol*. 2001;44:616-623.
- Moed H, Boorsma DM, Tensen CP, et al. Increased CCL27-CCR10 expression in allergic contact dermatitis: implications for local skin memory. *J Pathol*. 2004;204:39-46.
- Hansel K, Bellini V, Bianchi L, Brozzi J, Stingeni L. Drug reaction with eosinophilia and systemic symptoms from ceftriaxone confirmed by positive patch test: an immunohistochemical study. *J Allergy Clin Immunol Pract*. 2017;5:808-810.
- González de Olano D, González Mancebo E, Gandolfo Cano M, Menéndez Baltanás A, Trujillo Trujillo MJ. Flare-up-like phenomenon in a skin prick test after oral challenge with ibuprofen. *J Investig Allergol Clin Immunol*. 2007;17:414-415.
- Barbaud A, Gonçalo M, Bruynzeel D, Bircher A. Guidelines for performing skin tests with drugs in the investigation of cutaneous adverse drug reactions. *Contact Dermatitis*. 2001;45:321-328.

How to cite this article: Tramontana M, Hansel K, Bianchi L, Agostinelli D, Stingeni L. Flare-up of previously negative patch test and intradermal test with amoxicillin after oral provocation. *Contact Dermatitis*. 2018;1-2. <https://doi.org/10.1111/cod.13045>