Acta Derm Venereol 2005; 85: 171–172

Taylor & Francis
Taylor & Francis Group

LETTERS TO THE EDITOR

Drug-induced Bullous Pemphigoid with Positive Patch Test and *In vitro* IgE Sensitization

Jakob E. Borch[1], Klaus E. Andersen[2], Ole Clemmensen[3] and Carsten Bindslev-Jensen[1]
[1]*Allergy Center,* [2]*Department of Dermatology, and* [3]*Department of Pathology, Odense University Hospital, Sdr Boulevard 29, DK-5000 Odense C, Denmark. E-mail: jakob.borch@allergi.sdu.dk*
Accepted August 23, 2004.

Sir,

Bullous pemphigoid (BP) is a relatively common autoimmune skin disease characterized by blister formation, eosinophilia, chronicity and a relatively old age of onset (1). Drugs, including penicillin (2), may trigger BP, but this is a far less common event than drug-induced pemphigus vulgaris (1). The literature describes no clinical or laboratory features that distinguish idiopathic and drug-induced BP; however, a detailed patient history is essential. The chronology of drug intake and development of disease, and the observation that patients with drug-induced BP are often younger than patients with idiopathic disease (3) is supportive of this diagnosis. The prognosis of drug-induced BP is good, provided that the drug is withdrawn early in the course of the disease (3).

CASE REPORT

An 80-year-old man with Parkinson's disease, with no previous atopic diseases or contact dermatitis, but with a known history of adverse cutaneous reactions to penicillin, was mistakenly treated with penicillin for an infection of a traumatic wound. Two MIU penicillin G was given in the emergency room and oral penicillin V (1 MIU) was prescribed. After the first dosage of penicillin V (phenoxymethylpenicillin, Nycomed, Denmark), taken at home, he developed a rash. His family physician stopped penicillin treatment and gave erythromycin instead. Seven days after the last penicillin administration the exanthema became bullous, and the patient was admitted. The previous reaction to penicillin was in the 1950s in Africa. No records about the incident were available, and the patient failed to recall any details.

Clinically he had an itchy generalized maculo-papular rash confluent in the loins, over the knees and forearms with scattered widespread large vesicles, small tense bullae with serous exudate and denuded areas at the trunk and extremities. A 4-mm punch biopsy from the chest showed a slightly smudged dermo-epidermal interphase with focal subepidermal blistering. A few eosinophils were scattered within the epidermis, and in the papillary dermis a mixed inflammatory infiltrate of eosinophils, lymphocytes and neutrophils was seen. Direct immunofluorescence showed linear deposits of IgG and C3 along the basement membrane zone, but no deposits of other immunoglobulins including IgE. The histopathological diagnosis was BP.

Blood analyses showed elevated CRP (54 mg/ml) and leukocytes (13.6×10^9/l). Eosinophils were increased from 0.41×10^9/l on admission to 1.07×10^9/l during hospitalization. Kidney and liver function were not affected.

Specific IgE and histamine release were measured routinely prior to investigation for penicillin allergy (Table I). Total IgE was not measured.

Three weeks later the patient was tested. Skin prick tests were performed with penicillin G, benzyl penicilloyl-polylysine and minor determinant mixture (BPO-PL & MDM, Allergopen®, Allergopharma, Reinbek, Germany), carbidopa/levodopa, hydroxyzine HCl, paracetamol and erythromycin. All tests were negative. Intradermal tests with penicillin V, BPO-PL, MDM and erythromycin were also negative. Patch tests using routine procedure with Finn chambers on Scanpore were performed with penicillin G, ampicillin trihydrate, amoxicillin trihydrate, dicloxacillin sodium salt hydrate, cefotaxime sodium salt (all at 10% petrolatum). Also, hydroxyzine HCl (1% pet.), cefuroxime (30% pet.), carbidopa/levodopa (25 mg/100 mg, 30% pet.), paracetamol (30% pet.) and erythromycin (10% pet.). The tests were read according to ICDRG guidelines and the positive results are shown in Table II. The patient did not consent to biopsy of the patch test reactions or to any further investigations.

In BP, systemic drug challenge is considered to be contraindicated except for vital indications, so no further investigations were performed.

Table I. *Specific IgE (CAP Pharmacia, Stockholm, Sweden) and basophil histamine release (HR) (RefLab, Copenhagen, Denmark) to β-lactam antibiotics*

	Specific IgE		
Drug	Concentration	IgE class	HR
Penicillin V	3.72 kU/l	3	Negative
Penicillin G	2.79 kU/l	2	Negative
Penicillin minor determinants	0.46 kU/l	1	–
Ampicillin	2.24 kU/l	2	Positive
Amoxicillin	<0.35 kU/l	0	Positive
Dicloxacillin	–	–	Negative
Cefuroxime	<0.35 kU/l	0	Positive
Cefotaxime	<0.35 kU/l	0	Negative

 ISSN 0001-5555
DOI: 10.1080/00015550410024391

Table II. *Positive patch test with penicillins read on two occasions*

Drug	Day 4	Day 7
Penicillin G	++	+
Ampicillin	+	+?
Amoxicillin	+?	+?
Dicloxacillin	+	+

The eruption healed after withdrawal of penicillin and treatment with topical steroids. There has been no recurrence of the disease during a follow-up of 8 months.

DISCUSSION

We present a case of drug-induced BP with positive patch tests, specific IgE and basophil histamine release to penicillins.

BP is an immunological disease with antibodies to components of the basement membrane (1). The fact that the BP lesions in this patient healed rapidly after withdrawal of penicillin and have not recurred suggests that the disease was drug-induced. Bullous contact allergy resembling BP clinically and microscopically has been described, but is not associated with positive immunofluorescence (4).

Nothing in the known pathogenesis of BP indicates a role for IgE or basophils, so a coincidental IgE sensitization is the most likely explanation, although no clinical symptoms of an IgE-mediated reaction occurred.

Many drugs capable of eliciting BP have sulphur in the molecule and thiol formation is suspected to be involved in the pathogenesis (5). Many non-thiols contain sulphur atoms too, and some can form active thiol groups by metabolism ('masked thiols') (6).

Pemphigus can be elicited by drugs and thiols in particular. The thiol penicillamine is often the culprit drug, but the non-thiol penicillin is also frequently the cause of drug-induced pemphigus. This is explained by the fact that penicillin derivatives can transform to penicillamine during breakdown (7). This mechanism could apply for drug-induced BP as well.

REFERENCES

1. Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC. Dermatology, 2nd edn. Berlin: Springer Verlag, 2001.
2. Alcalay J, David M, Ingber A, Hazaz B, Sandbank M. Bullous pemphigoid mimicking bullous erythema multiforme: an untoward side effect of penicillins. J Am Acad Dermatol 1988; 18: 345–349.
3. Porter SR, Scully C. Adverse drug reactions in the mouth. Clin Dermatol 2000; 18: 525–532.
4. Goh CL, Ng SK. Bullous contact allergy from cinnamon. Derm Beruf Umwelt 1988; 36: 186–187.
5. Breathnach SM, Hinter H. Adverse drug reactions and the skin, 1st edn. Oxford: Blackwell Scientific Publications, 1992.
6. Brenner S, Bialy-Golan A, Ruocco V. Drug-induced pemphigus. Clin Dermatol 1998; 16: 393–397.
7. Brenner S, Livni E. Pemphigus vulgaris probably induced by penicillin. J Am Acad Dermatol 1987; 17: 514–515.

 DOI: 10.1080/00015550410024157