

from lupine IEF and SDS-PAGE separations (7).

IgE-binding proteins migrated to a pH ranging from 5 to 7. Those ones not inhibited by peanut extract migrated to pH 5 and to pH 6.05–6.3. Sera IgE from both patients recognized proteins of approximately 34 kDa and in the 40–65 kDa range. Patient 2 serum also recognized 7–15, 38, 77, 162 and 195 kDa proteins. Inhibition with lupine extract was complete for both sera. Serum preincubation with peanut extract did not inhibit patient 1 bands. On the other hand, it completely inhibited the 7–15 and 77 kDa bands and partially the 38, 40–65, 162 and 195 kDa components recognized by patient 2. Band of 34 kDa was never inhibited.

In this study, the clinical picture, skin prick tests and serum IgE to lupine and to peanut were suggestive of a sensitization to lupine not related to peanut allergy. The complete inhibition of lupine-specific IgE by lupine extract (90%) vs the only partial inhibition by peanut extract (65% and 75%) strongly supports this hypothesis. Immunoblotting studies performed by IEF as well as SDS-PAGE showed that some lupine IgE-binding proteins were inhibited by peanut extract, but they also evidenced bands only partially inhibited and others that suffered no inhibition at all, namely the 34 kDa protein and some of the proteins in the range of 40–65 kDa. These results clearly support that lupine is capable of inducing allergic sensitization out of the context of cross-reactivity with peanut. Taking them into account, we reinforce the need of including the lupine content in mandatory food labeling.

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References

1. Moneret-Vautrin DA, Guerin L, Kanny G, Flabbee J, Fremont S, Morisset M. Cross-allergenicity of peanut and lupine: risk of lupine allergy in patients allergic to peanuts. *J Allergy Clin Immunol* 1999;**104**:883–888.
2. Kanny G, Guerin L, Moneret-Vautrin DA. Risk of serious acute asthma due to lupine flour associated with peanut allergy. *Rev Med Interne* 2000;**21**:191–194.
3. Matheu V, de Barrio M, Sierra Z, Gracia-Bara MT, Tornero P, Baeza ML. Lupine-induced anaphylaxis. *Ann Allergy Asthma Immunol* 1999;**83**:406–408.
4. Hefle SL, Lemanske RF, Bush RK. Adverse reaction to lupine-fortified pasta. *J Allergy Clin Immunol* 1994;**94**:167–172.
5. Leduc V, Moneret-Vautrin DA, Guerin L. Allergenicity of lupin flour. *Allerg Immunol* 2002;**34**:213–217.
6. Tomaz E, Viseu R, Martins L, Reis R, Lourenço M, Inácio F. Allergic sensitization to lupin seed. XXIII EAACI Congress, 2004, Poster 1022.
7. Martins LM, Peltre G, Faro C, Pires E, Inácio F. The *Helix aspersa* (brown garden snail) allergen repertoire. *Int Arch Allergy Immunol* 2005;**136**:7–15.
8. Westermeier R. Method 6: agarose IEF. In: *Electrophoresis in practice – a guide to theory and practice*. Weinheim: VCH, Verlagsgesellschaft GmbH, B-6940, 1993:145–151.
9. Westermeier R. Method 9: semi-dry blotting of proteins. In: *Electrophoresis in practice – a guide to theory and practice*. Weinheim: VCH, Verlagsgesellschaft GmbH, B-6940, 1993:189–196.

Amoxicillin-induced exanthema in patients with infectious mononucleosis: allergy or transient immunostimulation?

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Key words: amoxicillin allergy; drug allergy; Epstein–Barr Virus infection; infectious mononucleosis; patch test.

Amino-penicillins are a major cause of delayed type reactions to penicillins. Furthermore, 70–100% of patients

receiving amino-penicillins during a florid Epstein–Barr virus (EBV)-infection develop a maculopapular rash

Delayed-type allergic reaction to amoxicillin triggered by EBV-infection can persist.

(1), the percentage being 14% for penicillin G, cloxacillin or tetracycline (2). This phenomenon may also occur with herpes simplex-, cytomegaly-, HI-virus- and, probably, many other viral infections. Hypotheses concerning the patho-mechanism are (i) that the immune system of patients with infectious mononucleosis has decreased tolerance and/or (ii) enhancement of immune reaction to certain drugs or its metabolites (3). The general opinion documented even in high ranked review articles on drug eruptions (4) as well as allergy text books is that in most cases an EBV-associated amoxicillin rash is reversible and, as a consequence, a differentiated allergy diagnostic test is not considered or recommended (4).

To test the hypothesis that some EBV-infected patients in contrast might develop a 'true' allergic drug reaction to amino-penicillins, 41 Dermatology out-patients presenting with drug eruptions following the intake of amino-penicillins were consecutively investigated for additional acute infectious mononucleosis (fever, tonsillopharyngitis, lymphadenopathy). In case of suspicion, anti-EBV-IgM and -IgG antibodies were investigated. After complete resolution but not earlier than 3 months after the diagnosis of acute EBV-infection had first been confirmed, allergy diagnostic tests consisting of IgE-detection against amoxicillin, ampicillin, penicillin and cefaclor with CAP-FEIA (Phadia, Freiburg, Germany), skin prick tests and patch tests with amoxicillin trihydrate, cefotaxim sodium and benzyl penicillin 10 000 IE with readings after 48 and 72 h were performed. Eight out of 41 had a florid infectious mononucleosis at the time of the drug eruption, five of eight patients had positive patch tests to amoxicillin and two of five additionally to penicillin (Table 1). One patient out of five was challenged with verum and developed a rash after 48 h which resolved under systemic treatment with

Table 1. Patients with EBV-associated drug rash to amoxicillin: synopsis of the allergy diagnostic test results

Patient no.	SPT	Patch test AMX	Patch test penicillin	Patch test cefotaxim	Challenge AMX	Challenge penicillin	Challenge cephalosporin	Challenge refused
1	Negative	Positive	Negative	Negative	–	Negative	–	
2	Negative	Positive	Negative	Negative	Positive	–	Negative	
3	Negative	Positive	Positive	Negative	–	–	–	yes
4	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	–	<i>Negative</i>	
5	AMX at 48 h +	Positive	Negative	Negative	–	–	–	yes
6	Negative	Positive	Positive	Negative	–	–	–	yes
7	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	–	–	–	yes
8	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	<i>Negative</i>	–	–	

Results written in italics describe those individuals who most probably only have a transient EBV-associated drug intolerance. EBV, Epstein–Barr virus; SPT, skin prick test; AMX, amoxicillin; –, not done.

anti-histamines and topically applied glucocorticosteroids without the necessity for hospitalization. After resolution, the oral challenge test with a cephalosporin was well tolerated.

Another amoxicillin patch test positive patient tolerated the oral challenge with penicillin, thereby revealing an isolated allergy to amoxicillin. As a challenge test would involve the risk for the patients to experience the same signs and symptoms of the previous drug reaction, the decision of four out of eight patients not to perform an oral challenge test was respected. Two of three patients, who were completely negative in the allergy diagnostic tests, agreed to an oral challenge with verum and revealed tolerance to the drug. It can be hypothesized that the third patch test negative subject may also have tolerated amoxicillin challenge. These three individuals may belong to the population, which only has a transient decrease in drug tolerance during EBV infection. Two amoxicillin patch test positive patients could be examined in a follow-up visit 2.2 and 1.5 years, respectively, after the first patch testing. Those patients revealed a patch test reaction similar in strength to the preliminary test result, which is indicative for a persistent delayed-type reaction to amoxicillin.

In conclusion, this study does not only provide additional evidence that true delayed-type allergic reactions to aminopenicillins may develop during a florid viral infection, but that they may be definitely more prevalent than previously assumed and published (5, 6). Additionally, follow-up investigations on two

patients revealed the persistence of the delayed-type reactions to amoxicillin, an approach, which has to the best of our knowledge not been published before. These observations should encourage the investigation of patients with aminopenicillin-induced exanthema for both, EBV-infection and true drug allergy. Particularly young women should be recommended an oral challenge with cephalosporins and maybe penicillins because the latter are antibiotics which may be given safely during pregnancy.

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References

1. Leung AKC, Rafaat M. Eruption associated with amoxicillin in a patient with infectious mononucleosis. *Int J Dermatol* 2003;**42**:553–555.
2. Partel BM. Skin rash with infectious mononucleosis and ampicillin. *Paediatrics* 1967;**40**:910–911.
3. Partel A. Amoxicillin hypersensitivity reaction in a patient with infectious mononucleosis: a case report. *Conn Dent Stud J* 1986;**6**:12–13.

4. Gruchalla RS, Pirmohamed M. Antibiotic Allergy. *New Engl J Med* 2006;**354**:601–609.
5. Nazareth I, Mortimer P, McKendrick GD. Ampicillin sensitivity and infectious mononucleosis – temporary or permanent? *Scand J Infect Dis* 1972;**4**:229–230.
6. Renn CN, Straff W, Dorfmueller A, Al-Masoudi T, Merk HF, Sachs B. Amoxicillin-induced exanthema in young adults with infectious mononucleosis: demonstration of drug-specific lymphocyte reactivity. *Br J Dermatol* 2002;**147**:1166–1170.

Oral reactions to sublingual immunotherapy: a bioptic study

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Key words: biopsies; eosinophils; local reactions; mast cells; sublingual immunotherapy.

Sublingual immunotherapy (SLIT) is currently considered a feasible option to traditional subcutaneous immunotherapy (SCIT) for treating allergic rhinitis caused by sensitization to seasonal or perennial allergens, with a significant advantage in terms of safety (1, 2). However, local reactions to the allergen extract following

Mast cells and eosinophils are not the elicitors of local reactions to SLIT.