

Table 1. Tienam continuous IV desensitization protocol*

Tienam concentration (mg/ml)	Fluid infusion rate (ml/min)	Tienam infusion rate (mg/min)
0.0001	1.0	0.0001
0.001	0.33	0.00033
0.001	1.0	0.001
0.01	0.33	0.0033
0.01	1.0	0.01
0.1	0.33	0.033
0.1	1.0	0.10
1.0	0.33	0.33
1.0	1.0	1.0

* Tienam infusion rate was increased every 10 min when no adverse effects were noted. When adverse effects occurred, infusion rate was decreased as specified in text.

patient, its development usually relates to the vancomycin drug infusion rate, suggesting a similar mechanism for which either imipenem or cilastatin could have accounted.

Failure of the conventional β -lactam desensitization protocol prompted successful performance of continuous prolonged "desensitization" as in that employed previously for vancomycin (10). Whether a similar mechanism underlies both drug-induced adverse reactions is questionable; nevertheless, the prolonged desensitization protocol may be employed in future cases of adverse reactions to Tienam.

Key words: β -lactam; desensitization; intravenous; Tienam.

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Oral allergy syndrome from pork

G.E., a 16-year-old girl, presented at this allergy unit because of recurrent episodes of itching and angioedema of the lips and oral mucosa which appeared a few minutes after she had eaten several kinds of pork (salami, both raw and cooked ham, and bacon); the first symptoms had been noted about 2 years before, and each episode lasted up to 15 min. By contrast, the patient tolerated cooked pork (chops, sausages) well. No other kind of food elicited such symptoms, and no episode took place under different circumstances. There was a family history of allergic diseases

A typical case of OAS with IgE antibodies to a 65-kDa protein, probably albumin.

(both father and brother had pollinosis), and the patient herself had noted the onset of moderate rhinoconjunctivitis after exposure to horse dander in recent years. Moreover, she complained of gastrointestinal symptoms after the ingestion of fresh milk.

The patient underwent diagnostic SPTs with a large series of both respiratory (Allergopharma) and food (Dome Hollister-Stier) allergens. Wheals equal to or greater than 2+ (i.e., 50% of the one elicited by histamine 10 mg/ml) were considered positive (1). Anti-horse-dander IgE were detected immunochemically by Allercoat (Kallestad, Austin, TX, USA) and expressed both in Allercoat arbitrary units per milliliter (AU/ml) and in classes, 0-4. Classes equal to or greater than 2 (i.e., >0.7 AU/ml) were considered positive. In view of the reported association between pork allergy and cat dander allergy (2, 3), IgE specific for cat epithelium was also measured.

IgE specific for pork, whole milk, β -lactoglobulin, and casein were measured immunochemically by the CAP-System (Pharmacia, Uppsala, Sweden) and expressed both in kU/l and in seven classes,

0–6. Again, only classes equal to or greater than 2 (i.e., >0.7 kU/l) were considered positive.

Pork proteins were extracted at 10% w/v from raw meat, cooked meat, and both raw and cooked ham by overnight incubation with 0.15 M PBS, pH 7.2. Particulate material was removed by centrifugation at 18 000 g for 30 min; the supernatant was exhaustively dialyzed against 5 mM ammonium bicarbonate, pH 8, and lyophilized. Protein contents were determined according to Bradford (4), with BSA as standard, and proved to be 0.56, 0.25, 1.5, and 0.14 mg/ml, respectively. Electrophoresis was carried out according to Laemmli (5) with a 10–15% polyacrilamide gradient gel in a Mini-Gel SW 250 Hoefer apparatus (Prodotti Gianni, Milan, Italy). The samples (mol.-wt. markers and pork extracts) were diluted in running buffer (Tris-HCl 0.125 M, pH 6.8, 5% β -mercaptoethanol, and 2% SDS) and then boiled for 3 min before the electrophoretic run at 40 mA. The resolved protein components were stained with 0.1% Coomassie brilliant blue or, alternatively, transferred onto a nylon-cellulose membrane (Fluorotrans 0.45 μ m, Pall, Milan, Italy) by a WB2 electroblotting unit (SCIE-PLAS, Prodotti Gianni, Milan, Italy). After 2 h of incubation with the saturation buffer (Tris 20 mM, pH 7.6, NaCl 0.9% and 5% fat-free milk), the membrane was incubated with the serum diluted 1:2 in saturation buffer. Bound specific IgE antibodies were detected by peroxidase-conjugated antihuman IgE antibodies from goat (1:1000 in saturation buffer), with an ECL Western blotting kit (Amersham, Milan, Italy) as substrate.

SPTs were strongly positive (4+) for both horse dander and pork. No positivity for other respiratory or food allergens was noted. The patient's serum strongly reacted to horse dander (>17.5 AU/ml; class 4), whereas no cat reactivity was found (class 0); moreover, it showed moderate reactivity to pork (3.81 kU/l; class 3); no milk allergen was positive (all class 0). The total IgE level, measured immunoenzymatically (Kallestad), was 332 UI/ml.

On Western blot experiments (Fig. 1), the patient's serum reacted mainly to four bands (from 20 to >100 kDa) in raw pork blots. By contrast, reactivity to a single band at about 65 kDa (probably pork serum albumin) was observed in both raw and cooked ham blots, and a further band at about 37 kDa was recognized in raw ham blots. Notably, serum reactivity to cooked ham was much weaker than to raw ham. No reactivity was observed to cooked pork.

Pork allergy has rarely been reported in the medical literature (2, 3, 6), and, to our knowledge, only one case of pork-induced oral allergy syndrome (OAS) has been described (7). Our young patient had typical OAS. The clinical history suggested that heat-labile

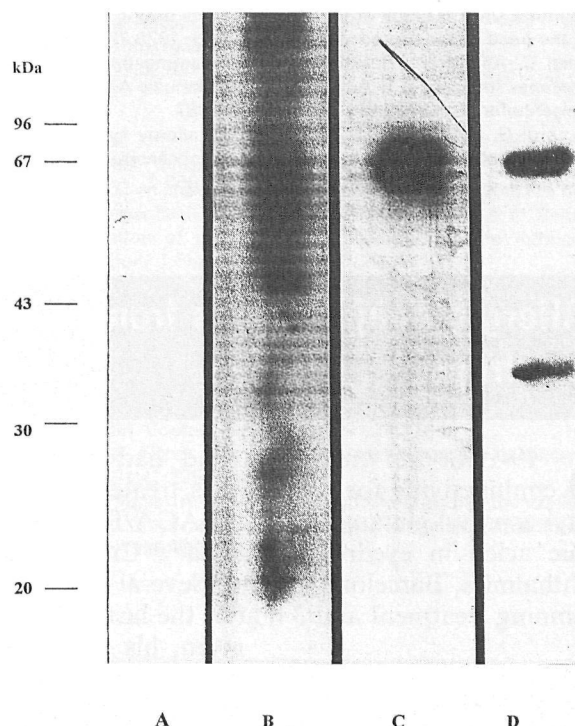


FIGURE 1.

allergen(s) were involved, and this was confirmed by Western blot analysis. Interestingly, cooked ham retained slight, but clearly detectable allergenic activity. In contrast to previous observations (2, 3), our patient never experienced systemic urticaria or angioedema; this fact might be due to the susceptibility of the causative allergen to the gastric acid environment and/or to digestive enzyme degradation.

Key words: oral allergy syndrome; pork allergy.

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Allergic conjunctivitis from eyedrops

A 19-YEAR-OLD man who had had perennial conjunctivitis for 4 years was treated with *N*-acetyl-aspartyl glutamic acid (NAAGA/DCI: spaglumic acid) in eyedrops (Naaxia[®], Ciba Vision Ophthalmics, Barcelona, Spain). Several days after beginning treatment and 3 h after the last dose was given, his symptoms worsened with ocular pruritus, hyperemia, chemosis of the conjunctiva, ocular redness, lacrimation, and eyelid edema. These symptoms subsided within a few days after withdrawal of the Naaxia

A case of allergic contact

blepharoconjunctivitis caused by spaglumic acid.

eyedrops. Other eyedrops such as Colircusi Gentadexa[®] (Cusi SA, Laboratorios, Barcelona, Spain), containing gentamicin and dexamethasone, and Oftalmowell[®] (Glaxo Wellcome, London, UK), containing polymyxin B, neomycin, and gramicidin, were well tolerated.

Three months later, patch testing was carried out with the European standard series (True Test, Pharmacia, Sweden), and the following eyedrops: nedocromil sodium (Tilavist[®], Fisons plc, Pharmaceutical Division, Loughborough, UK), Oftalmowell, Colircusi Gentadexa, and Naaxia as is. The components of Naaxia were provided by the pharmaceutical company and were similarly tested: the pharmacologic agent NAAGA 1% pet, and the preservatives benzalkonium chloride 1:1000 aq. (1) and phenylethyl alcohol as is. Patch testing and reading were carried out according to the International Contact Dermatitis Research Group recommendations. The results of the patch test are shown in Table 1. Patch testing with Naaxia was positive at 48 (+) and 96 (++) h. A similar reaction was observed to NAAGA 1% pet, but no response was observed to the excipients. Patch tests with these reagents in five control subjects yielded negative results. Skin prick tests with common

Table 1. Patch tests results

	D2	D4
European series	-	-
Eyedrops		
Oftalmowell [®]	-	-
Tilavist [®]	-	-
Colircusi Gentadexa [®]	-	-
Naaxia [®]	+	++
Naaxia components		
NAAGA 1% pet	+	++
Benzalkonium chloride 1:1000 aq.	-	-
Phenylethyl alcohol as is	-	-

Readings at D2 (48 h) and D4 (96 h).

inhalant allergens were negative. Total serum IgE was 59 kU/l.

■ Naaxia contains the magnesium salt of NAAGA, a naturally occurring dipeptide. It is found in the brain of many mammals (2). This substance inhibits mast-cell degranulation (3), the synthesis of certain leukotrienes (4), and the activation of the complement cascade (5). It has been reported to be effective in the treatment of seasonal and perennial allergic rhinitis and conjunctivitis (6, 7).

The clinical picture and results of patch tests clearly show that this patient developed contact allergy to NAAGA in eyedrops. Since control subjects did not react to this compound, an irritant mechanism is not suspected.

To the best of our knowledge, contact allergy to NAAGA has not been previously described. The concentration of NAAGA suitable for patch testing has not been reported. Although patch tests can be carried out with Naaxia eyedrops as is, specific tests with NAAGA are recommended to confirm sensitization and to rule out allergy to eyedrop preservatives.

Key words: conjunctivitis; spaglumic acid.

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