

Figure 1 (A/B) Multiple erythematous macules and papules on the lower extremities. (C) Western blot of kiwi extract with patient serum. (D/E) HE staining: neutrophilic infiltration in and around cutaneous vessels with leucocytoclasia.

banana, kiwi and pineapple in an unblinded manner. Six to ten hours after consumption of kiwi she reproducibly developed an itchy rash consisting of confluent 3–5 mm purpuric macules and papules on the legs, lower trunk and forearms with consecutive bleeding in the central part of the lesions. Oral provocations with apple, banana and pineapple were negative. Western Blot analysis of a kiwi fruit extract with the patient's serum showed IgG-, but no IgE-reactivity, corresponding to the major kiwi fruit antigen Act c 1 (Fig. 1C).

HE staining of a fresh lesion, that was taken soon after appearance, showed neutrophilic infiltration in and around cutaneous vessels with leucocytoclasia consistent with leucocytoclastic (allergic) vasculitis (Fig. 1D/E).

In the light of the patient's history, diagnostic findings and the reproducible induction of symptoms by oral provocation with kiwi, we diagnosed 'kiwi-induced allergic leucocytoclastic vasculitis'.

Elimination diet with avoidance of the consumption of kiwi lead to slow resolution of the purpuric lesions and hyperpigmentations over time. No recurrences of vasculitis were observed over a period of 3 years.

Using repeated oral food challenges we were able to identify kiwi fruits as a causal elicitor of allergic vasculitis. The presence of Act c 1-specific IgG strongly supports an antigen-specific process, but food-specific IgG antibodies are also frequent finding in healthy individuals (1). Foodstuff is rarely considered as a cause for allergic vasculitis in clinical practice and is reported only anecdotally in current literature (rye, carrot, cow's milk, hen's egg, cocoa products and additives) (2–4). Strikingly, in our patient mainly dependent body regions like legs and feet were affected by vasculitis and therefore, the formation of IgG immune complexes with kiwi antigen and their deposition in dermal postcapillary venules can be assumed as pathogenic process (5).

The authors report no conflict of interest.

J.G., S.K., and J.R. cared for the patient. J.G. and S.K. wrote the manuscript. M.O., M.M. and J.R. reviewed the manuscript. M.O. performed the western blot.

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Cow's milk allergy as a cause of anaphylaxis to systemic corticosteroids

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Keywords: contamination; corticosteroid allergy; cow's milk allergy; lactose; methylprednisolone.

Immediate IgE-mediated allergic reactions to corticosteroids are rather uncommon,

whereas causative agents usually involve the native steroid molecule or a pharmaceutical excipient, in most cases a

Lactose-free corticosteroid preparations should be exclusively used when treating patients with severe cow's milk allergy.

Table 1 Skin testing results in both patients with acute reaction to lactose-containing succinylated methyl-prednisolone

Drug tested	Original concentration	SPT		ID		Lactose-containing
		1/10	1/1	1/100	1/10	
Methyl-prednisolone sodium succinate 40 mg	40 mg/ml	–	+			Yes
Methyl-prednisolone sodium succinate 125 mg	62.5 mg/ml	–	–	–	–	No
Methyl-prednisolone acetate 80 mg	40 mg/ml	–	–	–	–	No
Hydrocortisone sodium succinate 250 mg	125 mg/ml	–	–	–	–	No
Dexamethasone sodium phosphate 8 mg	4 mg/ml	–	–			No
Prednisolone 25 mg	25 mg/ml	–	–			No
Methyl-prednisolone tablet 4 mg		+	+			Yes
Cow's milk extract			+			Yes

succinate ester bound to methyl-prednisolone or hydrocortisone (1, 2). We here report two cases of immediate reaction to methyl-prednisolone, attributed to milk allergen contamination.

A 9-year-old boy with a history of severe persistent cow's milk allergy (CMA) was seen at the Emergency Department due to a virus-induced asthma exacerbation presented with fever, wheezing & moderate dyspnea. The boy was administered nebulized salbutamol, as well as 40 mg of methyl-prednisolone by intravenous injection. Paradoxically, wheezing deteriorated, along with a slight fall in arterial blood oxygen saturation, so the boy was given another course of the same medication on assumption of clinical under-responsiveness. Within a few minutes the patient acutely collapsed, with hypotension, cyanosis and respiratory arrest and had to be immediately transferred to the IC Unit, where he was given epinephrine intramuscularly and was eventually intubated.

Another patient, a 7-year-old boy with severe CMA was similarly treated with salbutamol and intravenous administration of 40 mg methyl-prednisolone, following clinical diagnosis of a virus-induced asthma exacerbation. The therapeutic intervention resulted in a full-blown anaphylactic reaction, with aggravation of dyspnea & wheezing, immediate urticarial rash, emesis and ultimately hypotension.

Both children were evaluated within the next 6 months for assumed IgE-mediated reactivity to methyl-prednisolone. Skin testing (skin prick and intradermal tests when indicated) was performed using seven different corti-

costeroids to evaluate cross-reactivity pattern and identify the culprit agent (Table 1). Sensitization to the native steroid molecule and to the succinate ester was ruled out by negative skin tests, while both patients exhibited positive skin response exclusively to lactose-containing preparations.

Subsequent drug provocation tests were negative in both patients for a full therapeutic dose (125 mg) of non-lactose containing, otherwise identical to the one that elicited the reaction, succinylated methyl-prednisolone preparation (Solu-Medrol 125 mg, Pfizer). Diagnostic drug challenges with the lactose-containing preparation (Solu-Medrol 40 mg, Pfizer) were considered unethical due to the recent history of severe systemic reaction and were not performed.

By employing a highly sensitive ELISA assay (Veratox Total Milk Elisa kit; Neogen, St. Joseph, MI, USA, limit of detection = 0.5 ppm), we detected traces of milk proteins, within the range of 2.0–3.5 ppm, in samples from all five batches tested of the implicated product (Solu-Medrol 40 mg, Pfizer), confirming our hypothesis of milk allergen contamination.

Although uncommonly, pharmaceutical lactose, contained as an excipient in corticosteroid preparations may be an iatrogenic cause of anaphylaxis in children with severe CMA, due to milk protein contamination (3, 4). This is particularly relevant, since patients with severe CMA exhibit increased risk of concurrent asthma or other food allergies (5, 6). In the case of an acute allergic event or an asthma exacerbation, these patients are reasonable candidates for systemic administration of

(possibly lactose-containing) methyl-prednisolone. Given that the concurrent asthma exacerbation may potentially decrease threshold for anaphylaxis, intravenous injection of even minute amounts of cow's milk protein may be sufficient to elicit a severe reaction, e.g. by further aggravating preexisting bronchospasm. In any case, increased caution is warranted, as there is marked risk of mistaking the allergic reaction for apparent under-responsiveness to medication. This may justify additional administration of the allergen-containing drug, as in the case of one of our patients, especially since product information inserts typically do not caution patients with milk allergy about the rare possibility of an allergic reaction to contained milk proteins. It is of paramount importance that non-lactose containing preparations (Table 1) are exclusively used when treating such patients.

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Antigen-specific immune response to endotoxin-free recombinant P34

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Keywords: endotoxin; lymphocyte proliferative response; recombinant P34; soybean allergy.

Soybean allergy is one of the most important food allergies because soybeans are

widely used in processed foods. P34 has been identified as the main allergen in soybeans (1, 2). Producing and characterizing the recombinant

Endotoxin-free recombinant P34 induced the proliferation of lymphocytes from patients with soybean allergy.

allergen play crucial roles in the development of a diagnostic tool and the application of an allergen-specific immunotherapy. In particular, the lymphocyte proliferative response test against antigen is considered to be useful for evaluating T-cell activation (3). Therefore, we

investigated the antigen-induced proliferative responses to recombinant P34 (rP34) of peripheral blood mononuclear cells (PBMCs) from healthy control subjects and patients with soybean allergy.

The C-terminal hexa-histidine-tagged mature form of P34 (amino acid number, 123–379) was expressed in *Escherichia coli* BL21 (DE3). After purification

on Ni sepharose columns, the SDS/PAGE pattern showed a protein of approximately 30 kDa in the 500 mM imidazole elution fraction. We found that phase separation with Triton X-114 as described by Liu et al. (4) was not effective in reducing the amounts of endotoxin contamination in rP34. However, the endotoxin could be

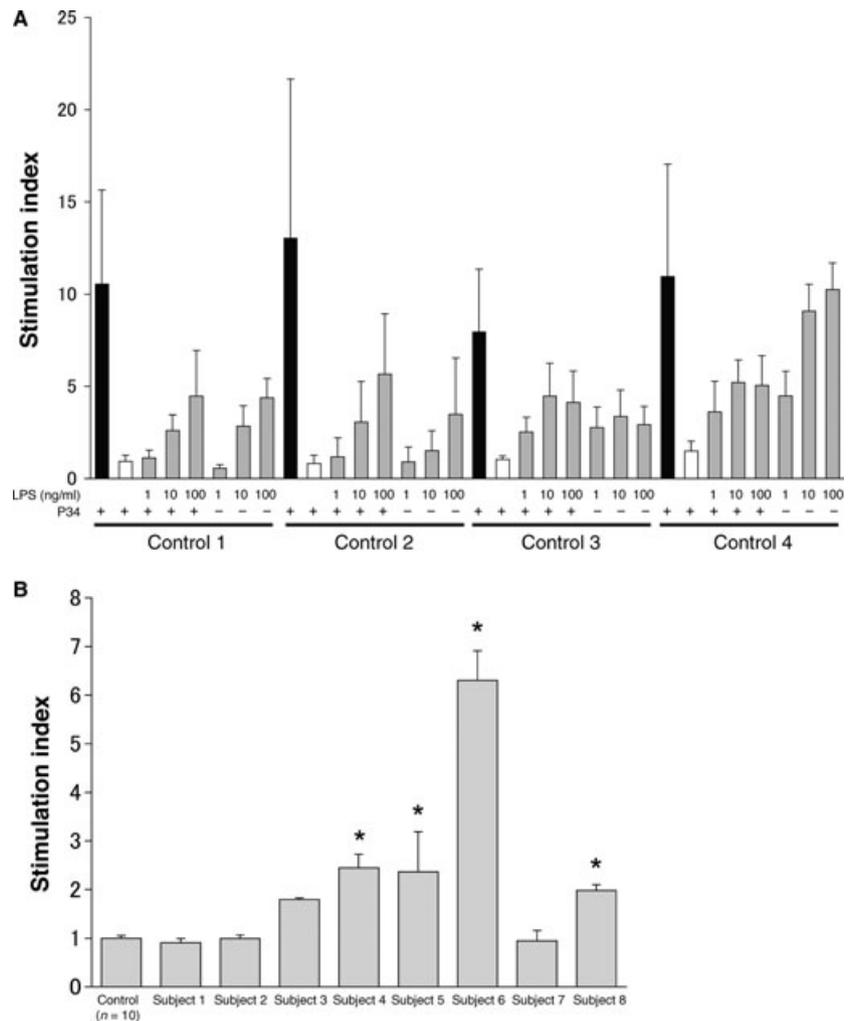


Figure 1 Proliferative response of peripheral blood mononuclear cells (PBMCs) to rP34. (A) Stimulation indices of PBMCs from four control subjects. PBMCs were stimulated with endotoxin-contaminated rP34 (non-SDS-treated rP34) (black bars) or endotoxin-free rP34 (SDS-treated rP34) (white bars) or 1, 10, and 100 ng/ml of LPS with or without endotoxin-free rP34 (gray bars). (B) Stimulation indices of PBMCs from ten control subjects, two subjects with outgrown allergy (subjects 1 and 2) and six allergic subjects (subjects 3–8). PBMCs were stimulated with endotoxin-free rP34. *Indicates a significantly higher stimulation index (SI) than those of controls after exposure to endotoxin-free rP34 ($P < 0.05$). To compare the responses between individuals, we expressed the results as SI using the following formula: counts per minute (cpm) incorporated into antigen-stimulated cultures/cpm incorporated into the medium-alone control.