

Anaphylaxis after consuming soy products in patients with birch pollinosis

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Many people use soy milk as an alternative to cow's milk, or ground and pressed soy beans as a replacement for meat (1–3). To date, more than 15 (putative) soy allergens have been described in the

Allergome database (<http://www.allergome.org>), of which six have been recognised by the WHO-IUIS Allergen

Nomenclature

Subcommittee. Gly m 1 and Gly m 2 are relevant in patients with asthma because of soy bean dust exposure, while Gly m 5 (vicilin-like 7S) and Gly m 6 (11S) have recently been reported as food allergens associated with severe allergic reactions to soy (4). Mittag et al. observed a prevalence of 10% of soy allergy among patients sensitised to birch pollen. This is presumed to be caused by IgE cross-reactivity between the major birch pollen allergen Bet v 1 and its homologue in soy, Gly m 4 (3). Recently, six patients with birch pollinosis presented in our outpatient clinics, who developed severe food

allergy upon first exposure to soy drinks or soy desserts (brand: Alpro).

All patients developed a swollen tongue, angioedema, urticaria, rhino-conjunctivitis and/or hypotension within 15–30 min after consumption and were treated for their anaphylaxis in the emergency department of our hospital.

All patients had strong IgE responses to birch pollen (specific IgE antibodies, demonstrated with CAP system and with skin-prick tests (SPT)), but tested negative for soy with the exception of one patient (#5). On the other hand, all had a positive ImmunoCAP (Phadia, Uppsala, Sweden) for Gly m 4 (6.45, 7.44, 1.80, 1.05, 21.3 and 11.2 kU/l, respectively), demonstrating insufficient sensitivity of soy CAP and SPT for detection of IgE against this allergen. All six patients tested positive to several other respiratory allergens and patient 1, 2 and 5 also reported oral allergy symptoms with birch-related foods, such as apple and hazelnut.

The demonstration of IgE antibodies against rGly m 4 clearly pointed towards the 'classical concept' of Gly m 4-induced birch pollen-related soy allergy. SDS/PAGE immunoblots of soy drink (10% v/v in PBS/0.1% Tween-20) and rGly m 4 were probed with patient's serum or rabbit anti-rGly m 4 (Fig. 1). In the soy drink, patients' IgE recognised doublets around 65 and 40 kDa and a strong band at 20 kDa. These bands could correspond to subunits of the two major allergenic storage proteins (Gly m 5 and Gly m 6). Despite the presence of IgE antibodies against Gly m 4 as demonstrated by rGly m 4 ImmunoCAP, IgE reactivity to the corresponding 17-kDa band could not be demonstrated on immunoblot. Rabbit anti-Gly m 4 antibodies did, however, bind weakly to a

band at 17 kDa, demonstrating that Gly m 4 is present, but most likely at insufficient level to be detected by serum IgE antibodies. To investigate whether any of the bands detected on soy drink immunoblot was related to recognition of Gly m 4, an immunoblot inhibition with rBet v 1 was carried out. None of the bands detected was affected, also when birch pollen extract was used as inhibitor. This indicates that birch pollen-independent soy sensitisation might exist presumably for storage proteins like Gly m 5/6.

Allergic reactions after digestion of soy by birch pollen allergic patients reported in literature, ranging from mild to severe anaphylactic shock, have generally been attributed to Bet v 1-Gly m 4 cross-reactivity (1, 3, 5, 6). Also in those reports, specific IgE to soy could not always be detected. On immunoblot, most serum samples with significant IgE titres to rGly m 4 in CAP did not show detectable IgE binding at 17 kDa but show strong binding to various higher molecular mass bands, i.e. similar to the observations in this study. Based on this, Ballmer-Weber et al. (1) concluded that Gly m 4 is underrepresented in total protein extracts of soybean. They therefore recommended determining specific IgE to rGly m 4 by ImmunoCAP in birch pollen-sensitised patients suspected to be allergic to soy. From their study, the authors concluded that IgE antibodies to Gly m 4 are linked to mild symptoms. Almost none of the patients with anaphylaxis demonstrated Gly m 4-specific IgE. Based on this and our own difficulties to unequivocally demonstrate that there is IgE binding to Gly m 4 in the products causing anaphylaxis, we cannot conclude that anaphylaxis of our patients is a result of Bet v 1-Gly m 4 cross-reactivity. Our immunoblot results

Birch pollinosis patients (n = 6) developed anaphylaxis after soy drink consumption: is Gly m 4 the causative allergen?

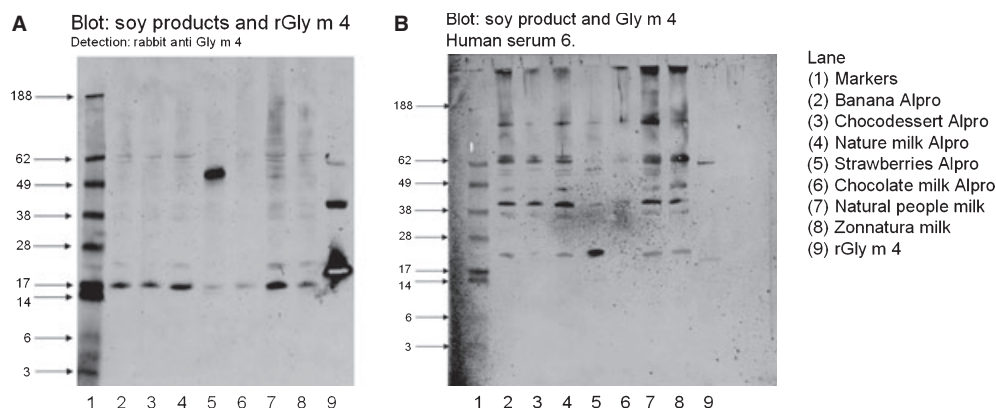


Figure 1 Blot (A + B): 2.5 µg soy extract or 0.25 µg rGly m 4 per lane was incubated with: (A) 1 µl rabbit anti-Gly m 4 in 10 ml PBS/0.1% TWEEEN/0.5% Milk powder (PBS/T/E) or (B) 300 µl patients' serum in 10 ml PBS/T/E. After washing, bound antibodies were detected with either anti-rabbit antibodies-IRD800 or anti-hIgE IRD800. Remark: blot A, lane 5, 54 kDa band is due to a-specific binding secondary antibody.

suggest that perhaps IgE responses against seed storage proteins are more likely candidates to cause the observed severe soy allergy. Therefore, it is important to realise that the presence of Bet v 1-Gly m 4 cross-reactivity does not exclude the possibility of simultaneous direct sensitisation to soy allergens.

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