

CLINICAL OBSERVATION

Severe reactions after the intake of soy drink in birch pollen-allergic children sensitized to Gly m 4

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ABSTRACT

Aim: To study the connection between reaction to soy milk and IgE sensitization to Gly m 4.

Methods: Four subjects who experienced unforeseen and severe symptoms after the ingestion of soymilk were studied.

Results: All children were birch pollen allergic, had high IgE responses to the PR-10 proteins from birch and soybean, Bet v 1 and Gly m 4. All reactions took place after the ingestion of soymilk during the peak pollen season.

Conclusion: This is the first time soybean-dependant pollen-food cross-reaction has been reported in children experiencing reactions during the birch pollen season. These findings may well be helpful to doctors in identifying individuals at risk of severe reactions upon the ingestion of soymilk, and we foresee an increase in the number of similar cases as soy drinks are promoted for health purposes.

INTRODUCTION

Soybean (*Glycine max*) is a species of the legume family and an important foodstuff in Asia. In the Western world, it is mostly used as a food additive in processed foods (1). Soybean-induced allergic reactions have been previously described, with symptoms ranging from mild to severe, systemic and fatal (2–4). Soybean allergy in children is known to be primarily mediated by allergen contact through the gastrointestinal tract, often in the form of soybean-based infant formula, particularly in infants with cow's milk protein allergy (4,5). The major soybean storage proteins, Gly m 5 and Gly m 6, seem to be the primary sensitizers (6). Soybean allergy may also be acquired after primary sensitization to birch pollen, because of IgE cross-reactivity between the major birch pollen allergen Bet v 1 and its homologous protein in soybean, Gly m 4 (7–9). Pollen-mediated soybean allergy has so far been mainly described in adults, although a few reactions in children have been reported (8). Here, we report four birch pollen-allergic children who experienced severe allergic reactions after the intake of soymilk during the pollen season. Our aim was to study a possible connection between the soybean reaction and IgE sensitization to Gly m 4 in children with a known birch pollen allergy.

MATERIAL AND METHODS

Subjects

Four children from Sundsvall, Sweden, were identified after they experienced severe symptoms shortly after the

ingestion of flavoured soymilk drink at the peak of the birch pollen season (Table 1). Two were admitted to emergency care, and two consulted their allergy specialist after the episode. All had birch pollen allergy and related oral allergy syndrome from fruits and/or vegetables, and none had reacted to soy protein previously. All had a normal diet containing soy but had not been exposed to soy milk before. They had not been exercising at the time of the reaction, and they were not infected according to the case report. An informed consent was obtained from all parents.

A 13-year-old boy, with allergic rhinoconjunctivitis, developed dyspnoea, cough and tightness of throat. He was treated at the emergency department with antihistamines and cortisone. His symptoms subsided within a few hours.

A 14-year-old girl, with allergic rhinoconjunctivitis and asthma, developed dyspnoea, swelling of lips, gastrointestinal pain and emesis. She was treated with antihistamines and her symptoms subsided within an hour.

A 10-year-old girl, with allergic rhinoconjunctivitis and asthma, developed dyspnoea, nausea and emesis.

A 10-year-old boy, with allergic rhinoconjunctivitis, developed dyspnoea, swelling of lips and tightness of throat. He was treated at the emergency department with antihistamines, oral corticosteroids and inhaled adrenaline. His symptoms subsided within a few hours.

Specific IgE measurements

Specific IgE to soybean extract, birch pollen, Gly m 4 and Bet v 1 was analyzed in sera using the ImmunoCAP®

Table 1 Demographic, serological and clinical characterization of subjects

Patient information			Reaction to soymilk	Specific IgE (kU/l)					
Case	Age	Sex	Symptoms	Birch	Soybean	Bet v 1	Gly m 4	Gly m 5	Gly m 6
1	13	M	dy, co, thi	163.5	0.1	117.2	24.7	nd*	nd
2	14	F	dy, git, s, em	99.6	0.3	81.8	40.9	0.0	0.0
3	10	F	dy, s, n, em	63.2	0.2	59.7	10.8	0.0	0.0
4	10	M	dy, s, thi	74.9	0.0	61.9	10.5	0.0	0.0

dy = dyspnoea, co = cough, thi = tightness of throat, git = gastrointestinal pain, s = swelling of lips, em = emesis, n = nausea.

*Analysis not performed because of shortage of sample.

method, and a level of 0.1 kU_A/l was considered positive (Phadia AB, Uppsala, Sweden). Specific IgE to Gly m 5 and Gly m 6 was analyzed in sera from three individuals using experimental ImmunoCAP[®] products. Native Gly m 5 and Gly m 6 were purified from soybean extract, and the purity was estimated to be >95%, as no other bands were visible using SDS-PAGE analysis.

RESULTS

Serum IgE antibody analysis showed no or very low levels to the soybean extract but high levels to Gly m 4, birch pollen extract and Bet v 1 (Table 1). No IgE responses were detected to Gly m 5 and Gly m 6.

DISCUSSION

Here, we report the cases of four birch pollen-allergic children, from one Swedish city, who experienced severe allergic reactions after the intake of soymilk during the birch pollen season. The subjects displayed similarities in their history as well as in the way they reacted after the intake of soymilk. None of them had previously reacted to soybean and all of them presented with severe reactions. All had earlier experienced mild OAS symptoms when eating Rosaceae fruits.

Birch pollen-mediated food allergy caused by, for example, apple and hazelnuts is common, and the symptoms are usually mild such as oral itch. However, a high number of severe reactions induced by soybean have recently been reported (7,8). This type of allergic reaction seems to be mediated by IgE cross-reactivity between the major birch pollen allergen Bet v 1 and its homologous protein in soybean, Gly m 4. In all four cases presented in this study, a higher IgE response to Bet v 1 than to Gly m 4 was detected. We therefore propose that the primary sensitizer was the birch allergen Bet v 1. The concentration of many PR-10 components in native allergen extracts is often low and, as they are also frequently heat labile, the concentration is further affected by degradation during extraction (1). All four children had low IgE responses to the soybean extract. Further, in the three children where IgE responses to the two major storage protein of soybean, Gly m 5 and Gly m 6, were also analyzed and no response was detected. All together, this indicated a very low or no IgE response to soybean proteins other than Gly m 4.

The concentration of Gly m 4 is highly variable in soybean products and is strongly dependent on the degree of food processing, heating and the total amount of soybean in the product (8). The soybean reaction in our subjects was most likely provoked by a high Gly m 4 content in the moderately processed soymilk. Soymilk is essentially whole soybeans extracted in water followed by heating for a short period of time (10). In addition, all four episodes occurred during the peak of the birch pollen season. We hypothesize from this that the time of intake could have contributed to the severity of the reaction. Soybean proteins are presently promoted for health benefits, and we foresee an increase in the number of similar cases of pollen-related soybean reactions. We therefore call to attention the possibility that individuals with moderate to severe birch pollen allergy are at risk of reacting to soy drinks during the pollen season.

To our knowledge, this is the first time this type of soybean-dependent pollen-food cross-reaction has been reported in children experiencing reactions during the birch pollen season. These findings may well be helpful to doctors in identifying individuals at risk of severe reactions upon ingestion of soymilk.

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Don't forget other causes of wheeze. ABPA in a boy with asthma. A case report and review of the literature

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ABSTRACT

Allergic bronchopulmonary aspergillosis (ABPA) is a rare pulmonary disorder caused by hypersensitivity to *Aspergillus fumigatus*. The prevalence is estimated to be about 1–2% in adult patients with asthma and 2–15% in patients with cystic fibrosis. In paediatric patients with asthma, only single case reports on ABPA exist. We report on a 13-year-old boy with allergic asthma complicated by ABPA. Despite the presentation of typical clinical symptoms, it took 6 years before he was diagnosed. The clinical course improved rapidly after ABPA therapy was started, and 12 months after diagnosis, the boy is still free of symptoms. Clinical symptoms of ABPA may be unspecific making a rapid diagnosis difficult in some cases.

Conclusion: A delay in diagnosis and treatment increases the risk for irreversible lung damage. Once bronchiectasis has developed, the outcome is unfavourable. Thus, ABPA has to be considered in patients whose asthma remains uncontrolled despite adequate therapy.

CASE REPORT

The boy described here was born in 1995. At age four, mild to moderate allergic asthma was diagnosed, which was initially well-controlled with inhaled corticosteroids. At the age of 7 years, he developed symptoms of daily episodes of wheezing, exercise-induced dyspnea and coughing with occasional expectoration of brownish plugs of sputum. In the following 6 years, serial chest radiographs (a total of 16) were carried out, showing varying patchy areas of consolidation and infiltrates in the right and left upper lobe. These findings were interpreted as pneumonia and clinical deterioration as asthma exacerbations. Therefore, the boy received antibiotics and/or short courses of systemic steroids more than five times. At age ten, a lung abscess was suspected and he was hospitalized for fourteen days. At this time, he had no fever and blood examinations did not reveal any sign of systemic inflammation. Despite the repeated therapies for presumed pneumonia and escalation of asthma therapy with at least 250 µg inhaled fluticasone and 50 µg salmeterol twice daily, the boy's symptoms persisted and reliever medication (inhaled salbutamol) was needed more than three times a week. He had to repeat the 7th grade because more than 30 school days were lost.

At the age of 13, he was referred to our hospital for further examination because of an infiltrate of the right upper

lobe that had persisted for at least 9 months. On admission, the patient was a lean adolescent appearing to be healthy with no signs of respiratory distress. Auscultation of the chest revealed a prolonged expiration but no adventitious sounds. Respiratory rate was 18 per minute; oxygen saturation measured by pulse oximetry was 96%; body temperature was 37°C. Further physical examination revealed no other pathological findings. A lung function test showed moderate obstruction (FEV1 72% predicted) without any signs of restriction [vital capacity (VC) 90% predicted]. Exhaled nitric oxide (FeNO) was markedly high 158 ppb (normally < 20 ppb). The white blood count at referral was $11.0 \times 10^9/L$ with 53% neutrophils, 20.6% lymphocytes, 7.3% monocytes, 1.1% basophils and 18% eosinophils.

In view of recurrent exacerbations of obstruction, brownish sputum plugs and persistent infiltrates in chest X-ray, a diagnosis of allergic bronchopulmonary aspergillosis (ABPA) on the background of bronchial asthma was considered. Further examinations revealed a strongly elevated total IgE (10 800 IU/mL) and elevated specific IgE to recombinant *Aspergillus* antigens (Asp f 2, Asp f 4 and Asp f 6) reported to be pathognomonic for ABPA. Intradermal skin test with *Aspergillus* antigen revealed a very strong immediate reaction and delayed reaction and *Aspergillus*-specific IgG was increased. High resolution computer