

Somnolence upon Allergen Provocation in a Child with Hen's Egg Allergy

Somnolenz nach Allergenprovokation bei einem Hühnereiweiß-allergischen Kind

Background

Recent epidemiological data reveal that food allergies highly affect the pediatric population and are an increasing cause for hospitalization. Typical food allergic symptoms range from mild, local symptoms, such as itching, swelling, nausea, vomiting and diarrhea, to systemic anaphylactic symptoms, like airway swelling, hypotension and arrhythmias (Boden SR et al., *Immunol Rev* 2011; 242: 247–257, Kirchlechner V et al., *Klin Padiatr* 2007; 219: 201–205). Although the appearance of these symptoms may facilitate the diagnosis of food allergy, diagnostics of food adverse reactions in the pediatric population is particularly difficult, as the patient or patient's parents can often not communicate allergic symptoms appropriately. Therefore, objective screening tests including measurements of total and allergen specific IgE, skin prick testing (SPT) and the golden standard of food allergy diagnosis, the double blind placebo controlled food challenge (DBPCFC), are conducted especially in the young age groups. DBPCFC is not only of importance for diagnostic purpose, but is substantial for determination of threshold levels, which enable physicians to adequately advise patients or parents. Oral allergen provocations are carried out under hospital settings, due to possible adverse reactions, such as anaphylaxis, following international guidelines of NIAID (National Institute of Allergy and Infectious Disease) (Boyce JA et al., *J Allergy Clin Immunol* 2010; 126: S1–58) and EAACI (European Academy of Allergy and Clinical Immunology). Increasing doses of the challenging food are given at 30min intervals until the top dose has been reached, or the patient reports an objective symptom, which ensures the correct diagnosis of food allergy and which is the basis for dietary recommendations or therapeutic measures.

In this case report, we report for the first time a 3-year-old child reacting repeatedly to allergy provocations by falling into a transient somnolence.

A 3-year-old girl was referred to the Medical University Pediatric Department to substantiate the clinical relevance of a suspected egg allergy.

From patient's history it was known that after hen's egg consumption she had repeatedly experienced exacerbations of atopic dermatitis lasting for several days. Due to inconsistencies with regard to symptom occurrence after hen's egg exposure, further diagnostic evaluation was initiated.

Routine diagnostic measures included SPT and measurement of total and allergen specific IgE (Table 1). The patient had substantially elevated total IgE levels and IgE specific for hen's egg white (CAP 4), hen's egg yolk (CAP 3) and cow's milk protein (CAP 2). These results indicated a polysensitization to hen's egg and cow's milk allergens, although symptoms occurred exclusively after egg consumption.

In SPT, the patient developed a positive skin reaction, a wheal diameter above 3 mm, to hen's egg white (10 mm), house dust mite (20 mm), cat (10 mm), hazelnut (6 mm) and horse dander (15 mm). Some minutes after SPT, the child felt nauseous, sleepy and turned pale. She fell asleep for 30 min, which was not reported by parents before. She did not show any skin lesions or other systemic allergic symptoms. The episode was self-limiting and the patient did not show any symptoms as soon as she was awake.

Due to these atypical symptoms, a rub test with cow's milk and hen's egg was performed one month later. Although the rub test is, due to its lack of clinical repro-

ducibility, a secondary diagnostic tool in diagnosis of food allergy, it represents a non-invasive method especially for highly sensitized patients. The patient did not show any reaction to native cow's milk. However, when the commercial prick testing substance containing hen's egg was used for testing, several urticarial wheals with a size of 2–3 mm on reddened skin appeared. Within 30 min the child felt sleepy again. According to the parents the time point did not correlate with her normal naptime.

To confirm the diagnosis of hen's egg white allergy, to clarify symptoms and in particular to identify a threshold dose being tolerated by the child, the patient was subjected to a placebo controlled egg white provocation. On the day of admission, the patient was healthy and well rested. The patient had been on a hen's egg free diet at home for several weeks. For oral provocation, increasing doses of hen's egg white masked with Sinlac mash (Nestle) were prepared according to standard procedures. The child was compliant and drank the test substance without any resistance. The first 2 doses were well tolerated. After the third dose (1.0g hen's egg white, cumulative dose: 1.5g), the patient developed a perioral erythema being followed by small urticarial lesions on the cheeks. Due to these weak local reactions, which could be induced by the contact with the hen's egg white provocation substance, and to objectify symptoms a fourth dose was given. 25 min after the fourth dose (3.5g hen's egg white, cumulative dose: 5g), corresponding to a cumulative dose of one-third to one-half of an egg, the child felt nauseous and vomited. Within the next minutes, the patient became sleepy and suddenly 45 min after the fourth egg white dose she was somnolent, which lasted for 30 min. During this time the patient could barely be awakened and had only reacted to painful stimuli, which was unusual for her normal sleep. Blood pressure, respiratory and heart rate and

Table 1 Specific IgE and sensitization status.

Specific IgE	IgE measurement		SPT mm
	kUA/L	CAP	
hen's egg white	27.4	4	10
cow's milk protein	2.91	2	3
hen's egg yolk	5.29	3	
house dust mite	n.t.		20
cat	n.t.		10
hazelnut	n.t.		6
horse	n.t.		15
Total IgE	1 842 kU/L		

n.t.: not tested, normal total IgE level <190 kU/L, normal specific IgE level <0.35 kUA/L.



Fig. 1 Fluctuation of vigilance during oral allergen provocation. Four doses of hen's egg white were given to the patient. Small urticarial lesions occurred on her cheeks and forehead after the third dose. The patient felt nauseous and vomited 25 min after the fourth dose. Somnolence appeared 45 min after the fourth dose. Hypnagogic theta curves especially around the temporal region T3–T5 (black rectangle) in EEG indicated fluctuations of vigilance.

capillary refill time were normal. Emergency medications, such as corticosteroids, antihistamine or epinephrine were not applied, because cardio-respiratory parameters were stable. An EEG (electroencephalography) was carried out, when vigilance was already improving. Theta rhythm over the temporal region occurred throughout the whole EEG indicating fluctuation in vigilance (◉ **Fig. 1**), which does normally not occur during oral allergen provocation. 1½ h after the last oral provocation dose, the girl had completely recovered from somnolence. Informed consent was obtained from the parents for all procedures.

On the next day, an open challenge with placebo was performed to confirm the egg-white-symptom causality. Placebo (Sinlac mash) was well tolerated up to the highest dose of 100 milliliters. The child did not sleep for at least 3 h after exposure to placebo.

The patient was advised to avoid high concentrations of hen's egg white, whereas traces might be tolerated by the child. Emergency medication was not prescribed due to the absence of anaphylactic reactions.

Discussion

In the literature, typical symptoms of a food allergic patient after allergen provocation

range from mild, local symptoms to systemic anaphylactic symptoms (Boden SR et al., *Immunol Rev* 2011; 242: 247–257). However, we observed somnolence as an objective, and reproducible symptom after hen's egg white challenge, SPT and rub testing in an egg allergic child. Up to date, sleepiness or hyporesponsiveness has been described in connection with circulatory signs of shock and anaphylaxis (Boyce JA et al., *J Allergy Clin Immunol* 2010; 126: S1–58). Only one case report in literature described a 6 year old cow's milk- and hen's egg white-allergic girl who developed unconsciousness, angioedema, sneezing, wheezing and stridor within minutes after MMR (measles-mumps-rubella) vaccination (Yavuz ST et al., *Acta Paediatr* 2011, 100: e94–96). Our patient had stable vital parameters and did not show any signs of anaphylactic shock. We presume that the appearance of somnolence was directly related to the allergic reaction and was not a consequence of an impairment of the cardio-respiratory system. Similar episodes of unresponsiveness have been described after diptheria-tetanus-pertussis-immunizations, where children became hypotonic and hypo-responsive within minutes after immunization (Heininger U et al., *Monatsschr Kinderheilkd* 1998; 146: 972–975). These events were often accompanied by paleness or cyano-

sis, which however was not the case in our case report.

The mechanisms underlying the food allergy related somnolence in this patient remains to be elucidated. An EEG, performed during recovering from somnolence did not reveal any signs of epileptiform activity, making any kind of seizure, including in particular absence seizure, very unlikely. Typical signs of fluctuations of vigilance were indicated by hypnagogic theta curves especially in the temporal region, which have not been yet described under normal conditions during allergen provocation. Hypnagogic theta curves are present especially in children during the first sleep phase, which might indicate a typical resting episode of our patient. The fact that the child did barely react to painful stimulus, which was unusual for her sleep onset phases, and that she was absolutely compliant during the whole procedure, makes the possibility of a normal nap unlikely. Additionally, as the patient reacted 3 times by falling asleep after SPT, rub testing and during oral provocation, we propose the unusual symptom of somnolence in our patient to be objectively valid and to be caused by the allergic reaction. The parents did not report of hyporesponsive episodes to any other stimuli but they could not rule out the possibility that the child might have fallen asleep after hen's egg consumption.

To the best of our knowledge, this is the first case report of a food allergic patient reacting with somnolence to allergen provocation. Positive allergen specific IgE and a positive reaction during SPT corroborate the objectivity of the patient's allergic reaction to hen's egg. The absence of somnolence during placebo testing strongly implicates that the symptom is directly associated with the allergen provocation. Therefore, unusual symptoms upon allergen encounter, such as somnolence, should be taken seriously and a relation with the suspected allergen should be confirmed with DBPCFC. Patients should be advised accordingly and emergency medications should be prescribed if necessary.

Conflict of interest: The authors have no conflict of interest to disclose.

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