FOLIA MEDICA CRACOVIENSIA
Vol. LVIII, 2, 2018: 89–101
PL ISSN 0015-5616
DOI: 10.24425/fmc.2018.124661

Component-resolved diagnosis (CRD) of food anaphylaxis

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Abstract: Anaphylaxis is an increasing problem in public health. The food allergens (mainly milk, eggs, and peanuts) are the most frequent cause of anaphylaxis in children and youth. In order to define the cause of anaphylaxis, skin tests, the determination of the concentration of specific IgE in the blood and basophil activation test are conducted. In vitro tests are preferred due to the risk of allergic response during in vivo tests. Component-resolved diagnosis (CRD) is an additional tool in allergology, recommended in the third level of diagnostics when there are diagnostic doubts after the above mentioned tests have been carried out.

The paper presents 3 cases of patients with anaphylactic response, and the application of CRD in these patients helped in planning the treatment. Patient 1 is a 4-year-old boy with diagnosed atopic dermatitis and bronchial asthma reported an anaphylactic shock at the age of seven months caused by cow's milk and the exacerbation of bronchial asthma after eating some fruit. Patient 2 is a 35-year-old woman who has had anaphylactic shock three times: in June 2015, 2016, and 2017 and associates these episodes with the consumption of dumplings with a caramel, bun, and the last episode took place during physical exertion few hours after eating waffle. Patient 3 is a 26-year-old man with one-time loss of consciousness after eating mixed nuts and drinking beer.

CRD offers the possibility to conduct a detailed diagnostic evaluation of patients with a history of anaphylactic reaction.

Key words: anaphylaxis, food allergy, component-resolved diagnosis.

Introduction

Anaphylaxis is defined as severe, life-threatening generalized or systemic oversensitivity that can occur in the immunological mechanism (IgE-dependent or IgE-independent) or not related to the immunological system (non-allergic anaphylaxis) [1].

It goes without saying that anaphylaxis is an increasing problem in public health. Due to the complexity of the clinical picture, gathering of fully reliable epidemiological data is difficult. It is reported that anaphylaxis occurs in adults in Europe with the frequency of 1.5–7.9:100,000 man-years, while this ratio fluctuates in children, depending on the data sources, from 0.19:100,000 up to the ratio occurring in adults [2]. In Poland in 2015, 3144 people received treatment for anaphylactic shock with an estimated prevalence rate of anaphylaxis of 8.2 per 100,000 (8.4 for females and 7.9 for males) [3]. The number of anaphylaxis cases has increased in the last decade, with the increase of food anaphylaxis at even 350%, and anaphylaxis induced by other factors grew by 230%. The number of anaphylaxis-related hospital admissions has also increased [4]. The annual mortality rate is 1–3 persons per one million. Bronchospasm is the main cause of anaphylaxis related mortality (96% of cases) [5].

The food allergens (mainly milk, eggs, and peanuts) are the most frequent cause of anaphylaxis in children and youth. In adults, it is venoms of Hymenoptera and medications (mainly antibiotics) prevail among other allergens. Approximately 20% of anaphylaxis cases have an unknown origin (the so-called idiopathic anaphylaxis) [5].

Regardless of the route of stimulating mastocytes and basophils, the anaphylaxis mechanism includes the releasing of a number of biologically active factors; the so-called preformed mediators, i.e. histamine, tryptase, heparin, and chymase, released within 5–15 minutes. Then, *de novo* synthesized mediators, which are platelet-activating factor (PAF), leukotrienes, and prostaglandins, are released within 10–30 minutes. It should be noted that in 20% of cases the anaphylaxis takes place in two stages, with the delayed response within 4–12 hours, and among others, cytokines and chemokines are responsible for the occurrence of anaphylaxis [6].

Clinically, anaphylaxis manifests itself in a severe response that mainly affects the skin, the respiratory, and/or cardiovascular systems. Food allergens most frequently induce symptoms in the respiratory system, and insect venoms induce the response of the cardiovascular system, while medications cause skin lesions. Currently, there are 3 groups of anaphylaxis criteria that are presented in Table 1 [1]. Anaphylaxis comes on in several tens of minutes after the contact with the allergen, and references cite medians of response time after 5, 15, and 30 minutes, which corresponds to response elicited by medications administered parenterally, insect venoms, and foods. Left untreated, the response progresses fast and may cause death [7]. After the anaphylactic response, the patient should be monitored for 8–24 hours, because the symptoms of the response can be delayed and such symptoms can be more severe than previous ones [8].

Table 1. Criteria for diagnosing anaphylaxis.

1. A sudden onset the disease (from several minutes to several hours) associated by lesions of the skin and/or mucous membranes (e.g. systemic urticaria, pruritus, itching, erythema, swelling) and symptoms in at least one of the following systems: a) Respiratory tract (e.g. shortness of breath, bronchospasm, stridor, hypoxia) b) Cardiovascular system (e.g. blood pressure drop, fainting)
2. Symptoms of two or more following systems which occur soon after the first systems (from several minutes to several hours) after exposure to the probable allergen in specific patients: a) Skin / mucous membranes (e.g. generalized urticaria, itching or erythema, swelling) b) Respiratory tract (e.g. shortness of breath, bronchospasm, stridor, hypoxia) c) Cardiovascular system (e.g. blood pressure drop, fainting) d) Alimentary tract (e.g. stomach cramps, vomiting)
3. Hypotension after the exposure to a known allergen affecting the specific patient (from several minutes to several hours): a) Infants and children — low arterial systolic pressure or a drop in the systolic pressure o >30% b) Adults — arterial systolic pressure <90 mm Hg or a drop in the systolic pressure >30% in comparison to the initial value

Asthma predisposes to a more severe progress of anaphylaxis, especially caused by food. Other risk factors for the severe systemic response are co-existing diseases such as mastocytosis, deficiency of platelet-activating factor acetylhydrolase, and cardiovascular diseases, especially those that require administration of β-blockers, angiotensin-converting-enzyme inhibitors, and anaphylaxis in the medical history. The main cofactors for anaphylaxis include alcohol, physical exercise, severe infections, premenstrual period, or stress [9].

Past mild or moderate response does not preclude subsequent severe episodes in the future. That is why after each anaphylaxis incident, regardless of its severity, the patient must be supplied with a rescue drug kit (epinephrine in a pre-filled syringe, antihistamine, and glucocorticoid administered orally) [10].

Diagnosing anaphylaxis is confirmed by the increased tryptase concentration in the blood (optimal testing time 15–180 minutes following the response to the inducing factor) or histamine (optimal testing time 15–60 minutes). The procedure applied in the allergic outpatient clinic includes gathering medical history and the identification of the inducing factor using additional tests that should be carried out no earlier than after 3–4 weeks following the anaphylactic response, optimally up to 1 year. In order to define the cause of anaphylaxis, skin prick tests (SPT), intradermal test (IDT), prick by prick tests, the determination of the concentration of specific IgE (sIgE) in the blood and basophil activation test (BAT) are conducted. *In vitro* tests are preferred due to the risk of allergic response during *in vivo* tests [6].

Component-resolved diagnosis (CRD) is an additional tool in allergology, recommended in the third level of diagnostics when there are diagnostic doubts after the above mentioned tests have been carried out. CRD is especially useful in

the allergic response to food, because the detection of sensitising molecules provides information on the severity of the allergy and potential cross reactions [11].

Milk, eggs, and peanuts

Cow's milk protein (CMP) is the most frequent cause of food allergy in children, and it occurs in 1–3% of the youngest population. Most of this population becomes tolerant by the age of 5, but, at present, the age of becoming tolerant has been increasing, even up to 16–17 years [12]. Allergy to cow's milk protein in adults can remain after the childhood or start at an older age, which applies to 0.1–0.5%. CMP are responsible for 13% of all fatal anaphylactic responses caused by food allergens [13].

Cow's milk contains about 30–35 g of proteins per litre, and it consists of two fractions: curd (coagulum) — 80%, and whey (lactoserum) — 20% [14]. The main allergens are caseins, alpha-lactoglobulin, and beta-lactoglobulin, and most patients are hypersensitive to several various proteins [15].

The application of CRD in an allergy to CMP is helpful in the risk assessment of severe responses to unprocessed milk and thermally treated milk. CMP belong to class I of food allergens due to its resistance to heat. The casein fraction is very resistant to high temperatures, and the bond with IgE is strong after 90 minutes of boiling at a temperature above 90°C. Due to the above, the high concentration of sIgE against Bos d 8 is connected with the sensitivity to milk, even in the baked form. Whey fraction is more sensitive to thermal treatment than caseins, and the bond with IgE is broken down after 15–20 minutes of heating above 90°C (Table 2) [11].

Table 2. Allergens in the cow milk, hen egg, peanuts, heat stability taken into account.

Cow's milk allergens Curd (coagulum)	Bos d 8 (Caseins)*, Bos d 9 (Alpha$_{S1}$-casein)*, Bos d 10 (Alpha$_{S2}$-casein)*, Bos d 11 (Beta-casein)*, Bos d 12 (Kappa-casein)*
Cow's milk allergens Whey (lactoserum)	Bos d 4 (Alpha-lactalbumin), Bos d 5 (Beta-lactoglobulin), Bos d 6 (Bovine serum albumin), Bos d 7 (Immunoglobulins), Bos d LF (Lactoferrin)
Egg white allergens	Gal d 1 (Ovomucoid)*, Gal d 2 (Ovalbumin), Gal d 3 (Ovotransferin/conalbumin), Gal d 4 (Egg lysozyme)
Egg yolk allergens	Gal d 5 (Phosvitin/α-livetin), Gal d 6 (Apovitellenins I), Apovitellenins VI/apoprotein B)
Peanut allergens	Ara h 1 (Cupin/vicilin-type,7S globulin)*, Ara h 2 (Conglutin, 2S albumin)*, Ara h 3 (Cupin, 11S globulin)*, Ara h 5 (Profilin), Ara h 6 (Conglutin, 2S albumin)*, Ara h 7 (Conglutin, 2S albumin)*, Ara h 8 (Pathogenesis-related protein), Ara h 9 (Non-specific lipid transfer protein type 1)*, Ara h 10 (Oleosin)*, Ara h 11 (Oleosin)*, Ara h 12 (Defensins), Ara h 13 (Defensins), Ara h 14 (Oleosin)*, Ara h 15 (Oleosin)*, Ara h 16 (Non-specific Lipid Transfer Protein 2)*, Ara h 17 (Non-specific Lipid Transfer Protein 1)*

* Heat stability.

CRD is significant in the monitoring of the natural course of an allergy, in the evaluation of the probability for the acquisition of immunologic tolerance and the regression of symptoms. The probability of "growing out" of the CMP allergy is higher in children with a lower level of sIgE against milk, alpha-lactoglobulin, beta-lactoglobulin, and casein [16]. CRD determination can help in taking the decision on a possible allergen challenge or immunotherapy/desensitization. Kuitunen *et al.* studied profiles of sIgE against milk proteins before and after oral immunotherapy (OIT) in 76 children between 5 and 17 years old. It was indicated that the high level of sIgE against alpha-lactoglobulin, beta-lactoglobulin, and casein was related to the lower probability of OIT success [17].

The occurrence of the rate of allergy to hen egg was estimated at 0.5–2.5% of the population. Its frequency ranks second in children suffering from food allergies [13]. The main allergens of the egg white include ovomucoid, ovalbumin, ovotransferin, lysozyme, and livetin (Table 2) [11].

The resistance of specific proteins to denaturation is clinically significant, because the modification of the allergen structure enables some patients to consume safely products with thermally treated eggs [11]. Ovalbumin and ovotransferin are thermolabile, and lysozyme is moderately resistant to heating, and the ovomucoid, the antigen mostly responsible for clinical symptoms of hypersensitivity, is thermostable. The determination of sIgE for thermosensitive ovalbumin helps in the differentiation of patients reacting to various forms (raw, baked) of eggs (Table 3) [18].

Table 3. Dependence between sIgE concentrations for molecules versus hen egg tolerance.

Positive (low or medium) sIgE against egg white, negative or low sIgE against ovomucoid and ovalbumin → patients can consume eggs in any form.
Positive (low or medium) sIgE against egg white, negative or low against ovomucoid; positive sIgE against ovalbumin → patients do not tolerate raw eggs, but can consume boiled eggs.
Positive (medium or high) sIgE against egg white, increased sIgE against ovomucoid and ovalbumin → patients are sensitive to eggs in any form.

Some studies show that the determination of sIgE to ovomucoid is significant in the predication of the acquisition of tolerance to thermally treated eggs. Ando et al. found that in the case of the concentration of sIgE to ovomucoid amounting to 10.8 kU/l, there is 95% allergy risk to boiled eggs [19]. In another, similar study, the cut-off point was determined at 6.9 kU/l [20]. Patients with persistent allergy to eggs have a higher level of sIgE to ovomucoid and ovalbumin in comparison with children who tolerate eggs [18].

Jessadapakorn *et al.* conducted CRD of allergies to cow's milk and egg white in Thai children with symptoms of sensitivity in order to estimate the dependence

between the clinical symptoms and sensitising allergen, and sIgE against milk and egg white was measured. It was found that casein and beta-lactoglobulin are the most frequent milk allergens in studied children, while for eggs, these are ovomucoid and ovalbumin. In the case of allergy to milk, the concentration of sIgE against casein was higher in patients with urticaria compared to patients with atopic dermatitis. Patients with allergy to egg white, without atopic dermatitis (with symptoms related to the alimentary tract, urticaria, and anaphylaxis in medical history) presented higher concentrations of sIgE to ovomucoid in comparison to patients suffering from atopic dermatitis [21].

Peanuts often cause a severe anaphylactic response to food, and the frequency of sensitization is estimated at 11% in children and 1–2% in adults [22, 23]. They have a rich protein content (25% of the mass), which means a plethora of various potential allergens. In the component diagnostics for an allergy to peanuts, the content of sIgE to molecules Ara h 1–17 with various sensitising potential is determined (Table 2). Thermostable allergens (Ara h 1, 2, 3, 6, 7) show the ability to induce more severe responses compared to thermolabile allergens [11].

The way of product preparation and processing [24] is significant to the severity of anaphylaxis. The most frequent form of peanut consumption, i.e. roasted, is connected with the intensified Ara h 1 and 2 allergic potential, while the cooked peanuts consumed mainly in China have a decreased allergic potential [25, 26].

CRD application helps predict the level of response to peanuts and the efficacy of potential immunotherapy. The double-blinded randomized study showed that Ara h 2 and Ara h 6 are good predictors of severe allergic symptoms [27]. The studies on the application of sublingual immunotherapy (SLIT) in an allergy to peanuts are underway. It was proved that patients with the initial low concentration of sIgE to Ara h 2, Ara h 3, and seed extract are relatively the most susceptible to desensitisation extract [28].

Nonspecific lipid transfer proteins

Anaphylaxis has been associated with certain components, such as seed storage proteins (2S albumins, 7S vicilins, and 11S legumines) or nonspecific lipid transfer proteins (nsLTPs). International Union of Immunological Societies Allergen Nomenclature Sub-Committee cites the list of 41 sensitizing nsLTPs, which derive from fruit, tree and grass pollens, vegetables, peanuts, and natural latex. One of the first described proteins was molecule Pru p 3 found in peaches. Its structure and composition imposes resistance to temperature and pH changes, which means that this protein remains unchanged in the human organism. Three main epitopes binding sIgE were identified, and they are considerably similar to proteins of other plants (e.g., apple, apricot, cherry, strawberry, grape and plum), which indicates the possibility of the

occurrence of cross responses dependent on the similarity level. Symptoms of nsLTP hipersensitivity include the following: oral allergy syndrome (OAS), nausea, vomiting, diarrhoea, urticaria, exacerbation of asthma and anaphylactic response [11, 29].

nsLTP are also described as a risk factor of anaphylaxis induced by physical exercise (food-dependent exercise-induced anaphylaxis, FDEIA) [30]. Calvani *et al.* report a case of a patient with FDEIA in their medical history who consumed products containing popular allergens such as milk, eggs, cacao, and peanuts before physical exercises, but the basic allergic tests showed negative results. Molecular diagnostics revealed the presence of sIgE against Pru p 3 [31]. Avoiding consumption of food that are related to FDEIA before exercise prevents subsequent episodes of anaphylaxis [32, 33].

The paper presents 3 cases of patients with anaphylactic response, and the application of CRD in these patients helped in planning the treatment.

Patient 1

A 4-year-old boy with diagnosed atopic dermatitis and bronchial asthma reported an anaphylactic shock at the age of seven months caused by cow's milk and the exacerbation of bronchial asthma after eating some fruit. The sIgE panel revealed positive results for a dozen or so of foods, and the boy was administered a restrictive diet on this basis (Table 4). The diagnostics was extended by a determination of allergic components (ImmunoCAP ISAC sIgE) to verify the tests. Positive results for main

Table 4. Results of sIgE laboratory tests and dietary recommendation for patient 1.

Food panel (sIgE against extracts)	hazelnut (103 kU/l, Class 6), peanuts (300 kU/l, Class 6), walnut (21 kU/l, Class 4), almond (59 kU/l, Class 5), milk (581 kU/l, Class 6), casein (490 kU/l, Class 6), egg white (5 kU/l, Class 3), egg yolk (11 kU/l, Class 3), celery (234 kU/l, Class 6), carrot (221 kU/l, Class 6), tomato (101 kU/l, Class 6), cod (3,6 kU/l, Class 3), peach (311 kU/l, Class 6), apple 281 kU/l (Class 6), soya 127 kU/l (Class 6), wheat flour (182 kU/l, Class 6), sesame (222 kU/l, Class 6), rye flour (35 kU/l, Class 4)
Diet on the basis of the food panel	Forbidden consumption for: milk, eggs (in any form), nuts, almonds, fruit (peach, apple), vegetables (potato, celery, carrot, tomato), cod, soy, wheat and rye flours, sesame.
CRD (IgE Multiplex FABER)	alpha-lactoglobulin (Bos d 4): 85 ISU-E, beta-lactoglobulin (Bos d 5): 31 ISU-E, casein (Bos d 8): 48 ISU-E); walnut (7S globulin (Jug r 2, storage protein): 17 ISU-E), soy (glycinin (Gly m 6, storage protein): 6,1 ISU-E) hazelnut (Cor a 1.0401): 15 ISU-E, apple (Mal d 1): 21 ISU-E, peach (Pru p 1): 18 ISU-E
Diet on the basis of CRD	Complete ban on consumption of cow milk including products thermally treated, walnut, soy. Cautious consumption of fresh fruit, vegetables and nuts.

allergic components of milk, walnut, and soya were found (Table 4). There were also positive results for the main components of birch inhaled allergens (Bet v 1): 27 ISU-E and grass allergens (Phl p 1: 116 ISU-E, Phl p 2: 3,3 ISU-E, Phl p 5: 132 ISU-E).

Comment

Patient 1 should be recommended a restrictive diet without cow's milk and derived foods, including thermally treated products. Due to the high concentration of milk components (Bos d 8: 48 ISU-E, Bos d 4: 85 ISU-E, Bos d 5: 31 ISU-E) oral allergen challenge is not recommended although 3 years elapsed after the anaphylactic shock. The presence of the above mentioned molecules shows a high risk of surviving cow's milk allergy. There were negative results of tests for the main protein components (Gal d 1, Gal d 2, Gal d 3) and yolk (Gal d 5), which enabled adding eggs to the recommended diet. Reported symptoms of bronchial asthma after fresh fruit can be caused by components from Pathogenesis-related (PR-10) family. Due to the presence of Bet v 1, Phl p 1, Phl p 2, Phl p 5 components, the probability of successful immunotherapy with specific birch and grass allergens is high.

Patient 2

A 35-year-old woman has been a patient of the Center of Clinical and Environmental Allergology of the University Hospital in Krakow since June 2012 due to atopic dermatitis (AD). She has suffered from AD since early childhood. There is no data on CMP allergy in her medical history. She reports rhinitis without dyspnoea in the autumn-winter season. She underwent house dust mite immunotherapy in 1995–1998 with partial relief of symptoms. The family history for atopy is positive, and her mother and her brother have AD. The results of additional tests performed in the clinic were as follows: concentration of total IgE 3429 IU/ml, sIgE egg white: 0.73 kUA/l (Class 2), sIgE egg yolk: 0.34 kUA/l (Class 0), sIgE milk: 34.4 kUA/l (Class 4), sIgE Dermatophagoides pteronyssinus >100 kUA/l (Class 6), sIgE Dermatophagoides fararinae >100 kUA/l (Class 6), sIgE cat: 80.2 kUA/l (Class 5). A dairy-free diet, an oral antihistaminic drug, and local treatment (emollient, corticosteroids, and calcineurin inhibitor) has been ordered.

The patient has remained in periodic control in the clinic. Even though the condition of the skin improved due to the introduced diet, she has had periodic exacerbations, including those requiring hospitalization in the Dermatological Clinic. She has introduced products containing processed goat milk into her diet without any consultations, with good tolerance and without affecting skin lesions as she has claimed.

The patient has had anaphylactic shock three times: June 2015, 2016, and 2017. The symptoms were as follows: utricaria, dyspnea, abdominal pain, and vomiting.

She associates these episodes with the consumption of dumplings with a caramel, bun, and the last episode took place during physical exertion few hours after eating waffle. The results of repeated additional tests were as follows: sIgE milk: Class 6, sIgE casein: Class 6, sIgE egg white: Class 6, sIgE egg yolk: Class 2, sIgE flour: Class 0, sIgE Dermatophafoides pteronyssinus: Class 6, sIgE cat: Class 6.

The diagnostics has been extended to the determination of the allergens' components (IgE Multiplex FABER). Positive components among food allergens were as follows: Bos d 8: 133.54 FIU/ml; Gal d 1: 10.61 FIU/ml, Gal d 2: 13.52 FIU/ml, Gal d 3: 1.61 FIU/ml, and Gal d 4: 4.69 FIU/ml. Positive components among respiratory allergens were positive for house dust mites and cats, as follows: Der f 1: 7.3 FIU/ml, Der f 2: 123.19 FIU/ml, Der p 1: 18.06 FIU/ml, Der p 2: 147.01 FIU/ml, and Fel d 1: 105.05 FIU/ml.

Comment

Patient 2 must undergo a restrictive diet without cow's milk and its derivatives, including thermally treated products. Due to the high concentration of sIgE against Bos d 8, desensitization to cow's milk was not attempted.

There is a 90% homology in the amino acid sequence between cow's milk casein and casein of milk from other mammals, e.g., sheep or goats. It is a cause of frequent cross reactivity [14]. Despite a high concentration of sIgE against Bos d 8, the patient could eat goat's milk without allergic symptoms. It can be attributed to the lower casein content in goat's milk. There are reports on allergies to casein present in milk of a single animal species [34–36]. Besu *et al.* studied concentrations of sIgE against goat milk proteins in patients suffering from recurrent aphthous ulcers associated with allergies to CMP. It was observed that the levels of sIgE against goat's milk were significantly lower than sIgE against CMP. It indicates a possibility of the safe consumption of goat's milk by some patients with CMP allergy [37]. The determination of a high concentration of sIgE against Gal d 1 implies applying an egg-free diet, even if eggs are thermally treated. Due to continued symptoms of allergic rhinitis and the concentration of Der f 1: 7.3 FIU/ml, Der f 2: 123.19 FIU/ml, Der p 1: 18.06 FIU/ml, Der p 2: 147.01 FIU/ml a specific immunotherapy against dust mite allergens is recommended.

Patient 3

A 26-year-old man was consulted at the Center of Clinical and Environmental Allergology of the University Hospital in Krakow due to a one-time loss of consciousness after eating mixed nuts and drinking beer. He reported chronic rhinitis with no concomitant skin lesions or dyspnoea. The patient did not remember his last consumption of nuts, and he did not recall any symptoms after eating his normal

diet. He denied taking medicines or receiving any kind of chronic treatment. SPT of inhalant allergens was positive for grass, rye, birch, filbert, alder, and timothy. The concentrations of sIgE were very high for peanut, sesame, citrus fruit, celery, peach, tomato (Class 6).

The diagnostics has been extended to determination of allergens' components (IgE Multiplex FABER). The results of allergen-specific IgE serum testing were positive for the peanut extract (Ara h: 4.83 FIU/ml) but negative for all of the main peanut molecules (Ara h 1-NT, Ara h 2, Ara h 3, Ara h 6, Ara h 8, Ara h 9, Ara h Agglutinin). Increased levels of sIgE were measured against nsLTP molecules of walnut (Jug r 3; 0.58 FIU/ml), peach (Pru p 3; 2.13 FIU/ml), hazelnut (Cor a 8; 4.33 FIU/ml), pomegranate (Pun g 1; 1.5 FIU/ml), and maze (Zea m 14; 1.17 FIU/ml).

Comment

In Patient 3, a positive result of sIgE for peanut extract was obtained, while sIgE for the determined allergen components (Aha h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8.0101, Ara h 9, Ara h Agglutinin) were not present. The positive result for sIgE related to the extract could be caused by a cross reaction with inhaled allergens or an allergy to a molecule not determined in the conducted tests [11].

During the medical interview, our patient mentioned the consumption of alcoholic drinks which could contribute to the occurrence of response to nut mixture. The European Anaphylaxis Registry reports that alcohol can be a cofactor of as many as 15% of responses [38].

Detection of sIgE against nsLTP present in peach (Pru p 3), hazelnut (Cor a 8), walnut (Jug r 3), grenade fruit (Pun g 1), and maze (Zea m 14) enabled a precise formulation of dietary recommendations. The patient must avoid food containing nsLTP, especially in the presence of anaphylaxis cofactors.

Summary

CRD is a new diagnostic method that employs the determination of sIgE against specific allergen molecules, thus increasing the specificity of the test [39]. In this way, dietary recommendations can be verified that are very significant in the context of indications found during medical interviews for patients with anaphylactic shock. The diet should eliminate potentially dangerous foods, but it should also maintain the patients' life quality to the maximum extent [40].

Contribution statement

MB contributed to the concept and design of the article, enrolled patients, and approved the final version of the manuscript, DB wrote the description of patient 1 with a comment, ML wrote the description of patient 2 with a comment, WM and AW wrote the description of patient 3 with a comment, JS and MC wrote introduction, EC contributed to the concept and design of the article, and read and approved the final version of the manuscript.

Funding

The study project was financed from the statutory task fund of Jagiellonian University Medical College K/ZDS/007936.

Conflict of interest

None declared.

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