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Severe atopic dermatitis in a boy with potato allergy

Ciężki przebieg atopowego zapalenia skóry u chłopca uczulonego na alergeny ziemniaka

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Abstract

Food allergy is an important problem in the paediatric population. Food products that are most likely to induce allergic reactions include cow's milk, wheat, peanuts, hen's eggs, fish and seafood. Food-allergy-related diseases include, among other things, atopic dermatitis, urticaria and asthma. Anaphylactic shock is the most severe form of allergic reaction. Intramuscular adrenalin at a dose of 0.01 mg/kg body weight (maximum dose 0.3–0.5 mg) is the primary treatment for anaphylaxis. An elimination diet is the treatment of choice in food allergy. If symptoms persist despite dietary intervention, extended diagnosis using skin prick tests and/or specific IgE measurements should be performed. We present a clinical case of a 2.5-year-old boy with erythroderma secondary to atopic dermatitis, who was referred to our Department due to the lack of improvement after outpatient treatment. It was found during hospital stay that the symptoms were caused by potato allergens.

Keywords: atopic dermatitis, potato allergens, food allergy, erythroderma, IgE

Streszczenie

Alergia pokarmowa jest istotnym problemem wśród populacji dziecięcej. Do produktów spożywczych, które najczęściej wywołują reakcje alergiczne, zaliczają się: mleko krowie, pszenica, orzechy ziemne, jajo kurze, ryby i owoce morza. Choroby związane z alergią pokarmową to między innymi: atopowe zapalenie skóry, pokrzywka lub astma. Najcięższą postacią reakcji alergicznej stanowi wstrząs anafilaktyczny. Podstawowym lekiem stosowanym w leczeniu anafilaksji jest adrenalina w dawce 0,01 mg/kg m.c. (maksymalnie 0,3–0,5 mg) podawana domięśniowo. Leczeniem z wyboru alergii pokarmowej jest dieta eliminacyjna. W przypadku objawów utrzymujących się mimo zastosowania interwencji żywieniowej należy rozszerzyć diagnostykę, wykorzystując punktowe testy skórne i/lub przeciwciała IgE swoiste. W pracy przedstawiono przypadek kliniczny 2,5-letniego chłopca z erythrodermią w przebiegu atopowego zapalenia skóry, skierowanego do Kliniki autorów z powodu braku poprawy w leczeniu ambulatoryjnym. W przebiegu hospitalizacji udało się ustalić, że przyczyną objawów u dziecka były alergeny ziemniaka.

Słowa kluczowe: atopowe zapalenie skóry, alergeny ziemniaka, alergia pokarmowa, erythrodermia, IgE

INTRODUCTION

Food allergy is an undesirable, repetitive and reproducible body's immune reaction to food. The body's immune response includes type 1 reaction (early, IgE-mediated) and type 4 reaction (late, cellular reaction). Similar reactions to food may be due to food intolerance; however, immune mechanisms are not involved in these responses. Secondary deficit in digestive enzyme activity (e.g. adult hypolactasia) is an example of intolerance. Symptoms of food allergy may involve almost all body systems, e.g. the skin (atopic dermatitis, urticaria, angioedema), the respiratory system (rhinitis, asthma), the gastrointestinal tract (vomiting, abdominal pain, diarrhoea and gastroesophageal reflux), as well as systemic reactions.

Anaphylactic shock is the least common, but at the same time, the most severe allergic reaction⁽¹⁾. Anaphylaxis is a severe, life-threatening, systemic or generalised rapid hypersensitivity reaction, which may be fatal. Food allergens are the main triggers of this type of reactions. Airborne allergens, hymenoptera venom, or latex are less common causative factors. Adrenaline administered intramuscularly into the lateral quadriceps of the thigh at a dose of 0.01 mg/kg body weight (maximum dose 0.3–0.5 mg) is the primary treatment for anaphylaxis. Adrenaline doses may be repeated every 5–15 minutes⁽²⁾.

The diagnosis of food allergy uses both skin prick tests, patch (contact) tests, specific IgE measurements, as well as provocation tests. An elimination diet is the treatment of choice⁽¹⁾.

Food products that are most likely to induce allergic reactions include cow's milk, wheat, peanuts, hen's eggs, fish and seafood⁽³⁾. In everyday medical practice, however, it should be also remembered about much more common products, which are less often suspected of causing food allergies. Potato is an example of such a food product. The incidence of potato allergy ranges between 2.5 and 14.5%⁽⁴⁾.

CASE REPORT

A 2.5-year-old boy was admitted to the Department of Paediatrics, Paediatric Nephrology and Allergology, Military Institute of Medicine due to highly severe skin lesions in the lower limbs with a tendency to generalise, which were accompanied by severe pruritus of the skin.

Medical history revealed erythematous skin lesions on the cheeks, which had occurred since infancy and intensified after milk intake. IgE antibodies specific for selected allergens were measured in the first year of life due to increased occurrence of skin lesions. Increased levels of antibodies against allergens of cow's milk protein, nuts and egg white were observed. Total IgE was measured and was 5,000 IU/mL (normal: 50 IU/mL). At the age of 2 years, the boy suffered from obstructive bronchitis twice and had an episode of anaphylactic shock after consuming goat's milk. A month later, the child was hospitalised for lower gastrointestinal

bleeding. Coeliac disease was excluded at that time. The boy was breastfed until 24 months of life. There was positive family history for allergy, with an allergy to cow's milk protein in his 5-year-old brother.

On admission, the child was on a dairy-free, egg-free and nut-free diet. Physical examination showed severe erythematous-papular eruptions all over the body with lichenisation and excoriations. Extensive dermatitis covered more than 90% of the boy's body surface, which could be classified as erythroderma. Furthermore, the child presented with cervical, occipital, axillary, and inguinal lymphadenopathy, with soft and mobile lymph nodes.

Laboratory findings included leukocytosis ($20 \times 10^3/\mu\text{L}$) and eosinophilia ($2.27 \times 10^3/\mu\text{L}$); other inflammatory parameters were within the laboratory limits (ESR: 2 mm after 1 hour, C-reactive protein, CRP: 0.0 mg/dL). Serum IgE was measured as part of diagnosis for allergic atopy, and was elevated (9,225 IU/mL; normal for age: 50 IU/mL).

Diagnosis for enteropathies and immune deficiency was performed. The protein fraction pattern was unremarkable. The levels of IgA (25 mg/dL), IgG (978 mg/dL), IgM (93 mg/dL), as well as C3 (93 mg/dL) and C4 (22 mg/dL) components of the complement system were within limits of normal. Serum levels of 25(OH)D (43.0 ng/mL) were also normal. Netherton's syndrome, an autosomal recessive genetic disorder combining primary immunodeficiency, erythroderma, atopy and hair fragility was excluded.

Serology was performed due to generalised lymphadenopathy, and excluded cytomegalovirus (CMV), Epstein-Barr virus (EBV), *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Toxoplasma gondii* infections. General urine test showed no signs of infection. No parasites were detected in the stool. Enzyme-linked immunosorbent assay (ELISA) for *Toxocara canis* was negative. Based on the clinical picture and laboratory findings, the boy was diagnosed with allergic atopic dermatitis, which particularly intensified after contact with food allergens. It was the cause of generalised erythrodermic skin lesions in the child.

Symptomatic treatment was included for extensive skin lesions. Topical cholesterol ointment with hydrocortisone 1%, baths in potassium permanganate and starch were used. The skin was lubricated with emollients. Oral desloratadine 1×5 mL or rupatadine 1×2.5 mL was used for pruritus. Furthermore, the child's diet was continued while awaiting the results of IgE food panel. Oral prednisone at 2×5 mg and diazepam at 2×2.5 mg were included due to lack of improvement after 2 days of treatment. Mupirocin ointment was applied topically to severe skin lesions. Local skin improvement was achieved.

On the next day of hospitalisation, laboratory findings showed high levels of IgEs specific for egg white and yolk, cow's milk protein (class 5), hazelnut (class 6) and potato (class 5), which was one of products included in the anti-allergy elimination diet. Due to the strong immune response to the potato allergen, a decision was made to eliminate it from the boy's diet and discontinue starch baths.

Parameter measured		Hospital stay 1, February 2016	Hospital stay 4, December 2016	Hospital stay 5, June 2017	Hospital stay 6, July 2018
CRP [mg/dL] (normal 0–0.8)		0.0	0.1	<0.1	0.1
Serum WBC [$\times 10^3/\mu\text{L}$]		20.00	10.93	12.11	7.85
Serum eosinophils [$\times 10^3/\mu\text{L}$]		2.27	0.67	0.22	0.14
Total IgE [IU/mL]		9,225	2,448	1,707	3,457
Specific IgE [kU/L]; (class)					
Food allergy panel	Potato (f35)	72; (5)	49; (4)	15.4; (3)	14.9; (3)
	Egg white (f1)	99; (5)	62; (5)	39; (4)	78; (5)
	Egg yolk (f75)	63; (5)	22; (4)	14.1; (3)	26; (4)
	Cow's milk (f2)	97; (5)	35; (4)	52; (5)	64; (5)
	Soy (f14)	2.2; (2)	0.45; (1)	0.41; (1)	0.44; (1)
	Peanut (f13)	2.6; (2)	<0.35; (0)	<0.35; (0)	0.44; (1)
	Hazelnut (f17)	>100; (6)	89; (5)	74; (5)	56; (5)
	Almond (f20)	1.0; (2)	<0.35; (0)	<0.35; (0)	2.2; (2)
	Tomato (f25)	0.36; (1)	<0.35; (0)	<0.35; (0)	<0.35; (0)
	Carrot (f31)	1.0; (2)	<0.35; (0)	<0.35; (0)	<0.35; (0)
	Celery (f85)	0.53; (1)	<0.35; (0)	<0.35; (0)	<0.35; (0)
Airborne allergy panel	Sweet vernal grass (g1)	5.0; (3)	22; (4)	17.4; (3)	25; (4)
	Cock's-foot grass (g3)	7.8; (3)	47; (4)	38; (4)	46; (4)
	Timothy grass (g6)	1.0; (2)	17.4; (3)	18; (4)	33; (4)
	Rye (g12)	1.5; (2)	25; (4)	39; (4)	34; (4)
	Alder (t2)	<0.35; (0)	0.53; (1)	42; (4)	55; (5)
	Birch (t3)	<0.35; (0)	13.3; (3)	69; (5)	99; (5)
	Hazel (t4)	<0.35; (0)	<0.35; (0)	4.2; (3)	67; (5)
	House dust mites (d2)	5.0; (3)	22; (4)	18; (4)	49; (4)
	Cat's fur (e1)	<0.35; (0)	11.2; (3)	8.1; (3)	48; (4)
	<i>Penicillium notatum</i> (m1)	2.4; (2)	0.36; (1)	<0.35; (0)	2.1; (2)
	<i>Cladosporium herbarum</i> (m2)	1.5 (2)	<0.35; (0)	<0.35; (0)	<0.35; (0)
	<i>Aspergillus fumigatus</i> (m3)	0.53; (1)	0.45; (1)	<0.35; (0)	<0.15; (0)
	<i>Alternaria alternata</i> (m6)	0.53; (1)	0.36; (1)	<0.35; (0)	<0.35; (0)

Tab. 1. Selected test results from subsequent hospital stays of the described patient with atopic dermatitis

Inflammation and pruritus subsided already on the first day of treatment. On day 4, a significant improvement in the condition of the skin and reduction of its dryness were observed.

The boy was discharged home in good general condition after 6 days of hospital stay. Potatoes were permanently excluded from the child's diet. Continuation of antipruritic and anti-inflammatory treatment with prednisone was recommended, with gradual dose reduction over the following 2 weeks.

Since the first hospitalisation, the boy was hospitalised in the Department five more times for follow-up examinations (Tab. 1). The diet and pharmacological treatment contributed to skin improvement and caused almost complete pruritus resolution, which had a calming effect on the boy and enabled normal psychophysical development. Physical examination still showed dry skin with a tendency

to lichenise, as well as cervical, occipital, axillary, and inguinal lymphadenopathy. However, no recurrence of generalised dermatitis was observed. Inflammatory markers (serum CRP and white blood cells) were within the limit of normal. Minor persistent eosinophilia and elevated total IgE were found. High titres of antibodies against food allergens, such as hazelnut, egg white, cow's milk protein (class 5), egg yolk (class 4), and potato (class 3), were still observed.

At the age of 4 years, the boy developed two episodes of dyspnoea. Based on the clinical picture and good response to inhaled corticosteroids, early childhood asthma was diagnosed. During his last (sixth) hospitalisation, the boy presented with erythematous fine papular skin lesions located in the popliteal and elbow fossa. Catarrhal lesions of the nasal mucosa were also found. A follow-up panel of inhaled allergens showed very high levels of IgEs specific for

hazel, birch, alder (class 5) and sweet vernal grass, cock's-foot grass, timothy grass, rye, house dust mites, and cat hair (class 4).

The boy was diagnosed with atopic dermatitis, food allergy, inhaled allergy and asthma. He received effective antipruritic treatment, nebulized budesonide $2 \times 250 \mu\text{g}$ and mometasone 0.05 mg in the form of a nasal spray. Further skin care with emollients, topical cholesterol ointment and continuation of the elimination diet were recommended. The child remains under the care of the Department.

DISCUSSION

Food allergy is an important clinical problem in the paediatric population. It may manifest cutaneously as urticaria⁽⁵⁾ or atopic dermatitis. The response to food allergens occurs within several hours after exposure in the case of immediate, IgE-mediated response or several days in the case of cellular IgE-independent response. Dermatitis manifests in increased erythema and pruritus⁽⁶⁾.

In some cases, generalised inflammation covering more than 90% of the skin, i.e. erythroderma, develops⁽⁷⁾. Such a clinical picture was observed in our 2.5-year-old patient. Erythroderma in atopic dermatitis should be differentiated from other forms of eczema and dermatitis, such as seborrhoeic dermatitis, psoriasis, immunodeficiency or Netherton's syndrome⁽⁷⁾. The treatment of mild-to-moderate forms of atopic dermatitis involves topical application of emollients, ointments, and ointments containing glucocorticosteroids and calcineurin inhibitors, as well as antipruritic therapy. Systemic immunosuppression with oral glucocorticosteroids, cyclosporine or azathioprine is used in severe and generalised cases⁽⁸⁾. European Medicines Agency (EMA) approval of dupilumab, an interleukin-4 receptor antagonist which is currently used in adults only, in July 2017 was a breakthrough in the treatment of severe atopic dermatitis⁽⁹⁾. Food allergy, which is still associated with the risk of developing a life-threatening condition, i.e. anaphylaxis, can still be managed only by avoiding the allergen (an elimination diet) and symptomatic treatment⁽¹⁰⁾. In the presented clinical case, an elimination diet free of cow's milk protein, eggs and nuts was used in the boy. It should be noted, however, that there are other common food products that may induce food allergy. A potato is one of these products.

Potatoes (*Solanum tuberosum*) are a staple food plant cultivated around the world. They were brought to Europe from South America at the end of the 16th century. Introduced into the diet of an infant between 17 and 26 weeks of age, they are one of the first supplementary products in this diet⁽¹¹⁾.

Hypersensitivity to raw potatoes in the adult population (mainly in restaurateurs, cooks and housewives) most often manifests in the form of oral allergy syndrome (OAS). It is a set of symptoms caused by the contact between a food allergen and the oral cavity and the pharynx, which is associated with IgE-mediated response triggered by cross-reacting protein determinants found in pollen, fruits

and vegetables⁽²⁾. Since allergens responsible for this type of response are thermosensitive (PR-10 proteins, profilins), cooked potatoes do not cause allergic reactions^(12,13). Profilins and PR-10 proteins belong to panallergens – a conserved group of proteins present in most plant species. Their structural similarity is the cause of cross-reactions between distantly related species. Bet v1, the major birch allergen, is an example of PR-10 protein. Profilins are represented by Bet v2 (birch) and Phl p12 (timothy grass)^(14–16). Allergy to thermally processed potatoes is observed only in the paediatric population. Seppälä et al.⁽¹⁷⁾ identified patatin, a storage protein of potato (Sola t 1), as one of the primary potato allergens. Patatin is a thermostable protein, which retains its allergenic properties despite heat or digestive enzyme activity. A number of studies have shown that this is not the only allergen found in potatoes. There are 6 different allergens responsible for the allergenic properties of potatoes: Sola t 2 – aspartyl protease inhibitor, Sola t 3 – cystatin, Sola t 4 – serine protease inhibitor, Sola t 8 – profilin, Sola t glucanase, and Sola t 1, which is still the main allergen⁽⁴⁾.

Many studies focus on the assessment of the type and incidence of allergic symptoms in children with cooked potato allergy. De Swert et al.⁽¹³⁾ showed that allergic eczema, which was found in 16 out of 17 patients with potato allergy, was the most common clinical manifestation. Gastrointestinal symptoms, wheezing and rhinitis were the second most common manifestations. Only 2 out of 17 children developed anaphylaxis in response to potato allergens. The majority of children participating in this study developed tolerance to potatoes at 4 years of age. It was also found that hypersensitivity to potato allergens is a risk factor for allergy to pollen in the child. The authors suggest considering an allergy to boiled potatoes in the differential diagnosis of children with atopy. Similar conclusions may be drawn from a paper by Dogru et al.⁽¹⁸⁾, who conducted a retrospective analysis of 40 children with potato allergy. Allergic eczema was the most commonly reported symptom (33 children). Severe anaphylaxis was observed in 4 cases. This indicates a strong relationship between hypersensitivity to potatoes and allergic eczema.

There is an increasing number of clinical case reports of children with cooked potato allergy. Martín-Muñoz et al.⁽¹⁹⁾ reported a case of a 21-month-old boy with allergy to potato skin Sola t 4 allergen. Eke Gungor et al.⁽⁵⁾ reported a case of a 3-year-old boy, while Monti et al.⁽²⁰⁾ described a case of an 8-month-old infant with atopic dermatitis. The latter authors also pointed to diagnostic difficulties in distinguishing between an anaphylactic reaction and a severe form of intestinal inflammation caused by food proteins⁽²⁰⁾. Despite severe symptoms of potato allergy, the child developed tolerance at the age of 3 years. This corresponds with the findings presented by De Swert et al.⁽¹³⁾.

In our clinical case, severe atopic dermatitis was caused by exposure to an atypical allergen – potato allergen, which is often the primary component of an elimination diet in clinical practice. In the event of lack of improvement following

a standard elimination diet, the suggested procedure is to extend the diagnosis to include atypical allergens, such as potato allergens. Several years of follow-up in the child showed how the allergen profile which triggered the symptoms changed and how the allergy pattern evolved – from skin lesions caused by food allergens to asthma and allergic rhinitis caused by airborne allergens.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organisations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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