Anaphylaxis following the consumption of pumpkin seeds in a two-year-old child tolerant to its pulp – a case study and a minireview

Julia Gawryjolek

Nicolaus Copernicus University Faculty of Medicine: Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy

Hanna Ludwig

Nicolaus Copernicus University Faculty of Medicine: Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy

Magdalena Żbikowska-Gotz

Nicolaus Copernicus University Faculty of Medicine: Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy

Zbigniew Bartuzi

Nicolaus Copernicus University Faculty of Medicine: Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy

Aneta Krogulska (✉ aneta.krogulska@cm.umk.pl)

Nicolaus Copernicus University in Torun: Uniwersytet Mikołaja Kopernika w Toruniu <https://orcid.org/0000-0002-5280-1876>

Case report

Keywords: pumpkin, seeds, pulp, food allergy, anaphylaxis, cross reactivity, child, case report

Posted Date: November 24th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-112102/v1>

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Abstract

Background

Pumpkin and its seeds are increasingly consumed by children for their potential health benefits. Each day, around 30% of teenagers consume nuts and seeds, including pumpkin seeds. However, there is some evidence that pumpkin seeds may exert allergenic effects and induce severe life-threatening anaphylaxis. Allergy for melon, cucumber, and zucchini, which belong to the same Cucurbitaceae family as pumpkin, are well known, opposite to pumpkin allergy. Few descriptions of allergic reactions associated with pumpkin have been published, especially in children. To date, three cases of pumpkin pulp and two seed cases have been reported among children. Our case report describes a case of pumpkin seed anaphylaxis in a child with good tolerance of pulp.

Case presentation

In the present study, a two-year-old child experienced anaphylaxis: generalized urticaria, swollen lips and increasing dyspnea following the consumption of pumpkin seeds. The history showed that although the child had been receiving elimination diet because of atopic dermatitis, the basic dietary element was pumpkin pulp. The skin-prick test was positive for pumpkin seeds (5 mm) but negative for pumpkin pulp (1 mm); allergen-specific IgE was 1.34 kUA/L for seed, and 0.37 kUA/L for pulp. The component resolved diagnosis found IgE to sesame seed, buckwheat and walnut (storage proteins). Based on these findings, severe anaphylactic reaction to pumpkin seeds was identified.

Conclusions

It is possible to develop pumpkin seed anaphylaxis in a child with a tolerance to pumpkin pulp. Pumpkin seeds allergens have not been well characterized. Homology between the amino acid sequences in storage proteins may indicate cross reactivity between different edible seeds and nuts.

Background

Like flax, poppy, sesame and sunflower seeds, pumpkin seeds are increasingly consumed for their potential health benefits. Their polyunsaturated fatty acid content bestows cardioprotective effects, and their phytosterols possess antioxidant, anti-inflammatory and immunomodulatory properties [1]. Each day, around 32.4% of teenagers consume nuts and seeds, including pumpkin seeds [2, 3]. However, there is some evidence that pumpkin seeds may exert allergenic effects and induce anaphylaxis. Few descriptions of allergic reactions associated with pumpkin have been published, especially in children [1,4–6].

Case Presentation

A two-year-old boy was referred to hospital for generalized urticaria, swollen lips and increasing dyspnea, observed around 10 minutes after eating pumpkin seeds for the first time in his life. Severe anaphylactic reaction was diagnosed.

Interview revealed a negative family history for allergies. The boy was born at 32 Hbd, body mass 1150 g/intrauterine hypotrophy; the pregnancy was the first one for the mother; delivery was by Caesarean section, Apgar score six points. From the age of two months, the child displayed loose stools and skin lesions characteristic of moderate atopic dermatitis (AD), with periodically-observed severe courses of AD. The child was breastfed up to five months of age (the mother was on a dairy-free and egg-free diet) followed by extensively hydrolysed formula based on whey protein at the end of breastfeeding. Due to persistent skin lesions (moderate-severe), an elimination diet was extended to the following months of life: wheat flour, soybean, carrot, apple, celery, pear, corn, broccoli and potato were excluded. At 15 months, the diet comprised whey hydrolysate, millet, rice, turkey, rabbit, watermelon, peach and bananas.

At around 16 months, the child entered the care to the Allergology outpatient clinic. It was proposed that the diet should be expanded to include potato, corn, broccoli and pumpkin pulp, which was introduced into the diet and well tolerated. From the age of 16 months, the pumpkin pulp become one of the most favourite meals; it was the basic dietary element and eaten daily in large

quantities. Until the age of two years, apart from the observed exacerbations of AD, no other symptoms were observed. The child had been receiving topical treatments and elimination diets.

At the age of 2.5 years, while at home, the child experienced a sudden episode of anaphylaxis within 10 minutes of consuming pumpkin seeds shelled by his mother. Generalized urticaria, lip swelling and dyspnoea were observed. Adrenaline, systemic glucocorticosteroids, salbutamol and antihistamines were administered at a nearby hospital, and the symptoms regressed. A pumpkin seed elimination diet was initiated. After the incident, the child was referred to our Clinic (the Department of Paediatrics, Allergology and Gastroenterology) for diagnosis. During his stay in the clinic, the only deviation from the norm during physical examination was the presence of mild symptoms of AD (Scorad 20 points). The skin-prick test (SPT) based on the prick-by-prick method was positive for raw pumpkin seeds (5 mm) but negative for roasted pumpkin seed (2 mm) and pumpkin pulp (1 mm); total IgE was 111.8 kU/L, allergen-specific IgE (asIgE) was 1.34 kUA/L for seed, and 0.37 kUA/L for pulp. In addition, asIgE against cow milk (20 kUA/L), egg white (6.3 kUA/L), sesame (0.78 kUA/L) and hazelnut (2.0 kUA/L) were identified. The component resolved diagnosis (CRD) found medium to high level IgE to cow's milk protein, egg white, sesame seed and buckwheat (ISAC test). Sensitization to inhalant allergens was also determined: the ISAC test revealed Der p 1 (7.7 ISU-E), Der f 1 (10 ISU-E), Phl p 1 (7.5 ISU-E). *Alternaria alternata* asIgE was present at serum concentrations of 0.72 kUA/L and birch pollen asIgE at 0.68 kUA/L (Table 1).

Table 1
Patient SPT, aslgE and CRD results.

ALLERGY TEST							
SPT*		aslgE [^]		CRD [#]			
Allergen extracts	Diameter (mm)	Allergen extracts	Concentrations (kUA/L)	Allergens			ISU-E ISAC
FOOD ALLERGENS							
Pumpkin seed	5	Pumpkin seed	1.34				
Pumpkin pulp	1	Pumpkin	0,37				
		Cow milk	20.0	Cow milk	Alpha-lactalbumin	Bos d 4	6.4
		Egg white	6.3		Casein	Bos d 8	2.5
		Egg yolk	0.40		Beta-lactoglobulin	Bos d 5	1.4
		Sesame	0.78	Egg white	Ovalbumin	Gal d 2	5.1
		Wheat flour	0.48		Conalbumin/Ovotransferrin	Gal d 3	1.8
		Peanut	0.44		Ovomucoid	Gal d 1	1.7
		Hazelnut	2.0	Buckwheat	2S albumin	Fag e 2	7.0
				Sesame	2S albumin	Ses i 1	2.3
				Walnut	7S globulin	Jug r 2	0.4
INHALANT ALLERGENS							
		D. pteronyssinus	0.33	D. pteronyssinus		Der p 1	7.7
		D. farinae	0.26	D. farinae		Der f 1	10
		Phleum pratense	0.16	Phleum pratense		Phl p1	7.5
*SPT – skin prick tests (using the prick by prick method); wheal diameter: positive control – 4 mm; negative control – 1 mm							
[^] aslgE – allergen-specific IgE antibodies (ImmunoCAP-FEIA, Sweden) (bold ≥ 0.7 kUA/L, i.e. ≥ 2 class)							
[#] CRD – component-resolved diagnostics (ImmunoCAP ISAC kits; Thermo Fisher Scientific, U.S.)(bold ≥ 0.9 ISU-E, i.e. moderate/high/very high)							

Based on the history, symptoms and results of the testing, anaphylactic reaction to pumpkin seeds was identified. A pumpkin seed elimination diet was recommended. In addition, it was planned to verify previous elimination diets and continue AD treatment. Currently, the child eats a standard diet apart from grains, peanuts, tree nuts, raw egg white and raw milk. It is planned

to perform further oral food challenges and to gradually broaden the diet; however, the mother of the child has strong concerns and reservations in this regard.

During follow-up, allergic asthma was diagnosed at the age of three years: the asthma is mild and seasonal, but well controlled. At the age of five years, the child is sensitized to birch pollen (> 100 kUA/L), gray alder pollen (1.9 kUA/L), rye pollen (0.96 kUA/L), timothy grass (0.48 kUA/L), *D. pteronyssinus* (30 kUA/L), *D. farinae* (15 kUA/L) and *A. alternata* (3.1 kUA/L). He receives medication during the allergy season i.e. spring (April/May) (montelukast and fluticasone 2×125 µg inhaled while walking). Exacerbations of asthma are also experienced after exercise. Since three years old, the AD has remained in remission, although it worsens around spring. On one occasion, a rash was observed on the skin following contact with raw milk. The anaphylactic reactions have not recurred.

Discussion And Conclusions

Pumpkin belongs to the Cucurbitaceae family, which comprises about 120 genera and 760 species of plants. Allergy for melon, cucumber, and zucchini are well known, opposite to pumpkin allergy (all Cucurbitaceae family) [7, 8]. For pumpkins, the pulp, skin and seeds all elicit allergic responses [7]; however, individual case studies mainly report seed allergies (Table 2) [1, 4–7, 9–12]. Among children, three cases have been reported for pumpkin pulp and two for seeds [1, 4–6].

Table 2
Pumpkin seed allergy - summary of published case reports.

References	Child	Adult	Pumpkin		Symptoms	Atopy	SPT		sIgE		OFC
			flesh	seeds			flesh	seeds	flesh	seeds	
Chatain et al [1] 2017	8 y ♀			+	grade 3 anaphylaxis with deep faintness, vomiting, facial and pharyngeal edema	+	-	+	-	3.75 KU/L	
Caubet et al [4] 2010	11 y ♂			+	urticaria, angioedema and dyspnea	+		-			+
Hagendorens et al [5] 2009	2.5 y ♂		soup		vomiting, coughing, dyspnea, urticaria and angioedema		+			25.20 KU/L	
La Shell et al [6] 2010	18 y ♂ 8 y ♀		cake contact with pumpkin		generalized pruritus, shortness of breath, and throat tightness; nasooocular pruritus, sneezing, eyelid swelling, and chest tightness while carving a pumpkin	+	+	+		33.50 KU/L	
Figueredo et al [7] 2000		28 y ♀	soup		several episodes of itching of the mouth, angioedema of the lips and face, generalized itching, and mild dyspnea		+				+
Fritsch et al [9] 1997		49 y ♀ 29y ♀ 46y ♀		+	oropharyngeal itching and swelling, dyspnea	+		+			+ (2 class) + (2 class) + (2 class)

References	Child	Adult	Pumpkin		Symptoms	Atopy	SPT		sIgE		OFC
			flesh	seeds			flesh	seeds	flesh	seeds	
Doll et al [10] 2017		70 y ♀		+	nausea, sense of impending doom, syncopal episodes, consciousness, shock	+		+			
Rodríguez-Jiménez et al [8] 2011		33 y ♀		+	facial oedema, erythema, dyspnea	+		+			
Baur et al [12] 2002		18 y ♀ and 3 years later		+	oropharyngeal swelling and dysphagia, contact urticaria						

Our report is a valuable complement to previous studies in which children experienced anaphylaxis after ingestion of seeds, with good tolerance of pulp [1, 4–6]. Another two children experienced anaphylaxis after consuming the pulp in the form of pumpkin soup or cake [5, 6].

Although pumpkin allergy (PA) usually develops following consumption, reports suggest the possibility of exposure through skin contact and/or inhalation of raw pumpkin or pumpkin seed allergens, e.g. while carving pumpkin [6, 9, 13]. Also, PA appears to be more common in males, especially atopic patients; our patient is a boy with co-existing AD and asthma.

Among adults, only one case with anaphylaxis to pumpkin flesh has been described, and six with anaphylaxis to pumpkin seeds (Table 2) [6, 12].

PA can range from mild oral symptoms to severe life-threatening anaphylaxis. Most reactions are mild, manifesting as only local symptoms in the mouth and throat [7]. However, some patients display vomiting, angioedema (face and throat), urticaria, erythema, dyspnoea, syncope and shock [1, 4, 10, 11]. Pumpkin pulp allergy can also manifest as food protein induced enterocolitis syndrome [14].

Similar to our case, most previous patients displayed positive prick-by-prick ST for pumpkin seeds, and positive serum asIgE for pumpkin seeds. The high allergenic potential of pumpkin seeds means that allergy symptoms, including severe anaphylaxis, can occur at low asIgE levels. In addition, it is important to consider pumpkin seed allergy in patients with an unclear history of anaphylaxis, even following a negative SPT [4].

In our patient, the interview was unambiguous, i.e. symptoms appeared immediately after the consumption of pumpkin seeds shelled from pumpkin by the child's mother, and tests confirmed IgE sensitization. Hence, the food challenge test was abandoned.

Some patients with PA have cross sensitization to plants from the Rosaceae and Cucurbitaceae families and to pollen such as ragweed [6].

The development of pumpkin seed allergy is not precisely understood as the allergens have not been well characterized [1, 11]. Immunoblotting has identified proteins with a molecular weight of 14 kDa, possibly a profilin homologue, and 12 kDa, possibly an LTP homologue, in the sera of patients with pumpkin seed allergy [9, 11]. In the present patient, CRD did not identify asIgE for the cross-reactive panallergens LTP and profilin, which may indicate that other proteins are involved in the anaphylactic reactions, e.g. 2S albumin, 7S and 11S globulin; these are highly anaphylactogenic storage proteins present in the seeds of many plants, including sesame and sunflower [15].

Sensitization to cross-reacting allergens may contribute to exacerbations of food allergy; however, the testing performed at 2,5 years did not indicate the possibility of cross-reactivity to liable allergens. Only a very low concentration of sIgE to birch pollen and a high level anti-Phl p 1 antibodies (the main allergen marker of sensitivity to various grasses such as Timothy grass) were found.

Co-factors may play a significant role in the development of anaphylactic reactions, including those associated with pumpkin seeds. While squash-dependent anaphylaxis has previously been observed in a child following exercise [16], the anaphylactic reaction observed in our patient was not accompanied by any additional factors which could enhance systemic reaction, such as exercise or medications.

High and medium asIgE levels were found for 2S sesame seed and buckwheat albumin, suggesting their presence in pumpkin seeds. 2S albumin proteins are present in peanuts, some tree nuts and many seeds (including sunflower and sesame seeds), and due to their disulphide bonds and glycosylation, they can cause severe IgE-dependent allergic reactions [11, 15]. PA has been found to co-occur with allergies to sunflower, poppy, almond and hazelnut seeds [1, 11].

Anaphylaxis case reports show that symptoms may develop after eating roasted seeds, indicating high allergen thermostability [1, 4, 10]. The prick-by-prick test with roasted pumpkin seeds was negative in our subject. The negative test result rules out the possibility that storage proteins may play a role, due to their exceptional stability; however, it does not negate the potential role played by other protein allergens. In a similar way to peanuts, raw pumpkin seeds contain specific allergens, together with a suitable epitope composition, while roast seeds may possess proteins with different allergenicity: roasting may lead to the development of new epitopes, which are not recognised by the asIgE prepared for the raw pumpkin seeds. However, little data is available on this topic.

In addition, the activity of other potential allergens, such as LTP proteins and oleosins, which are also found in other seeds (e.g. peanuts, hazelnuts, sesame seed, soya and sunflower) should also be taken into consideration. LTP proteins show relatively low amino acid sequence homology with allergenic LTP proteins from other sources, and therefore may not give a positive result for other LTPs in the ISAC test. Both the oleosins and LTP demonstrate less resistance to thermal processes than storage proteins, which may be the cause of a negative prick-by-prick test result based on roast pumpkin seeds. It is not possible to rule out the possibility that these proteins may have played a role in the sensitisation of our patient. Therefore, it appears certain that these proteins present in raw pumpkin seed participated in the anaphylactic reaction in the described patient.

In our case report, asIgE was found for the walnut allergen Jug r 2–7S globulin. The 7S and 11S globulin proteins are contained in the seeds of legumes (soybeans, peanuts), also in tree nuts and sesame seeds. Hazelnut allergen Cor a 9 11S globulin asIgE has previously been identified in an eight-year-old boy with anaphylaxis after ingesting pumpkin seeds [1]. Homology between the amino acid sequences in storage proteins may indicate cross reactivity between different edible seeds, peanuts and tree nuts [15].

It is possible to develop pumpkin seed anaphylaxis in a child with a tolerance to pumpkin pulp. Pumpkin seeds allergens have not been well characterized. Homology between the amino acid sequences in storage proteins may indicate cross reactivity between different edible seeds and nuts. Our findings are of special value, particularly in children, considering the current trend toward health foods. Pumpkin, sesame, sunflower, linen and poppy seeds should be included in the standard diagnostic procedures for food allergy.

Abbreviations

AD - atopic dermatitis

SPT - skin-prick test

asIgE - allergen-specific IgE

CRD - component resolved diagnosis

PA - pumpkin allergy

Declarations

1. The study was approved by Ethical Committee of CM Bydgoszcz, NCU Torun, no KB 74/2020.
2. Consent for publication: yes.
3. Availability of data and materials: The datasets analysed during the current study are available from the corresponding author on reasonable request.
4. Competing interests: The authors declare that they have no competing interests.
5. Funding: No funding.
6. Authors' contributions: J.G., H.L. and A.K. equally contributed to the conception and design of the research; J.G., H.L., M.Ž.G., Z.B. and A.K. contributed to the acquisition and analysis of the data; H.L., J.G. and A.K. contributed to the interpretation of the data; and H.L., J.G. and A.K. drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.
7. Acknowledgements: Not applicable.

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