LETTER TO THE EDITOR

Allergy to peanuts and peanut oil: a new severe italian phenotype?

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To the Editor,

peanut allergy is one of the most common food allergy throughout Europe and USA.
There are 17 registered peanut allergens in the WHO/IUIS list.

- Ara h 2, 6 and 7 are 2S albumins.
- Ara h 9, 16 and 17 are ns-LTP.
- Cupins: Ara h 1 and Ara h 3.
- PR-10: Ara h 8 (1).

More recently discovered allergens are defensins: Ara h 12 and 13; Oleosins: Ara h 10, 11, 14, 15 are heat-stable and digestion resistant proteins. Both defensins and oleosins have a lipophilic structure, hence are underrepresented in aqueous extracts used in the diagnostic phase, and they can cause severe clinical reactions (2,3,4).
Ara h 18, who is a recently discovered cyclophilin could carry a risk of severe symptoms and reactions (5).
We present the clinical case of a female patient aged 15, with an infantile history of pruritus after peanut consumption, for which she hasn't eaten any ever since. In June 2022 she reached us seeking medical attention because after eating a lemon sorbet, on whose packaging was stated the possible presence of peanuts, she manifested pruritus, labial angioedema and dyspnea.
We therefore performed a food allergen prick test which resulted positive for peanut (++++) and negative for egg (yolk and albumen), milk (alpha-lactoglobulin, beta-lactoglobulin, casein), peach, hazelnut, cod, shrimp and soy flour. Inhalant allergen prick test revealed positive for mugwort and dust mites, and negative for animal epithelia, alternaria, Gramineae, pellitory, cypress, birch, olive tree.
The same day we sampled her blood for specific IgE dosage that tested negative for peanut, soy seeds, tomato, cod, apple, rice, grain, Tri a 14, Tri a19, gliadine, Pru p3, Pru p 7; positive for dust mites and negative for Art v 1 and Art v 3; total IgE resulted 49 UI/ml and basal tryptase was 3.3 ng/ml.
We scheduled a prick by prick, performed with store-bought products and ALK steel lancets, with every food tested at least 10 centimeters far from the next; it resulted negative for lemon, positive for raw and roasted peanut, peanut butter, peanut oil. After a few minutes a pruriginous satellite erythema showed on her left shoulder and right scapula.
In the meanwhile she had presented urticaria and difficulty in breathing while eating fried food in a fast-food restaurant, and urticaria while others were eating peanuts at her table.
To exclude laboratory errors, we performed specific IgE dosage a second time, which resulted <0.10 kUA/l for peanut and its molecules (Ara h 1, 2, 3, 6, 8, 9). We additionally performed markers for celiac disease and anti-thyroid antibodies, all negative, TSH within range.
We consequently prescribed auto-injectable adrenaline and trained the patient and her family to its usage and complete avoidance of peanut and its derivatives.

Later, new episodes manifested with dyspnea in open air next to peanut oil used for frying (she denies food consumption on this occasion), hives and shortness of breath after eating bread (not the bread she usually ate, her family suspects contamination or wrong packaging).
As soon as possible we performed test multiplex ALEX 2: IgE<0.1 kUa/L for Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8, Ara h 9, Ara h 15 and all other tested allergens except Der p 1, 2, 21, 23 and Der f 2.
Patient is now on a free diet and avoids exclusively peanuts and its derivatives. She tolerates every other food, including nuts.
Oral challenge test with peanut oil was not performed for safety concerns after the positivity of prick by prick and subsequent pruriginous satellite erythema. Basophil activation test was not available.
Since Ara h 11 shares a high sequence identity with Cor a 13 from hazelnut and Ses i 5 from sesame, testing for Tahini could've been useful for confirming oleosin sensitization and was not performed since our patient tolerates hazelnut and sesame.
Our patient had systemic reaction likely due to a mono sensitizing peanut protein, with characteristics of resistance to processing and heat, possibly an oleosin other than Ara h 15 or less likely a defensin, both related to a moderate-severe risk of systemic reaction.
Peanut oleosins have limited sequence homology, the peak for Ara h 15 is reached with Ara h 11 and is equivalent to 47%: little cross-reactivity could hence hide a primary sensitization to another oleosin. Currently allergy to oleosins is believed to be underdiagnosed, both for the absence of oleosins in standard singleplex tests, and for the frequent cosensitization with major allergens to whom symptoms are ascribed.
Peanut defensins Ara h 12 and Ara h 13 have a lipophilic structure and are also underrepresented in diagnostic extracts, they seem to be related to greater severity of symptoms and could therefore be implicated in this clinical case, however evidences on this purpose are still limited and commercial test are not yet available.
This clinical case represents an exception, since to our knowledge it is the first confirmed cases of peanut oil allergy, and the first of oleosin allergy without sensitization to other known peanut allergen; underreporting and misdiagnosis are although a well known possibility. The patient has an important limitation in quality of life due to reactions to peanut proteins contamination, including oil, and due to suspected reactions to airborne transmitted allergens, representing a new clinical challenge. This last kind of reaction, although not demonstrated in our case and needing further evidence is hypothesized and has been studied in experimental settings (6).

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MM: investigation, methodology, review & editing
GD: resources, supervision, validation.
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