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CORRESPONDENCE

Gibberellin-regulated protein allergy and orange-induced anaphylaxis

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Dear Editor,

I have read the article titled, "Allergy to gibberellin-regulated proteins in an adolescent: A case of orange-induced anaphylaxis mediated by cofactors" by Kàtcheff et al. with great interest.[1] However, it is not clear as to which allergen actually caused cross-reactivity in this case and which co-factor triggered the reaction here. Therefore, clarifying these would be of great use to the reader.

First: Pollen-food allergy syndrome (PFAS) is known to induce oral allergy syndrome (OAS). Many patients who develop an allergic reaction to fruit are diagnosed as having OAS, and only a few cases of food-dependent exercise-induced anaphylaxis (FDEIA) are reported. A rare syndrome of immediate hypersensitivity reaction necessitates both ingestion of an allergenic food and exercise to initiate anaphylaxis.[2-4]

It seems difficult to attribute anaphylaxis to orange, even if specific IgE is positive in a case where oral food challenge (OFC) is negative. Although a similar reaction has been described with strawberries, in this case, a positive response to OFC with exercise was found.[5] A provocation test with a combination of orange intake and exercise should have been performed. This would have revealed whether the anaphylaxis was due to OAS or FDEIA.[2-4] Also, skin/serum allergy tests or exercise provocation tests were not performed with tomatoes and wheat. These foods are the most common culprits in FDEIA, and this patient had consumed them before anaphylaxis.

The fact that a suspected allergic food is tolerated after a short period makes it more likely a reaction due to these cofactors. Again, the negative finding of orange OFC supports this. Cofactors (exercise, nonsteroidal anti-inflammatory drugs, and alcohol) are reported to mediate the development of allergy to gibberellin-regulated protein (GRP). Shouldn't each of these cofactors be tested separately? Also, although cofactors (exercise, alcohol, ibuprofen, and cannabis) are mentioned, no attempt has been made to find out which of these is involved except for nonsteroidal anti-inflammatory drugs.

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As mentioned in this article, yes, it is always stated in the literature that GRP-induced allergy depends on cofactors,[5,6] especially exercise, but then would it be called PFAS-OAS or FDEIA?

Second: The prevalence of GRP sensitization was found to be high in Japanese fruit allergy patients except for PFAS patients.[6] Contrary to what was reported in this article, in this case, anaphylaxis is attributed to PFAS-associated OAS.[1]

The specific IgE against GRP molecule Pru p 7 (peach allergen) was detected in this case[1]. Pru p 7 has a high homology and 87% identity with orange Cit s 7, forcing the cross-reaction leading to anaphylaxis. It is then argued that reactions due to Cit s 7 are milder.[1] Why is this reaction explained by *Gibberellin* and cypress cross-reactivity when profilins are also major allergens in orange and the patient is allergic to timothy grass, a profilin?[7] Reactions due to gibberellin should be negative for profilin-specific IgE antibodies, as is the case for Timothy (shown in Figure 1).[1] In this patient, however, the opposite is the case and he was positive for both.[1] Profilin is defined as a major orange allergen in a study.[8]

Thaumatin-like protein (TLP) has been identified as a novel pan-allergen found in plant-based foods (i.e. fruits and vegetables), and it is associated with food allergy. A recent article reported a rare case of FDEIA to oranges with evidence of possible underlying TLP allergy.[3]

Therefore, it is possible to explain the anaphylactic reaction in this patient by mechanisms such as TLP and profilin allergens found in orange, and it is not necessarily based on GRP.

Minor points: The differential diagnosis between PFAS-associated OAS and FDEIA is not well addressed. Various foods can cause type I hypersensitivity symptoms such as in oral allergy syndrome and FDEIA. Each disease is associated with specific food groups: apples, peaches, and melon in oral allergy syndrome; and shrimp, wheat, celery, and tomato in FDEIA.[2-4]

Recently, GRP has been identified as an allergen that causes generalized/systemic symptoms in allergies associated with peaches, apricots, oranges, apples, and plums.[5,6,9,10] Was there a reaction with any of these fruits other than oranges in this case? In our opinion, the answer to this question could be referring to a fruit other than orange.

While I thank the authors for this beautiful and useful case presentation, I think it would be useful to clarify the points I mentioned above.

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