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Anaphylactic shock to raspberry

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Raspberry (*Rubus idaeus*) is a shrub belonging to the *Rosaceae* family: sub-family *Rosoideae*, gender *Rubus*, and species *Rubus idaeus*. The homonymous fruit is a drupe and is a very enjoyed food. Recently, Marzban and colleagues identified four IgE-reactive proteins in raspberry (1). These authors initially detected two potential allergens Rub i 1 and Rub i 3, using polymerase chain reaction. Rub i 1 and Rub i 3 showed high sequence identity to proteins in Rosaceous species: like Mal d 1 and Mal d 3 from apple. Further, Marzban and colleagues identified a new protein with high sequence homology with class III chitinases. Finally, they detected a raspberry cyclophilin, homologous to Bet v 7. These findings could suggest that raspberry ingestion might cause allergic symptom occurrence, such as IgE-mediated, in sensitized patients.

However, a case alone of allergic reaction to raspberry has been described so far. In fact, a first report concerned a case of anaphylaxis in a milk-allergic child after ingestion of milk-contaminated kosher-pareve-labeled "dairy-free" dessert. The described case occurred after ingestion of "pareve"-labeled raspberry sorbet in a child with milk allergy (2). Actually, anaphylaxis was due to milk-allergy and not to raspberry, as the food was contaminated by milk. The true case of raspberry allergy was occupational. This case concerned a 35-year-old woman who complained of hay fever symptoms, wheezing and breathlessness 2-3 times a month, exclusively in association with inhalation of raspberry powder, used for coating chewing gum (3). Both skin prick test and serum IgE assay were positive for raspberry. Therefore, this was the first and unique description of allergic reaction due to inhalation of raspberry powder.

We report a case of a 52-year-old woman who had an anaphylactic shock immediately after ingestion of raspberry during a quite walking tour in the Alps. She ingested raspberry 4 hours after the last meal, during a pause. She suddenly presented intense itching to palms, dyspnea, and intense flushing, rapidly

followed by syncope with sphincters' relaxation. She was assisted and transported by a rescue helicopter to the nearest hospital. After adequate treatment, she recovered without *sequelae*.

During a first allergist visit, she denied any previous allergic reaction. Skin prick test (performed using commercial extracts) was positive only to birch and hazelnut (mean wheal 2 mm; histamine wheal 3 mm). Serum IgE were measured only by ISAC methods, as specific IgE to raspberry is not assayed in the laboratory of the referential hospital. ISAC results showed that rPru p 3 was 1.0 ISU-E and nJug r 3 was 0.6 ISU-E. Then, serum was assayed by ImmunoCAP system: rPru p 3 was 1.94 kUA/L and rCor a 8 was 0.06 kUA/L. The patient was re-evaluated after the results: a more detailed history confirmed that she felt itching after the contact with the peach peel. After 2 months, a prick by prick was performed: raspberry fruit induced an 8 mm wheal. Therefore, the clear relationship between ingestion of raspberry and sudden anaphylaxis (*post hoc ergo propter hoc*), the positive prick by prick testing, and serum positivity to *Rosaceae* fruits allows to determine the causality. The explanation of the cross-reactivity between *Rosaceae* family fruit allergens derives from the matter that fruit proteins with high primary sequence similarity display also homologous tertiary structures, resulting in similar epitopes to IgE molecules (4).

This is the first description (at our best knowledge) of anaphylactic shock after ingestion of raspberry. We would like to emphasize the clinical relevance of history and molecular diagnosis. In fact, to detect positivity to lipid transfer proteins gives important information about the severity of allergic reaction, the prognosis, and mainly the dietary restriction.

The diagnostic workup of severe anaphylaxis should be based on the rigorous demonstration of a cause-effect relationship between suspected food ingestion and documented sensitization, using skin testing and/or serum allergen-specific IgE measurement. In fact, food challenge must be avoided for legal reason. Therefore, consistent history and proved allergy should be sufficient for identifying the causal allergen. However, it should be recommendable also in the routine practice, if available, to use component resolved diagnosis for obtaining more valuable information about risk factors and possible co-sensitizations or co-recognitions.

In the present clinical case, history and prick-by-prick were consistent in defining the culprit allergen protein, such as raspberry. Furthermore, CRD, based on findings of the ImmunoCAP and ISAC, allowed to identify co-sensitization with other *Rosaceae* fruits, mainly concerning LTP proteins. This information was useful both for interpreting past reaction to peach and for advising preventive food rules.

In conclusion, also a fruit believed to be harmless may be dangerous, and positivity to LTP should suggest to be cautious with *Rosaceae* fruits.

References

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