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Omega-5 gliadin anaphylaxis: an integrated diagnostic approach

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KEY WORDS

Anaphylaxis, exercise-induced anaphylaxis, omega-5-gliadin, recombinant allergens, wheat

SUMMARY

We report the case of a 62-year old man who presented a wheat-dependent, exercise-induced anaphylaxis (WDEIA). The case illustrates the usefulness of skin prick test not only with wheat extract, but also with native gliadin extract. Moreover we confirm the value of recombinant IgE dosage with rTri a 19 omega-5 gliadin in the diagnostic pathway of this condition.

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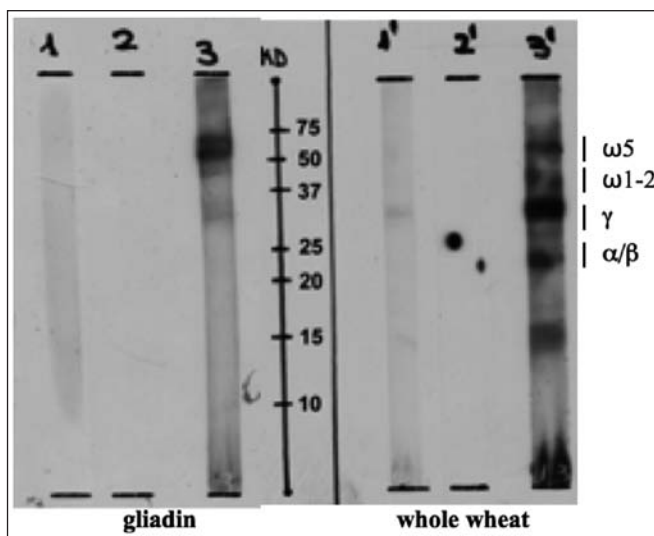
Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a well described life-threatening clinical presentation of food allergy, that occurs when a wheat-sensitized subject practises exercise in the few hours following ingestion of foods containing wheat proteins. Correlation between the amount of wheat and the intensity of exercise with the severity of the hypersensitivity reaction is unclear. Diagnostic pathway consists of an accurate clinical history including trigger factors (besides exercise, also aspirin and cold may play a role as cofactors), skin prick test (SPT), and IgE dosage for allergenic extracts and specific allergenic molecules.

We report a case of WDEIA in a 62-year-old, non-smoker man in good health, who had been suffering of recurrent urticaria, in the absence of known trigger factors, in the previous two years. He used to successfully treat his symptoms with an antihistaminic drug on demand. He reported also the first episode of acute generalized urticaria, lip angioede-

ma and hypotension (Systolic blood pressure: 50 mm Hg, diastolic blood pressure not measurable), four months before being visited at our clinic. This episode required systemic corticosteroids and antihistaminic therapy in the Emergency Unit. These symptoms occurred while taking a walk in a wood a few minutes after Easter lunch, consisting of pasta, cheese, eggs, beef, Cremona's mustard (preserve made from candied fruits in grape must or sugar with mustard), milk chocolate, cake with candied fruit, red and sparkling wine. One month later, he reported a similar episode while he was dancing. Also on this occasion, he had just ended a lunch consisting of salted fritter (made by wheat, milk, yeast and olive oil), French fries, pork, and white wine. Also this episode required systemic corticosteroids, antihistaminic therapy and Ringer's lactate solution in the Emergency Unit. In this occasion he was discharged with the diagnosis of: "neurologically mediated syncope" and he was prescribed epinephrine auto-injector on demand. Before being visited

at our clinic, the patient had already performed SPT with common food allergens, which yielded negative results: total IgE were 122 kU/L (normal value <100 in this laboratory); serum specific IgE for a standard group of food allergens, which scored negative, with the exception of a low value for whole wheat (ImmunoCAP® Phadia: 0.22 kU/L), at that time not considered clinically relevant. During the evaluation at our Hospital, SPT with commercial food allergens extracts (ALK Abellò A/S, Hørsholm, DK) including whole wheat were performed and resulted positive only for gliadin, that elicited a 9 mm diameter wheal. The determination of specific IgE for omega-5 gliadin (rTri a 19 omega-5 gliadin) was assessed both with ImmunoCAP-

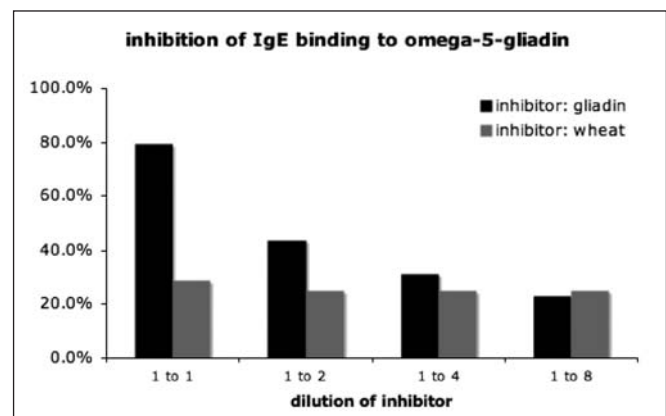
Figure 1 - Different omega-5-gliadin content in wheat versus gliadin extract. Gliadin extract (left panel, lanes 1, 2, 3) and whole wheat extract (right panel, lanes 1', 2', 3') for skin prick testing (ALK Abellò, Madrid, Spain) (1/20 W/V) were run in non-reducing conditions in 12% sodium dodecyl sulphate (SDS) polyacrylamide (PAGE) gel electrophoresis. Proteins were transferred to a nitrocellulose membrane (Hybond ECL, Amersham Pharmacia Biotech) and reacted onto single strips with 1:5 diluted sera from one non allergic control individual (lanes 1 and 1') and subsequently with probe (HRP-conjugated rabbit anti-human IgE, DAKO), with probe only (lanes 2 and 2') and with a pool of sera from patients with wheat allergy (level of IgE to *Triticum aestivum*: RAST class 3), which served as positive control, followed by the anti-IgE probe (lanes 3 and 3'). Bound antibodies were revealed by enhanced chemiluminescence autoradiography (ECL, Amersham Pharmacia Biotech). Molecular weight (MW) markers (Bio-Rad, Richmond CA, USA) were run in a different strip and reported visually with a pencil. The expected migration pattern of known gliadins is reported on the right.



ISAC (Immuno Solidphase Allergen Chip,) and with ImmunoCAP (Phadia), and scored respectively 5,8 ISAC Standardized Units (reported normal value < 0.3 ISU) versus 20.5KU/L (reported normal value <0.10 kU/L). These last results, together with the clinical history, allowed to confirm the diagnosis of wheat-dependent exercise-induced anaphylaxis, mediated by sensitization to omega-5 gliadin. After the diagnosis the patient returned to practise his leisure activities (dancing and trekking) and he did not experience new allergic reactions by avoiding the ingestion of wheat.

In order to justify the discrepancy between SPT results, immunoblotting was performed with natural wheat and gliadin extracts used for SPT (Alk Abello, Madrid, Spain - Figure 1). It demonstrates a low content of omega-5 gliadin in the whole wheat commercial extract, and also a different allergen content in the two extracts; moreover, to explain negative SPT with whole wheat and positive with gliadin, we performed a RAST inhibition of patient serum with commercially whole wheat and gliadin extracts (ALK-Abellò A/S, Hørsholm, DK), which confirmed the low content of omega-5 gliadin in whole wheat extract for SPT (Figure 2). In conclusion WDEIA is a well-described clinical entity, that usually affects young adults and adolescents². Our case emphasize the role of a multifaceted diagnostic approach, combining different in vivo and in vitro tools. In particular,

Figure 2 - Inhibition of IgE binding to Tri a 19 (omega-5-gliadin allergen component) by gliadin extract and wheat (*Triticum aestivum*) extract (ALK Abellò, 1/20 W/V), as measured by ImmunoCAP. One volume of serum from patient C.P. was pre-incubated with 1.5 volumes of either saline solution or allergen extracts for prick testing at different concentrations (the latter were obtained by dilutions in saline, indicated on the x axis) and specific IgE binding was measured. Results are expressed as percent inhibition (on the y axis) versus serum diluted with saline.



our case underlines: 1) the importance of performing SPT with gliadin extract to detect omega-5 gliadin sensitization. This could overcome the lack of standardization of the different commercial extracts due to the technical difficulties in obtaining the different allergenic molecules, especially in whole extracts; 2) the importance to use a 0.10 kU/L threshold value for specific IgE level (rather than 0.35 which is still used in some laboratories) and in WDEIA the possible clinical relevance of low specific IgE level for wheat; 3) the diagnostic value of specific IgE dosage for recombinant molecules, and the better sensitivity of CAP over ISAC for omega-5 gliadin. Finally, WDEIA should be con-

sidered not only in young people but also in elderly subjects, even in the absence of any previous IgE-dependent allergic clinical history.

References

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