Allergol Immunopathol (Madr). 2011;**39(5)**:313–314

Allergologia et immunopathologia

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LETTERS TO THE EDITOR

Is food anaphylaxis a cause of antiphospholipid syndrome and thrombosis or a coincidence?

To the Editor,

I read with great interest the article by Armentia et al.[1] recently published in Allergologia et Immunopathologia on food anaphylaxis in antiphospholipid syndrome (APS) and thrombosis. The authors suggested that seed lipoproteins might have a potential role in the APS and related thrombosis. I think that there are certain issues, which need clarification by the authors.

The first issue in need of explanation is about the randomisation of the patients. The authors mentioned that 52 patients with anaphylaxis were selected randomly from among patients with severe anaphylaxis. The number of patients with severe anaphylaxis (grade III–IV by Muller) is not clear. If the authors made this selection from among 21,879 patients, we could say that approximately, 28% of 21,879 patients may have thrombosis. This implies that development of thrombosis in patients with anaphylaxis is very high in these group patients. However, there is no clear evidence in the literature showing increased development of thrombosis in patients with anaphylaxis. Therefore the authors should give us the number of patients with severe anaphylaxis and clear information about randomisation. It seems to me that the selection of patients was made according to whether the patients have thrombosis or not. This could have led to a selection bias. The authors reported four cases with food anaphylaxis followed by thrombosis before.[2] Were these patients included in this study?

Secondly, in this study, of 52 patients with anaphylaxis, 15 (28%) had ACA IgG positivity with medium or high titre. The authors described medium or high titre as 20–80 GPL medium, >80 GPL high positive, respectively. In Table 1A, the number of patients having positive ACA IgG with medium or high titre were only seven and one in Table 1B. As a result, unlike that mentioned by the authors in the text and Tables, only eight patients had ACA IgG antibody positivity with medium or high titre (15%).

Thirdly, it is seen in the Tables that vascular involvement exists in patients with anaphylaxis and the patients with APS. It is likely that some of these patients may use aspirin for the secondary prophylaxis for thrombosis. As is well known, aspirin may enhance wheat anaphylaxis or skin prick test results.[3–5] Although this effect of aspirin may be seen in exercise-induced anaphylaxis, aspirin can be also an augmentation factor in wheat allergy without exercise.[3–5] For this reason, it would be necessary to know the number of the patients using aspirin in both groups. In explaining their results, the authors should have mentioned this as a confounding factor.

Fourthly, there is no clear explanation as to what criteria were used to select the patients with APS in the text. The authors re-tested ACA IgG two months after initial testing. According to classification criteria for APS published in 2006,[6] antibodies should be re-evaluated after three months to make a clear decision in patients with antibody positive. Why did the authors evaluate ACA IgG antibodies after two months? And did they use second antibody titres in their analysis.

In conclusion, we need well-designed studies investigating whether or not anticardiolipin antibody positivity and thrombosis are secondary to food allergies or a coincidence.

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DOI of refers to article: 10.1016/j.aller.2010.06.011

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doi:10.1016/j.aller.2011.03.003

The association of food anaphylaxis in antiphospholipid syndrome and thrombosis cannot be considered a coincidence

To the Editor,

We have read with great interest the comments on our study ''Food anaphylaxis in antiphospholipid syndrome and thrombosis.[1] We are very grateful to the authors for the opportunity that our colleagues bring us to clarify some details.

Severe anaphylaxis, fortunately, is an uncommon disease. The actual incidence of anaphylaxis is unknown but is estimated to be 10 to 20/100,000 patients/year. The biggest study on anaphylaxis among hospitalised patients in the previous decade was conducted as a retrospective study of adult patients between 1992 and 2001 at a tertiary care centre in Bangkok. Of 448,211 admissions, 80 events of anaphylaxis in 79 patients (0.017%) were found.[2] So, it was very difficult to find a big sample to anaphylaxis due to seed or fruit. We had to revise the records of 21,879 patients admitted to our Allergy Department in the last 22 years to find the number of patients necessary for a good statistical analysis. The sample size was calculated by simple random sampling in a control:case ratio of 1, with confidence limits of 98%, a power of 90% and an average of exposition among controls of 25%. A stratified analysis was performed in order to estimate the confounding and artefactual factors among the different independent variables, avoiding the selection bias. We finally selected 52 patients who suffered from severe anaphylaxis and 28% of them had anticardiolipin antibodies and 17.3% had thrombosis. This percentage can be considered not too big, but the fact that 75% of patients' diagnoses as having antiphospholipid primary syndrome with thrombosis had specific IgE against vegetal allergen, should not be considered a coincidence. Although it is true that given the heterogeneity of the clinical manifestations of APS it is likely that more than one pathophysiological process may play a role. Recent studies about vegetal food-induced anaphylaxis in Italy found that LTP is the most important allergen causing food-induced anaphylaxis, peach being the most frequently offending food. These data are very similar to our data but obviously geographic and environmental differences both between Italy and other countries and within Italy seem to play a relevant role in the pattern of sensitisation to foods.[3]

In the tables, we included as a medium level the patient number 33, who presented 18 GPL/ML in the first determination and 26 GPL/ML in the second analysis. We only presented in the table the first tests performed. None of our allergic patients were taking aspirin at the moment of anaphylaxis. The patients that suffered from thrombosis were treated with anticoagulants or aspirin after the diagnosis. We agree with our colleagues that antibodies should be reevaluated after three months. All patients with thrombosis were evaluated every three months. Those with anaphylaxis were tested again two months after discharge from the Hospital, in the third month of their process.

The rise in the incidence of anaphylaxis over the two decades of the study period is alarming. Raising the awareness of anaphylaxis management among healthcare providers and the public is warranted. Thank you very much again for the criticism that undoubtedly has improved our work.

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doi:10.1016/j.aller.2011.03.002