A New Triad: Sensitivity to Aspirin, Allergic Rhinitis, and Severe Allergic Reaction to Ingested Aeroallergens

Mario Sánchez-Borges, MD, Caracas, Venezuela
Arnaldo Capriles-Hulett, MD, Caracas, Venezuela
Eric Capriles-Behrens, Med Stu, Caracas, Venezuela
Enrique Fernandez-Caldas, PhD, Madrid, Spain

Goal
To describe the relationship between ingested allergens and sensitivity to aspirin.

Objectives
1. To identify the response pattern in patients allergic to nonsteroidal anti-inflammatory drugs (NSAIDs).
2. To present case studies in which there was an allergic response to ingestion of mite-contaminated wheat flour products.
3. To speculate on the relationship between NSAID sensitivity and ingestion of mites.

CME Test on page 324

Increasing attention has recently been paid to a group of patients who experience anaphylaxis after ingestion of foods prepared with mite-contaminated wheat flour. We present three cases of this syndrome, which occurs more often in young adults with allergic rhinitis and/or asthma. We have observed an increased frequency of sensitivity to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), manifested as urticaria or angioedema, in patients with this condition.

Max Samter described a syndrome of severe asthma, nasal polyposis, and "intolerance" to acetylsalicylic acid (ASA) more than twenty years ago.[1] Patients with this syndrome were usually older, required treatment with corticosteroids for adequate control of respiratory symptoms, and were characteristically nonatopic. Stevenson and Simon have expanded our knowledge on the clinical syndromes occurring in relation to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs).[2] Through results of challenge studies and measurements of pulmonary function, a clearer picture has emerged, better delineating aspirin-induced asthma and dispelling some of the intricacies of coexisting tartrazine sensitivity. Even a "desensitization" protocol has been proposed for persons who must take aspirin on a regular basis for a variety of medical reasons.[3]

Another aspect of the clinical response to aspirin is the pattern of urticaria/angioedema, for which a relationship to atopy is less than clear. Most aspirin-sensitive patients have either aspirin-induced asthma or skin manifestations, rarely both. Stevenson has also pointed out the existence of two additional ASA-induced syndromes: one he designated as anaphylactoid, because it is manifested as hypotension; and the other being interstitial pneumonitis.[4]

We emphasize that the pattern of urticaria and angioedema triggered by NSAIDs occurs very frequently in patients with allergic rhinitis and severe (anaphylactic) reactions provoked by the ingestion of the most ubiquitous aeroallergen: house dust mite.

Inhalant allergens (ie, pollens such as those of ragweed) can induce systemic symptoms when inhaled during the pertinent season. Food allergens, when ingested, can likewise produce systemic anaphylaxis.[5] We report

From the Pediatrics Department, Centro Médico-Docente "La Trinidad," Caracas, Venezuela, and the Research Laboratory, C.B.F. Leti, SA, Madrid, Spain.
REPRINT REQUESTS to POBA International, PO Box 02-5255, #635, Miami, Florida 33102-5255 (Dr. Sánchez-Borges).

FIGURE 1. Suidasia spp. mite present in wheat flour package used to prepare pancakes ingested by Case II.

here the occurrence of systemic symptoms, including anaphylaxis, after the inadvertent ingestion of mite-contaminated foods prepared with wheat flour, in atopic patients with a previous history of urticaria/angioedema triggered by ASA and other NSAIDs.

Case Reports

Case I—A 15-year-old girl was first seen for evaluation of dyspnea, rhinorrhea, eyelid edema, and itching appearing fifteen minutes after the ingestion of homemade pancakes. She also complained of cough and abdominal cramps, and at physical examination dysphonia and wheezing were present. Emergency treatment with subcutaneous epinephrine, intravenous hydrocortisone, and chlorpheniramine-induced symptomatic improvement. Her family history documented asthma in her mother and allergic rhinitis in her father. The patient had allergic rhinitis and a previous history of urticaria caused by diclofenac.

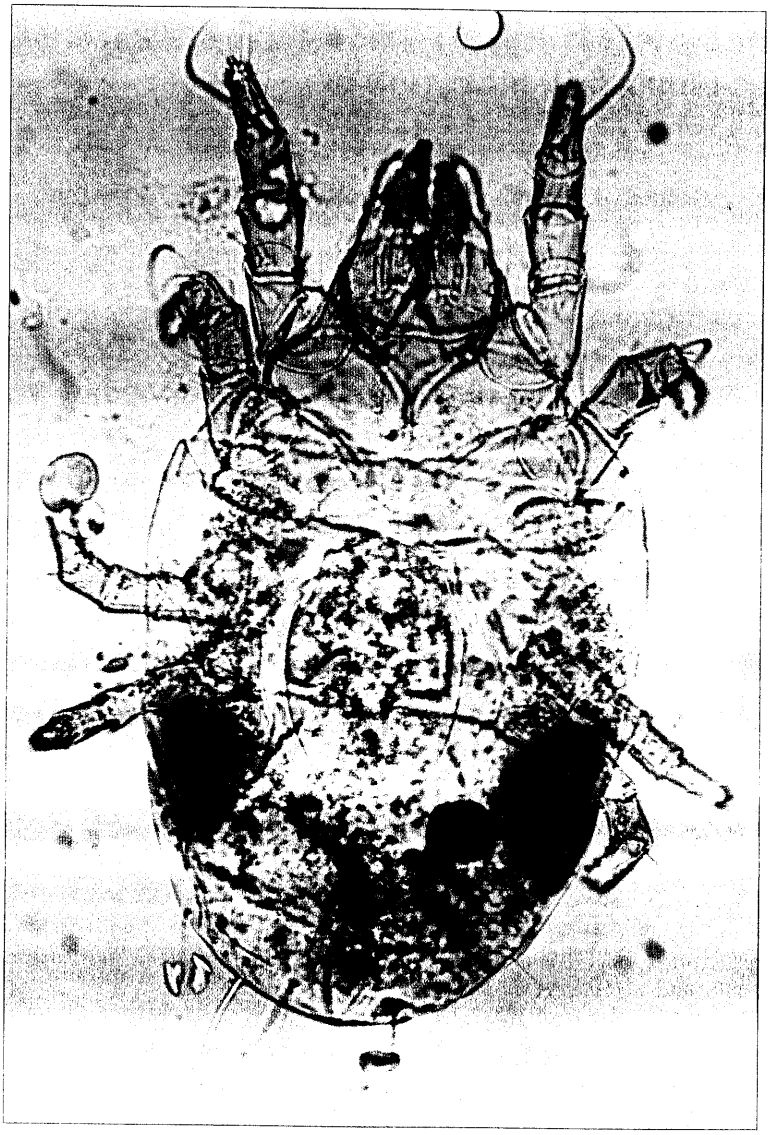

FIGURE 2. Aleuroglyphus ovatus present in a second, unopened, package from Case II.

Results of prick skin tests included formation of wheals of the following sizes: house dust extract, 8 mm; *Dermatophagoides farinae* extract, 10 mm; wheat extract, 0 mm (Center Laboratories, Port Washington, NY); mite-contaminated wheat flour, 9 mm; 1 percent histamine phosphate, 6 mm; and glycerosaline solution, 0 mm. Nasal eosinophilia was 28 percent (right nostril) and 10 percent (left nostril).

Microscopic examination of the flour disclosed 5,000 *D. farinae* mites per gram of flour, and results of enzyme-linked immunosorbent assay showed 0.4 µg Der p 1 allergen and 100 µg Der f 1 allergen per gram of flour.

Case II—A 39-year-old woman had a fifteen-year history of allergic rhinitis. She noticed eyelid edema, dyspnea, cough, rhinorrhea, nasal obstruction, and wheezing thirty minutes after eating homemade pancakes. Her previous history included angioedema due to ASA, ibuprofen, mefenamic acid, and paracetamol. One brother and one daughter also had allergic rhinitis.

Skin test results from this patient were as follows: house dust, 6 mm wheal; *D. farinae* extract, 9 mm; dog, 4 mm; wheat extract, 0 mm; mite-contaminated wheat flour (used to prepare the pancakes), 10 mm; histamine, 8 mm; and glycerosaline solution, 0 mm.

Microscopic examination of the flour revealed, in the same package used to prepare the pancakes, *Suidasia* spp. 2,500 mites/gm flour (Figure 1) and *Aleuroglyphus ovatus* 2,500 mites/gm flour. In a second, unopened, package from the patient's home were found *A. ovatus* 1,600 mites/gm of flour (Figure 2).

Case III—A 25-year-old woman had a previous history of hypersensitivity to pyrazolone, allergic rhinitis, and asthma. She was admitted to the emergency room because of breathlessness, facial angioedema, and wheezing that began fifteen minutes after eating pasta (cannelloni) stuffed with homemade béchamel sauce. Treatment was immediately given consisting of subcutaneous epinephrine and intravenous hydrocortisone plus brompheniramine. One hour later prick skin tests were carried out, with the following results: *D. farinae* extract, 8 mm wheal; wheat extract, 0 mm; béchamel sauce (same ingested by the patient), 12 mm; wheat flour (used to prepare the sauce), 12 mm; histamine, 6 mm; and glycerosaline solution, 0 mm.

Microscopic examination of the flour showed *D. farinae*, abundant mites (not quantified).

Comments

The first reports of systemic symptoms due to the ingestion of mite-contaminated foods were published in 1993 by Erben et al.[6] They described a patient who experienced anaphylaxis when eating beignets prepared with wheat flour bought in a New Orleans restaurant. A year later another patient was reported with similar findings, also due to wheat flour purchased at the same restaurant.[7] In both cases the flour was contaminated with *D. farinae*.

We have observed this phenomenon for more than fifteen years and, stimulated by these reports, we decided to gather our experience in order to alert the practicing physician about this not uncommon cause of angioedema/anaphylaxis. Most patients are young adults, with past history of allergic rhinitis and/or asthma. A significant proportion of them had previously been diagnosed as sensitive to NSAID, experiencing urticaria or angioedema in reaction to these agents. We have observed thirty cases of systemic anaphylaxis, exemplified by the three cases reported here, with similar clinical pictures. Some of these data have been published in abstract form.[8] Twenty of these patients (66.6 percent) are NSAID sensitive.

TABLE I

PUBLISHED DATA ON ANAPHYLAXIS INDUCED BY INGESTION OF MITE-CONTAMINATED FOODS

Author	Year	Number of cases	Age	Gender	Food(s)	Mite	NSAID sensitivity
Erben et al[6]	1993	1	48	M	Beignets	*D. farinae*	No
Spiegel et al[7]	1994	1	17	F	Beignets	*D. farinae*	No
Castillo et al[8]	1995	21	13–39	M 12 F 9	Various	*D. farinae* *Suidasia* spp. *A. ovatus*	Yes (66.6%)
Skoda et al[9]	1996	1	14	M	Pizza dough mix	*D. farinae*	Yes (familiar)
Matsumoto et al[10]	1996	2	11,14	M 1 F 1	"Okonomi-yaki" mix Hot cake mix	*T. putrescientiae*	No
Blanco et al[11]	1996	12	?	?	Various	?	Yes

Table I summarizes all published studies on this subject, including three papers with fifteen additional cases reported this year.[9-11] The two larger series found an increased frequency of NSAID sensitivity in this patient population, which deserves further study.[8,11] Since no relationship has been established between NSAID sensitivity and allergic IgE-mediated reactions, the observed increased prevalence of NSAID sensitivity in this group of patients remains unexplained. Do these patients have an increased predisposition to urticaria/angioedema and anaphylaxis after exposure to different precipitating factors? Is there a cross-reaction between mite components and NSAID? Do mites contain some chemical compound able to inhibit prostaglandin synthase? These questions will have to be addressed in future studies.

We propose that the association of atopy, oral anaphylaxis from aeroallergens (mites), and NSAID sensitivity is not a casual observation, and that it should be designated as a new aspirin sensitivity triad. In addition we think that this syndrome is more prevalent in locations with tropical or subtropical climates, where high humidity and temperature favor mite reproduction. If unsuspected or considered under the category of "idiopathic" anaphylaxis, it might leave patients unprepared for a future inadvertent event.

REFERENCES

1. Samter M, Beers RF Jr: Intolerance to aspirin. *Ann Intern Med* 68: 975, 1968.

2. Stevenson DD, Simon RA: Sensitivity to aspirin and nonsteroidal antiinflammatory drugs. In, Allergy (Middleton ER, Reed CE, eds), p 1747. St. Louis, CV Mosby, 1992.

3. Stevenson DD, Simon RA, Mathison DA: Aspirin-sensitive asthma: tolerance to aspirin after positive oral aspirin challenges. *J Allergy Clin Immunol* 66: 82, 1980.

4. Stevenson DD: Challenge procedures in detection of reactions to aspirin and nonsteroidal anti-inflammatory drugs. *Ann Allergy* 71: 417-418, 1993.

5. Sampson HA, Mendelson L, Rosen JP: Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 327: 380, 1992.

6. Erben AM, Rodriguez JL, Mc Cullough J, et al: Anaphylaxis after ingestion of beignets contaminated with *Dermatophagoides farinae*. *J Allergy Clin Immunol* 92: 846-849, 1993.

7. Spiegel WA, Anolik R, Jakabovics E, et al: Anaphylaxis associated with dust mite ingestion. *Ann Allergy* 72: 56, 1994.

8. Castillo S, Sanchez-Borges M, Capriles A, et al: Systemic anaphylaxis after ingestion of mite-contaminated flour. *J Allergy Clin Immunol* 95: 304, 1995.

9. Skoda-Smith S, Mullen GR, Oi F, et al: Angioedema following dust mite exposure presenting as suspected food allergy. *J Allergy Clin Immunol* 97: 1996.

10. Matsumoto T, Hisano T, Hamaguchi M, et al: Systemic anaphylaxis after eating storage-mite-contaminated food. *Int Arch Allergy Immunol* 109: 197-200, 1996.

11. Blanco C, Carrillo T, Castillo R, et al: Anaphylaxis after ingestion of wheat flour contaminated with dust mites. *J Allergy Clin Immunol* 97: 363, 1996.

CONFLICT OF INTEREST

The Conflict of Interest Policy of the College of Medicine requires that faculty participating in a CME activity disclose to the audience any relationship with a pharmaceutical or equipment company which might pose a potential, apparent, or real conflict of interest with regard to their contribution to the program. Dr. Sánchez-Borges reports no conflict of interest.