



Oral mite anaphylaxis (pancake syndrome) in Peru: an underestimated problem?

Anafilaxia por ingestão de ácaros (Síndrome da panqueca) no Peru: um problema subestimado?

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ABSTRACT

Urticaria and angioedema are known to have different etiologies, as they can be allergic, infectious, autoimmune, or spontaneous in nature. In single or recurrent episodes, a hidden triggering allergen should be considered, such as house dust mites (HDMs). Several reports have demonstrated that flours contaminated with HDMs can cause urticaria and angioedema, including severe life-threatening allergic reactions when ingested in large quantities from stored wheat flour. In this study, we report the clinical findings in 31 patients, including cases of anaphylaxis after the ingestion of mite-contaminated flour. We also found a relationship between a clinical history of hypersensitivity to nonsteroidal anti-inflammatory drugs and oral mite anaphylaxis syndrome in atopic patients, consistent with the theory of a “new aspirin triad,” as previously published, and now being described for the first time in Peru.

Keywords: Urticaria, angioedema, mites, anaphylaxis, flour.

RESUMO

Sabe-se que a urticária e o angioedema apresentam diferentes etiologias, pois podem ser de natureza alérgica, infecciosa, autoimune ou espontânea. Em episódios únicos ou recorrentes, deve-se considerar um alérgeno desencadeante oculto, como os ácaros de poeira doméstica (APDs). Vários relatos demonstraram que farinhas contaminadas com APDs podem causar urticária e angioedema, incluindo reações alérgicas graves com risco de vida quando ingeridos em grandes quantidades provenientes de farinha de trigo armazenada. Neste estudo, relatamos os achados clínicos de 31 pacientes, incluindo casos de anafilaxia após ingestão de farinha contaminada com ácaros. Também encontramos uma relação entre uma história clínica de hipersensibilidade a anti-inflamatórios não esteroides e síndrome de anafilaxia por ingestão de ácaros em pacientes atópicos, consistente com a teoria de uma “nova tríade do ácido acetilsalicílico”, conforme publicado anteriormente, e agora sendo descrito pela primeira vez no Peru.

Descritores: Urticária, angioedema, ácaros, anafilaxia, farinha.

Introduction

Urticaria, angioedema, and anaphylaxis can have different etiologies. These may include an allergic reaction, infections, and auto-immunity. If the trigger cannot be identified, these conditions are commonly

designated as idiopathic or spontaneous. In certain cases, a specific cause can be identified, including foods, venoms, or medications. However, in other cases the trigger is not easily recognized.

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When these diseases occur sporadically or as recurrent episodes, a hidden allergenic trigger such as mites should be considered in the investigation process.

A number of reports in the literature have shown that flours contaminated with mites can cause severe life-threatening allergic reactions and anaphylaxis if a patient ingests huge numbers of mites in these stored wheat flours.¹⁻⁴ The first report of systemic anaphylaxis after ingestion of food contaminated by storage mites was published in 1996 by Matsumoto et al.⁵

Methods

In the present study, we report clinical findings from 31 patients, including cases of urticaria, angioedema, and anaphylaxis occurring after ingestion of mite-infested flour. To the best of our knowledge, this is the first time that anaphylaxis caused by ingestion of mite-contaminated flour has been reported in Peru.

Results

The first patient was a 31-year-old man who had recurrent episodes of urticaria. He had a clinical history of rhinitis and hypersensitivity reactions to NSAIDs. He mentioned experiencing two episodes of anaphylaxis 10 years earlier after eating a pancake at home, for which he received treatment at the emergency department of a different medical service. On that occasion, he was treated at the emergency department of another hospital and we do not have access to any more information. While he was being treated for allergic rhinitis at our service (with intranasal corticosteroids), he presented two additional episodes of urticaria within two months; this time the diagnosis of anaphylaxis was not considered. On both occasions he had eaten spaghetti prepared with a white sauce containing mite-contaminated wheat flour.

Based on these findings, we started investigations to clarify the etiology of this recurrent urticaria, working from the hypothesis that the patient might have suffered from the Pancake Syndrome. The Pancake Syndrome, also known as “oral mite anaphylaxis”, is a new syndrome characterized by severe allergic manifestations occurring in atopic patients shortly after intake of foods made with mite-contaminated wheat flour.^{6,7}

The flour used to prepare the white sauce was examined by light microscopy and live mites were

detected (Figure 1). The wheat flour sample was sent to Inmunotek, Spain, to quantify and identify the mite species present in the flour. More than 300 *Tyrophagus putrescentiae* (Acaridae family) mites were present per gram of flour sample.

The patient was skin prick tested (SPT) with standardized allergenic extracts (Hollister Stier, Spokane WA, USA) from the house dust mites *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis* and whole wheat flour (IPI-ASAC, Sao Paulo, Brazil). The tests were read at 15 minutes and wheals with a diameter >3 mm greater than negative control were considered positive. Negative (50% glycerinated HSA–saline) and positive (histamine 10 mg/mL) controls were also tested. The SPT was positive for all 3 mite species and negative for the whole wheat flour extract. This patient tolerated all foods, including those made with uncontaminated wheat flour, without experiencing any reactions.

We concluded that the patient had a systemic reaction caused by ingestion of flour contaminated with *T. putrescentiae* mites. Since flour packages must be stored in a refrigerator to prevent mite



Figure 1
Mites in the wheat flour from the first case (*Tyrophagus putrescentiae*)

contamination and proliferation, we advised our mite-sensitive patient to store wheat flour products in his refrigerator. Since then, no more episodes of recurrent urticaria have occurred.

After this first case was diagnosed, we started a program to investigate patients evaluated at our clinic due to allergic symptoms after eating foods prepared with wheat flour. The objective of this study was to

investigate whether these patients might meet the criteria for diagnosis of Pancake Syndrome. From January 2016 to January 2017, we identified 30 cases with a high degree of suspicion (Table 1). This number represents about 2.2% of the total number of patients evaluated at the emergency room of our institution over this period. In 16 cases we could not obtain the offending flour samples, and, therefore, the diagnosis could not be fully ascertained.

Table 1
Patients in whom pancake syndrome was suspected

Patient	Age (years)	Mites in the flour	HDM SPT	Confirmed diagnosis
I	32	Positive	Positive	Positive
II	13	Positive	Positive	Positive
III	42	Positive	Positive	Positive
IV	16	NA	Positive	NC
V	22	NA	Positive	NC
VI	24	NA	Positive	NC
VII	30	Positive	Positive	Positive
VIII	41	Positive	Positive	Positive
IX	5	Positive	Positive	Positive
X	14	Positive	Positive	Positive
XI	9	NA	Positive	NC
XII	33	NA	Positive	NC
XIII	5	Positive	Positive	Positive
XIV	19	NA	Positive	NC
XV	12	NA	Positive	NC
XVI	11	NA	Positive	NC
XVII	23	Negative	Positive	Negative
XVIII	47	NA	Positive	NC
XIX	23	NA	ND	NC
XX	37	Positive	Positive	Positive
XXI	19	Negative	ND	Negative
XXII	13	NA	Positive	NC
XXIII	33	Positive	Positive	Positive
XXIV	44	NA	Positive	NC
XXV	27	Positive	Positive	Positive
XXVI	41	NA	Positive	NC
XXVII	12	NA	Positive	NC
XXVIII	19	NA	Positive	NC
XXIX	25	Positive	Positive	Positive
XXX	10	NA	Negative	Negative

HDM = house dust mites, SPT= skin prick test, NA = not available, NC = not confirmed.

Studies of the 14 flour samples that were obtained revealed that 12 (85.7%) flour samples contained mites. Microscopic examination using stereoscopes revealed presence of live mites in all the positive samples. In two cases we could not find any mites in the samples examined. However, the absence of live mites cannot rule out the presence of mite allergens. Since mite allergens were not quantified, the absence of these data could represent a weakness of the present study.

Skin prick tests were performed on these patients for house dust mites (Der p and Der f) and whole wheat flour using the same method as described above. The results showed sensitization to both mites in all the patients, suggesting a high degree of mite sensitivity. The tests for whole wheat flour sensitivity were negative and all the patients continued eating foods prepared with uncontaminated wheat flour without experiencing any reactions. These patients and/or their parents were also advised to keep flour in the refrigerator after opening the package.

Discussion

Some reports have demonstrated presence of house dust and storage mites in high altitude areas of South America, including Peru and Ecuador.⁸⁻¹³ These findings differ significantly from studies conducted in Europe, in which very low levels of mites and mite allergens are detected.

The best conditions to allow mite proliferation are relative humidity higher than 70%, mean temperature >25°C, and darkness. In our cases, we observed that flour packages had been stored for a few weeks and some of them for more than 3 months, including beyond expiry dates, in conditions that were optimal for mite proliferation. This fact is important, since it has been shown that there is a direct correlation between the duration of storage of the flour package and the number of mites.¹⁴

In vitro cross-reactivity among house dust and/or storage mites could also explain the sensitization of these patients from Lima to house dust and storage mites and their clinical symptoms.

Some mite proteins are thermostable and may induce symptoms after ingestion, even after cooking, as in cakes, pancakes, or white sauces. Der p2, a major mite allergen, is a thermostable protein, which can resist high temperatures and continue to provoke symptoms after exposure to high temperatures.¹⁵

Therefore, as previously suggested, this allergen may be the culprit responsible for these reactions.

Another relevant finding of this study is confirmation of the relationship between a clinical history of hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) and the OMA syndrome. There are several reports in the literature of sensitivity to aspirin and other NSAIDs, manifested as urticaria or angioedema, in patients with OMA. In 1997, Blanco et al. showed that up to 87% of patients affected with the Pancake Syndrome were sensitive to Aspirin.⁶

Our first patient has the same co-morbidity; allergy to NSAIDs and oral mite anaphylaxis (OMA). There were seven patients allergic to NSAIDs (54%) among the 13 positive Pancake Syndrome cases, one of whom was allergic to acetaminophen. The results shown in Table 2 do not include the first case described above because he was not part of the group of patients evaluated during the period from 2016 to 2017.

Considering that sensitivity to NSAIDs is responsible for 21-25% of reported adverse drug events in the general population¹⁶ and 37% of patients with chronic spontaneous urticaria,¹⁷ the results observed in this and other studies suggest that patients allergic to NSAIDs are at a higher risk of suffering OMA than non-allergic patients. Sensitization to mites and NSAIDs seems to be a significant risk factor. Patients living in tropical and subtropical areas and suffering from these conditions should be advised to keep flour packages in their refrigerators.

Although the mechanism underlying this relationship between atopic patients who had oral mite allergic reactions and hypersensitivity to NSAIDs is unknown, some pathogenic pathways have been suggested and a “new aspirin triad” of allergic rhinoconjunctivitis, aspirin/NSAID hypersensitivity, and severe systemic reactions to mite-contaminated foods has been proposed.¹⁸

In conclusion, this is the first description of the Pancake Syndrome in Peru. Mite sensitized patients suffering from urticaria, angioedema, and anaphylaxis may experience these conditions after ingestion of foods contaminated with mites. Patients allergic to NSAIDs seem to be at a greater risk.

With this study, we hope to raise physicians' awareness about this condition, in order to prevent further life-threatening reactions. We acknowledge that this study has limitations, such as the absence of some flour samples for investigation. Some of the

Table 2

Relationship between pancake syndrome and hypersensitivity to nonsteroid anti-inflammatory drugs (NSAIDs)

Patient	Age (years)	NSAID hypersensitivity	Mites in the flour	SPT with house dust mite extracts	Confirmed diagnosis
I	32	+	+	+	+
II	13	Negative	+	+	+
III	42	+	+	+	+
VII	30	+	+	+	+
VIII	41	Negative	+	+	+
IX	5	Negative	+	+	+
X	14	Negative	+	+	+
XIII	5	Negative	+	+	+
XX	37	+	+	+	+
XXIII	33	+	+	+	+
XXV	27	+	+	+	+
XXIX	25	Negative	+	+	+

+ = positive, NSAID= nonsteroidal anti-inflammatory drug, SPT= skin prick test.

samples used in the cooking process were finished or had been discarded and thus no more samples were available. Based on this preliminary information, greater effort should be made in Peru, and Latin America in general, to disseminate the information available and avoid more severe life-threatening reactions due to ingestion of mite-contaminated flours. The worldwide information currently available about the OMA syndrome should be disseminated to reduce the number of patients affected by this syndrome.

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