ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Baker's rhinitis and asthma with concomitant wheat anaphylaxis: a rare overlap of clinical entities

Rinite e asma do padeiro com anafilaxia após ingestão de trigo: um caso raro de sobreposição de entidades clínicas

Filipa Rodrigues-dos-Santos[1], Inês Falcão[1], Borja Bartolome[2], Leonor Cunha[1]

ABSTRACT

Wheat is one of the fundamental sources of food worldwide. Baker's asthma and occupational rhinitis are both frequent and can be attributable to work exposure in bakers. However, the association between baker's asthma and wheat allergy is very rare. The authors report the case of a bakery worker who developed baker's asthma and occupational rhinitis after years of working in a bakery and later developed anaphylactic reactions after wheat ingestion.

Keywords: Occupational asthma, rhinitis, anaphylaxis, food hypersensitivity.

RESUMO

O trigo é uma das fontes alimentares mais importantes em todo o mundo. A asma do padeiro e a rinite ocupacional são frequentes e podem ser atribuídas à exposição a farinhas em padeiros. No entanto, a associação entre asma do padeiro e alergia alimentar ao trigo é muito rara. Os autores descrevem um caso em que um trabalhador de panificação desenvolveu asma do padeiro e rinite ocupacional após anos trabalhando em uma padaria, e posteriormente desenvolveu reações anafiláticas após a ingestão de trigo.

Descritores: Asma ocupacional, rinite, anafilaxia, hipersensibilidade alimentar.

Introduction

Wheat (*Triticum aestivum*) is one of the fundamental sources of food worldwide.[1] Depending on the route of exposure, wheat is responsible for different clinical manifestations of IgE-mediated allergy.[2] Ingestion of wheat can induce food allergy or wheat-dependent exercise-induced anaphylaxis; inhalation of wheat and rye flour is the main cause of baker's asthma.

Baker's asthma is a frequent form of occupational asthma, and affects up to 15% of bakers, millers, and pastry workers.[3] Inhalation of cereal flour proteins triggers an IgE-mediated bronchial reaction and can also result in rhinoconjunctivitis and contact urticaria.[3]

Proteins constitute approximately 10-15% of wheat grain and can be classified into two different fractions: salt-soluble proteins (albumins and globulins) and salt-insoluble proteins (prolamins, namely gliadins and glutenins).[4,5] Salt-soluble proteins, including alpha-amylase inhibitors, peroxidase, thioredoxin, nonspecific lipid transfer proteins (LTPs), serine

1. Centro Hospitalar Universitário de Santo António, Serviço de Imunoalergologia - Porto, Porto, Portugal.
2. Roxall, Research and Development Department - Bilbao, Bilbao, Spain.

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protease inhibitor, and thaumatin-like protein (TLP), are known allergens associated with Baker's asthma.[4,5]

Each of these fractions contains allergens that may induce a clinical reaction, although there is no consensus definition on either major or minor allergens, nor on their allergenicity after heating and processing.[1] Wheat flour LTPs (Tri a 14) have recently been identified as important allergens linked to both Baker's asthma and IgE-mediated food allergy.[4,5] Omega-5 gliadin (Tri a 19), associated with wheat-dependent exercise-induced anaphylaxis (WDEIA), has been associated with wheat food allergy.[3]

Recent studies in the United States in children and adults with wheat food allergy show a prevalence of about 0.5% in children and 0.8% in adults, with 50% being of adult-onset.[6] Although the association of Baker's asthma with wheat food allergy is very rare, overlapping between these two clinical entities may be possible through allergens such as alpha-amylase inhibitors, LTPs, and gliadins due to their sensitization potential through inhalation. Rarely, patients may develop symptoms after eating meals contaminated with uncooked wheat flour, but otherwise they do not report problems after ingestion of cooked wheat.[6]

Clinical case

The patient was a 45-year-old woman, resident in Porto, with a personal history of seronegative generalized myasthenia gravis, without any medication or other significant medical or surgical history. She worked as a counter attendant in a bakery shop for over two decades. Initially, she was asymptomatic, but after approximately 20 years she developed persistent symptoms of watery rhinorrhea, nasal itching, and nasal obstruction. She also experienced occasional wheezing and dyspnea after contact with flour in the workplace. She remained asymptomatic during holiday periods.

Two years after the onset of respiratory symptoms, the patient had 2 episodes of generalized maculopapular rash, with associated symptoms of pruritus, dyspnea, and throat tightness, approximately 15 minutes after ingestion of wheat bread. She had no history of infection, no drug or alcohol intake, or exercise prior to the episode. She presented at the Emergency Department and was treated with IM adrenaline 0.5mg/0.5ml, methylprednisolone 1 mg/kg IV, and clemastine 2g IV. Her serum tryptase level was 10.7 µg/L (reference value <10 µg/L) four hours after onset of symptoms, compared to 3.67 µg/L, obtained after the episode was resolved.

She was referred to the Immunology and Allergy clinic for further study. Skin prick tests were conducted for common inhalants and flours, which were positive (mm) for oat extract 6.5; rye extract 9, wheat extract 9, and histamine 9. The patient had a total IgE level of 100 kU/L. Specific IgE was positive (kUA/L) for wheat extract 11.20, rye extract 9.53, oat extract 0.77, and gluten 11.40, and negative for corn extract 0.21, rTri a 19 0.01 and rTri a 14 0.06. Spirometry findings were within the normal range. The post-bronchodilation test (with salbutamol) was negative. A bronchial provocation test with methacholine was positive. An open oral wheat provocation test was not performed due to the history of anaphylaxis. A bronchial provocation test with wheat flour was not performed due to the history of anaphylaxis. The ImmunoCAP™ ISAC test was negative.

SDS-PAGE Immunoblotting

Protein and Allergenic Profile

In order to study the IgE-binding protein profile, SDS-PAGE immunoblotting was performed in non-reducing conditions (without 2-mercaptoethanol). The patient's serum was incubated with gluten and extract from wheat seed and whole wheat flour. The IgE binding detected was much higher for the extracts of wheat seed and whole wheat flour than for the gluten sample. The wheat seeds and whole wheat flour extracts showed similar IgE binding profiles. Among others, two bands at approximately 15.5 kDa and 13 kDa were detected (Figure 1).

Based on her clinical history and the results of additional studies, the patient was diagnosed with occupational rhinitis, baker's asthma, and wheat-induced food allergy with anaphylaxis. An adrenaline autoinjector (Epipen® 0.3mg/0.3ml) was prescribed as well as desloratadine 5mg sos and prednisolone 60mg sos. A Mandatory Occupational Disease Report was submitted to the Portuguese Department of Protection against Occupational Risks, and a 100% work disability was assigned for a bakery work post. The patient underwent job reassignment with avoidance of inhalation of and contact with the cereal involved. Since then, she remains asymptomatic and maintains elimination of wheat ingestion, inhalation, and contact.

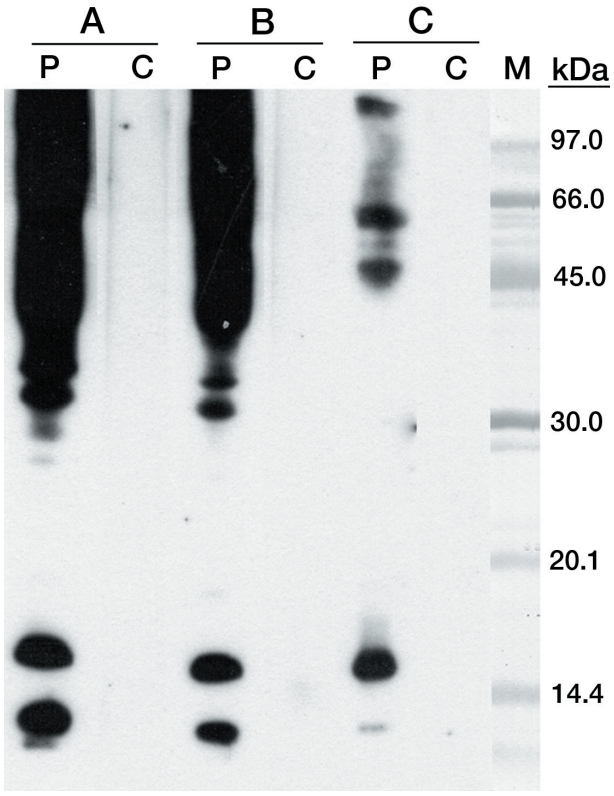

Figure 1
SDS-PAGE Immunoblotting

A) Wheat seed extract; B) Whole wheat flour extract; C) Gluten sample; Lane P = patient serum; Lane C = control serum; Lane M = Molecular mass marker.

Discussion

Food allergy to wheat in adults is a rare IgE-mediated hypersensitivity reaction, unlike baker's asthma, which is considered a significant occupational disease among bakery workers.[1] Most patients with baker's asthma do not show a concomitant food allergy. Bakers with occupational asthma typically consume bread and other foods containing wheat flour without developing adverse reactions. Our case is of particular interest, with an IgE-mediated mechanism being demonstrated both for baker's asthma and food allergy in the same patient.

In this case, sIgE to wheat proteins were detected in the patient's serum, which might be responsible for an allergic reaction upon exposure to, contact with, or ingestion of wheat. The IgE-binding band at approximately 15.5 kDa detected with wheat seed and whole wheat flour extracts has the same molecular weight as Tri a 30, described in the literature;[7] and the IgE-binding band of approximately 13 kDa detected in these same extracts has the same molecular weight as Tri a 28.[7]

The World Health Organization (WHO) allergen database lists 27 allergens for wheat, but the clinical relevance of many of them remains undetermined.[8] Tri a 28 and Tri a 30 are alpha-amylase/trypsin inhibitors and are members of the prolamin superfamily, one of the most allergenic proteins found in wheat. Wheat prolamins share sequence and structural homology with each other and with other proteins in rye and barley,[9] highlighting the importance of investigating cross-reactivity in this case. Alpha-amylase inhibitors have been associated with both baker's allergy and food allergy,[9-11] which is also described in our case.

Tri a 19 is by far the best characterized wheat allergen and is a major allergen for wheat-dependent exercise-induced anaphylaxis. It is also an important allergen in baker's asthma. However our patient seems not to be sensitized to Tri a 19. Other clinically relevant allergens include wheat Tri a 14, which has also been associated with baker's asthma[12] and food allergy.[13] Here we described an IgE-mediated allergy that is probably related to allergens other than Tri a 19 and Tri a 14.

In adults, food allergy to ingested wheat is uncommon and is normally observed as the WDEIA variant, in which symptoms of food allergy appear in response to a combination of wheat ingestion and physical exercise.[14] Moreover, most patients presenting with baker's asthma do not show concomitant wheat food allergy. In this case, we present a rare combination of baker's asthma and wheat-induced anaphylaxis after ingestion of wheat. We emphasize the need for referral of such patients to the Immunology and Allergy clinic, since identification of the causal allergen(s) has potential implications for accurate diagnosis and management of occupational exposition of these patients, with health and legal implications.

Management of IgE-mediated wheat allergy is mainly based on elimination of wheat from the diet and restriction of exposure to wheat flours is recommended in the case of baker's asthma[15] In case of accidental exposure and anaphylactic reaction, an epinephrine auto-injector can be a lifesaving treatment and therefore must be prescribed for all patients with anaphylactic history.

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Corresponding author:
Filipa Rodrigues dos Santos
E-mail: filipair.santos@gmail.com