

J. QUEIRÓS GOMES, L. BROSSERON, J. A. FERREIRA, I. ROSMANINHO, I. LOPES

Flour sensitization in a wooden door factory: what is the relationship?

Department of Allergy and Clinical Immunology, Centro Hospitalar Vila Nova de Gaia / Espinho EPE, Vila Nova de Gaia, Portugal

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Corresponding author

Joana Queirós Gomes
Department of Allergy and Clinical Immunology
Centro Hospitalar Vila Nova de Gaia / Espinho EPE
Rua Conceição Fernandes S/N
4434-502 Vila Nova de Gaia, Portugal
E-mail: joanarqueiros@gmail.com

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To the Editor,

Workplace exposures contribute substantially to asthma global burden, being related to 15-33% of adult asthma (1, 2). A wide variety of occupational substances have been associated to work-related asthma (WRA) (3). Over the last decades, significant changes occurred in workplaces with increasingly new agents introduced to work environment (3). Therefore, a complete occupational history of current and past jobs as well as hobbies is essential (2). Patients may not be aware of the exact work exposure, so all potential substances should be considered (1). We report the case of a 23-year-old woman with no relevant medical history, referred to our department for recurrent episodes of dry cough, dyspnea, nasal congestion and sneezing, along with nasal and ocular itching in the past 12 months. The patient had been working in a wooden door factory for 3 years, operating a glue applicator machine to unify wood veneers, being exposed to multiple substances without respiratory protection: wood dust, glue, paint vapors and thinners. Symptoms were exacerbated at workplace, especially one week a month when she prepared the

glue, which includes the addition of rye or wheat flour to several liquid products, as resins and hardeners. Symptoms improved on the rest of the month, vacations and weekends. She had no symptoms outside the workplace, tolerating cereal flour ingestion even with concomitant exercise. She also denied previous occupational exposure to flour (4). Improvement of symptoms was reported with inhaled budesonide/ formoterol 160/4.5 µg twice-daily and intranasal fluticasone 200 µg daily. Spirometry at first visit revealed normal baseline lung function with a moderate hyperresponsiveness to methacholine bronchial provocation test (PC20: 0.36 mg/ml) (5). Occupational asthma (OA) was based on FEV1 determined after the work shift on the week she prepared the glue, performed at the hospital's pulmonary function laboratory according to ERS/ATS criteria (mean FEV1 2.6 L [89.7%]; mean increased FEV1 post-bronchodilation 540 cc [16%]), and 6 weeks after the last period in which she made this task (mean FEV1 3.2 L [108%]; mean increased FEV1 post-bronchodilation 60 cc [2%]). Skin prick tests (SPT) with common inhalant and flours (Roxall-Aristegui, Bilbao, Spain) were positive to birch pollen and

to rye, wheat, barley, oats, and rice. Serum total IgE was 207 IKU/L. Serum specific IgE (ImmunoCAP, Thermofisher, Sweden) was elevated for rye (32.30 UK/L), wheat (9.10 UK/L) and barley (7.78 UK/L). Despite being sensitized to Tri a 14 (4.41 UK/L), a major allergen associated with baker's asthma, Tri a 19, commonly associated with wheat-dependent exercise-induced anaphylaxis (WDEIA), was found negative (0.01 UK/L) (6). She denied any symptom with ingestion of LTP containing foods. Patch-testing with Portuguese baseline, plastic and glues series, epoxy series (Chemotechnique Diagnostics™, Vellinge, Sweden) as well as wheat and rye flour (commercial flours without yeast diluted in isotonic saline solution) were negative (7). The patient was diagnosed with OA with sensitization to rye, wheat, and barley. In this factory, cereal flour (rye and wheat) was added to increase the viscosity of urea-formaldehyde glue used in veneer panels. We recommended her immediate removal from glue preparation area as well as exposure to flours. Six months after relocation the patient became asymptomatic and lung function returned to normal, despite remaining in contact with different woods and other chemicals such as formaldehyde. She preserved her job in another workstation without flour exposure. The case was reported to the appropriate public health authorities, in accordance with national regulation, waiting for evaluation.

In summary, we report a case of OA with sensitization to cereal flours in a wood industry worker. The diagnosis of OA was based on bronchial symptoms and lung function improvement on days away from work and decline with labor exposure, in a patient without previous diagnosis of asthma. Although specific inhalation challenge is considered an important tool in OA diagnosis, a negative challenge in a worker with evidence of OA does not exclude the diagnosis (8). It was not performed in our case, since it is not available in our hospital.

Our first suspicion was an occupational sensitization due to resins, woods, hardeners, isocyanates or glue formaldehyde, the most commonly used materials in this industry. We therefore investigated the different chemicals and woods used by the patient in past and current jobs and hobbies, and the contact with cereal flours became distinctive. In some veneer panels factories, cereal flours are used to increase glue viscosity. This addition reduces the cost and improves the look of final product (9).

Rye and wheat were the known flours used in this factory, however, the patient was also sensitized to other cereals such as barley. This sensitization pattern could be explained by small amounts of these cereals contaminating the rye and wheat flours. Another hypothesis could be the cross-reactivity between wheat, rye, and barley due to homology among inhibitors subunits of these cereals (10).

Wheat is the main culprit for OA caused by flours, also known as baker's asthma (BA). Although not yet entirely characterized, wheat proteins are the most studied among all cereals. Salt-soluble proteins, namely α -amylase trypsin inhibitor family and non-specific lipid transfer protein Tri a 14, seems to be the main proteins

associated with BA and wheat food allergy. Tri a 19 (Ω -5 gliadin), a salt-insoluble protein, is commonly related with WDEIA (4, 6). Component-resolved diagnosis using Tri a 14 can help to clarify the sensitization pattern and route. In BA, Tri a 14 was characterized by Palacin *et al.* (6) as a major allergen, in contrast with Sanders *et al.* (10) who reported it as a minor allergen.

In this case, a finding of a positive Tri a 14 (4.41 UK/L) along with negative Tri a 19 supports the sensitization by occupational exposure and not a wheat seropositivity based on cross-reactivity with grass pollens (11). Since the patient denied previous work in bakery industry or other area including cereal flours, the sensitization seems to have happened at the wooden doors factory. To our knowledge, our case report joins three other cases of flour sensitization in wood industries described by López-Rico *et al.* in Spain (9). Nevertheless, strong data about flour sensitization in wood industry was not found. OA produced by flour is well-known in bakers and millers but this finding in wood industry workers is unexpected and reveals the importance of a detailed occupational history.

Conflict of interests

The authors declare that they have no conflict of interests.

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