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Occupational asthma, rhinitis, contact dermatitis, and severe milk allergy caused by primary occupational exposure to casein



Respiratory allergy to milk proteins, including casein, remains rare in adults, and only a few case reports have been made in the context of occupational allergy.^{1,2} Moreover, casein is not listed as a substance that can cause occupational asthma.³

We report a case of occupational asthma, rhinitis, contact dermatitis, and severe milk allergy that started in adult life from occupational exposure.

A 22-year microbiology laboratory worker developed sneezing, watering eyes, cough, wheeze, chest tightness, and flushing within 5 minutes of exposure to culture media powder, despite wearing a basic dust mask. This happened on a weekly basis while preparing the culture medium. He began experiencing these symptoms 12 months after starting the job, and they took 12 hours to improve. He also reported worsening nasal congestion and chest tightness during the week, improving over the weekend and resolving completely on holidays.

Six months later, he developed allergic reactions after eating cheese and milk chocolate, developing generalized urticaria, lip swelling, abdominal pain, cough, and wheezing. This required admissions to the emergency department, where he was treated with

antihistamine, inhaled and systemic steroids, and intravenous fluids. Until this time, he was able to consume milk and milk products without any adverse reaction.

He also had episodes of acute allergic contact dermatitis whilst wearing latex gloves (Triflex, Baxter) with a clearly demarcated area of erythema under the glove. These latex gloves contain casein as a stabilizer.

He had no medical history of asthma, hay fever, or eczema.

CT-SMAC (0157 media powder) contains casein and is used in procedures for selective and differential isolation of Shiga toxin-producing *Escherichia coli* serotype O157:H7 from stool specimens. This powder can plume into the air when being mixed, easily coming into contact with mucous membranes, or be inhaled.⁴

Skin prick tests (SPT) to a standard panel of aeroallergens and latex were negative. The SPTs to milk proteins (raw and boiled milk, cheddar cheese) and to culture media containing casein were strongly positive (Table 1), whereas SPT to these reagents (containing casein) in 7 healthy negative control subjects were all negative. Specific immunoglobulin E (IgE; ISAC ImmunoCAP, Thermo Scientific, Uppsala, Sweden) to casein was elevated, and other milk proteins were negative (Table 1). Results of his routine spirometry were normal. Peak expiratory flow (PEF) variability was

Table 1
Skin Prick Tests and Specific IgE

Solution	Weal (mm)	Erythema (mm)
Positive control (histamine)	4	8
Negative control diluent	0	8
Soya	0	15
Milk (raw)	7	20
Milk (boiled)	3	15
Fresh milk	6	20
Gelofusin	2	8
Mature cheddar	10	30
<i>Candida albicans</i>	2	8x8
Latex	2	8
Culture medias (containing casein)		
BPW (buffered peptone water)	14 (pseudopodes)	40
Agar (XLD)	7 (pseudopodes)	40
0157:H7 (<i>Escherichia coli</i>)	10 (pseudopodes)	50
Specific immunoglobulin E (ImmunoCap ISAC)		
nBos d 8 (Casein)	2.3 ISU/L	
nBos d 4 (Alpha-lactalbumin)	Negative	
nBos d 5 (Beta-lactoglobulin)	Negative	
nBos d lactoferrin (Transferrin)	Negative	

between 670 L/min on day shift and 730 on a rest day. His exhaled nitric oxide was elevated, at 89 ppb.

Oasys is a computer program that plots and interprets PEF readings of patients suspected to have occupational asthma or work-related asthma, with 94% specificity for occupational asthma diagnosis and a 75% sensitivity.⁵

His Oasis work effect index was 2.67. Rest–Work PEF difference percent predicted was 0.90 (score of < 3.3 is associated with occupational asthma). The area between curves score on day shifts was 3.76 (A score of <15 is associated with occupational asthma.). Time point analysis showed 2 positive time points, with a significant drop in PEF to 400 L/min from 730 when he was preparing the culture media.

Our patient's history, the positive skin prick test, and positive specific immunoglobulin E (ImmunoCap and ISAC) sensitization to milk proteins used at work environment, and elevated exhaled nitric oxide along with positive Oasys-2 work effect index fulfilled the criteria for the diagnosis of occupational allergic asthma caused by milk protein (casein) sensitization.

The patient is now avoiding all dairy products. He has been successfully relocated at work and has been asymptomatic since. The causal relationship between symptoms and occupational exposure was also confirmed by disappearance of symptoms after removal from exposure.

Occupational allergic diseases are generally underreported, either because of the worker's reluctance to complain or the lack of an index of suspicion by the clinician. However, a wide variety of causative substances have been implicated in occupational asthma and rhinitis.^{1–3,6}

In adults, the reactions to cow's milk proteins are mostly cutaneous or gastrointestinal and are usually the consequence of a previous gastrointestinal sensitization.⁷

This case illustrates that sensitization to casein milk protein may occur via the respiratory tract in adults who are previously tolerant to milk, similar to other cases reported.^{7–10} The initial respiratory and later gastrointestinal allergic reactions that

resulted from milk product exposure began only after recurrent occupational exposure to a casein product over a period of 12 to 18 months.

Our patient developed acute contact allergic dermatitis on exposure to latex gloves; this is interesting because several brands of latex gloves contain casein.⁸ Ylitalo et al⁸ showed that the casein content of the glove used in preparing latex extracts use for natural rubber latex allergy screening (Triflex, Baxter) was rather high at approximately 400 µg/g of glove. Several brands of NRL gloves were found to contain casein, implying that extracts prepared from such gloves can cause false-positive SPT reactions secondary to milk protein sensitization. The use of casein as a stabilizer in glove manufacture also may be a cause of acute contact urticaria in individuals with cow's milk allergy.

In summary, allergy to milk proteins is not common in adults, and our case illustrates the rare occurrence of occupational allergy secondary to casein. All of the possible sources of sensitizing allergens in the work environment and mode of exposure to these substances should be considered carefully by clinicians investigating a suspected occupational allergy. A correct diagnosis and the subsequent allergen avoidance are critical, to enable patients to keep working, with a favorable socioeconomic outcome. Regulatory agencies need to include casein (milk proteins) as a potential occupational allergen and ensure appropriate labeling of casein and other milk proteins in different products (stabilizer in gloves, condoms, dummies, balloons, etc), where they can be a hidden allergen.

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