Case report

Adult-onset IgE-mediated cow's milk allergy—a rare phenotype

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Cow's milk allergy has been studied extensively in infants and young children and has public health importance around the globe. We describe the clinical and demographic characteristics of 3 cases of a rare presentation of adult-onset IgE-mediated cows' milk allergy. (J Allergy Clin Immunol Global 2023;2:100142.)

Key words: *Cow's milk allergy, adult-onset allergy, baked milk tolerance, milk allergy, alpha-lactalbumin, casein*

Abbreviations used
BM: Baked milk
CMA: Cow's milk allergy
OFC: Oral food challenge

Cow's milk allergy (CMA) is a common food allergy in infants and children, manifesting as an IgE-mediated or a non–IgE-mediated immune reaction.[1] Although most children outgrow CMA by age 6 years, the allergy can sometimes persist into adulthood.[1] Among children with CMA, 65% to 83% tolerate baked milk (BM)-containing foods. A low casein IgE level is a marker of BM tolerance.[2,3] Inclusion of BM in diets for children with CMA can accelerate resolution of allergy.[4] Epidemiologic studies highlight the growing incidence of adult-onset food allergy.[5] A recent US survey estimated a prevalence of 0.28 to 0.5% for IgE-mediated adult-onset CMA.[6] However, the literature on oral food challenge (OFC)-confirmed cases of adult-onset IgE-mediated CMA is scarce.[7] Here we describe the clinical features, diagnosis, and management of adult-onset CMA in a series of 3 patients with prior cow's milk tolerance.

PATIENT 1

A 32-year-old female presented with a suspected CMA. Her first reaction occurred during her second trimester of pregnancy at age 26 years. She experienced immediate-onset pharyngeal pruritus after milk ingestion that resolved spontaneously after several minutes. She subsequently avoided milk but was able to tolerate cheese and yogurt. At age 27 years, she developed lip angioedema immediately after eating cheese. Consequently, she began avoiding cheese. She continued to tolerate products containing BM. A few weeks before presentation, she developed lip angioedema, oropharyngeal pruritus, a globus sensation, and generalized urticaria within minutes of accidental cheese consumption. These symptoms resolved with oral diphenhydramine. She had no history of chronic urticaria. The results of serologic IgE testing were positive for milk and milk components (Table I). Six years ago, the patient's milk IgE level increased to 3.2 kU/L from 2.13 kU/L. Milk OFC resulted in oral pruritus, lip urticaria, and angioedema. The patient subsequently passed a BM OFC and continued regular consumption of BM products.

PATIENT 2

A 33-year-old female presented with an 8-year history of pharyngeal and ear pruritus following cow's milk consumption that had been progressively worsening. She denied dermal, respiratory, or gastrointestinal symptoms. She was able to tolerate cheese, yogurt, and BM products. The result of skin prick testing to milk was negative, but the patient's IgE levels for milk and milk components were elevated (Table I). CMA was confirmed by a positive OFC result. It was recommended that the patient avoid milk but continue intake of the dairy products (including BM), which she tolerated.

PATIENT 3

A 50-year-old male presented with multiple episodes of pharyngeal pruritus following milk consumption. His first reaction occurred in his mid-20s, when he moved from the United States to Japan. At that time, he experienced symptoms after consuming milk with cereal; his symptoms resolved spontaneously. He tolerated cereal without milk. His symptoms occurred after consumption of milk, butter, ice cream, chocolate, or certain cheeses. He started avoiding these foods but tolerated products containing BM. Three months before presentation, he accidentally consumed cow's milk in coffee and developed lower lip angioedema, oropharyngeal pruritus, and a globus sensation in his throat. His symptoms resolved over 30 minutes after taking oral cetirizine. The results of skin prick testing and serologic testing were positive to milk and milk components (Table I). The patient declined OFC to milk. The potential risk of anaphylaxis was discussed, and an epinephrine autoinjector was prescribed for all 3 patients.

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TABLE I. Characteristics of patients with adult-onset cow's milk allergy

Characteristic	Patient 1	Patient 2	Patient 3
Sex	Female	Female	Male
Race/ethnicity	Hispanic White	Hispanic White	White
Approximate age at symptom onset (y)	27	26	Mid 20s
Clinical reaction to cow's milk	Lip swelling, generalized hives, and oropharyngeal pruritus	Pruritus of oropharynx and ear	Lip swelling, oropharyngeal angioedema, and pruritus
Cow's milk IgE (kU_a/L)	3.2	4.82	3.97
Milk component panel (kU_a/L)			
A-lactalbumin	3.83	4.77	6.55
B-lactoglobulin	0.68	1.62	0.11
Casein	1.19	0.15	<0.10
Result of skin prick testing to cow's milk	Not performed	Negative	Positive (10 × 10-mm wheal)
OFC result	Positive at a cumulative dose of 30 mL of cow's milk	Positive at a cumulative dose of 240 mL of cow's milk	Patient declined OFC
Symptoms in response to OFC	Lip swelling, generalized hives, and oropharyngeal pruritus	Pruritus of oropharynx and ear	NA
Baked milk tolerance	Yes	Yes	Yes
Comorbid atopic conditions	Asthma and allergic rhinitis	Asthma and allergic rhinitis	Allergic rhinitis
Comorbid food allergies	None	Avocado, almond, and orange	None

NA, Not applicable.

Here we have reported 3 patients with adult-onset, IgE-mediated CMA. Written consent from all patients was obtained for publication of this case report. All 3 patients had nonsevere reactions and BM tolerance. In children, the majority of patients with CMA can tolerate BM products, and this is associated with allergy resolution. Although BM-containing diets accelerate the resolution of milk allergy,[4] their benefit in adults is not known. Interestingly, patient 3 in our cohort has continued to have milk allergy 25 years after symptom onset despite consuming BM products. Unlike children with BM tolerance, in this case, the allergy appears to be persistent.

In children, a casein IgE level less than 4.95 kU/L is a marker for BM tolerance,[4] which is a consistent finding in our patients with adult-onset CMA. BM tolerance was confirmed by OFC in patient 1 and by a history of consistent ingestion in patients 2 and 3. Casein has been the predominant source of sensitization among children with CMA allergy in our clinic population (data not shown), whereas α-lactalbumin was the predominant source of sensitization noted in all 3 adults in our cohort. In children, reports suggest that α-lactalbumin and β-lactoglobulin are weak predictors of BM tolerance,[2,3] but all 3 patients in our cohort were α-lactalbumin–sensitized and BM-tolerant. This is consistent with the thermolability of α-lactalbumin, which would be denatured by baking.[8]

All 3 patients in our cohort had tolerance to milk before onset of their symptoms. Their symptoms were progressive starting with native milk. The age of CMA symptom onset was between 25 and 30 years.

The prevalence of IgE-mediated adult-onset food allergy has increased in recent years.[5,9] Fish and shellfish are reported as being the most common culprits.[5] No apparent risk factors for adult-onset food allergies have been established, but some studies have postulated a role of genetic and environmental factors. These include infections, hygiene practices, food additives and processing, and exposure to agents that can change the homeostasis of gut mucosa (such as proton pump inhibitors, alcohol, and aspirin). In a recent survey of 78,851 US individuals meant to characterize the population burden of CMA in adults and children, 0.28% to 0.5% of the adult US population was estimated to have a convincing history of IgE-mediated adult-onset CMA.[6] Other demographic and clinical characteristics are not known. Further, literature on OFC confirmed CMA in adults is limited.[7] Adult-onset milk allergy may be underdiagnosed owing to nonsevere presentations, as seen in our cases. Sex and racial health care inequities may also contribute to underreporting because a higher prevalence of CMA was noted in females and those of non-Hispanic Black and Hispanic ethnicity.[6]

Adult-onset IgE-mediated CMA is likely an underreported phenotype linked to *de novo* α-lactalbumin sensitization. Our findings demonstrate that adult-onset CMA is associated with BM tolerance and does not manifest severe allergic reactions. Information from larger cohorts of patients with adult-onset CMA is needed to understand the risk factors, clinical features, and prognosis of this emerging phenotype.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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