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Sheep Rennet Food Allergy in a Child With Atopic Dermatitis: A Case Report

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Abstract

Rennet allergy is uncommon and has historically been described primarily as an occupational allergy among individuals with substantial exposure to powdered rennet, particularly cheese makers. We report a pediatric patient with atopic dermatitis who developed anaphylaxis following ingestion of Parmesan cheese containing sheep rennet, despite having previously tolerated Parmesan and other dairy products. Detailed review of the patient's exposure history revealed regular application of a goat milk-containing lotion for several years as part of the management of atopic dermatitis, raising concern for cutaneous sensitization to animal-derived proteins with subsequent cross-reactivity to sheep rennet.

Allergy evaluation was performed using skin-prick testing and measurement of serum specific IgE to sheep rennet. The combination of the clinical history and positive allergy testing supported a diagnosis of IgE-mediated hypersensitivity to sheep rennet as the likely cause of the patient's anaphylactic reaction. The absence of a prior clinical reaction to Parmesan, together with the history of prolonged topical exposure to goat milk proteins on an impaired skin barrier, suggested that sensitization may have occurred through repeated cutaneous exposure to the goat milk lotion.

This case demonstrates a rare presentation of anaphylaxis to sheep rennet in a child without occupational exposure and highlights a potential route of sensitization through topical exposure to animal milk proteins in the setting of atopic dermatitis. It underscores the importance of evaluating lesser-known ingredients, including processing agents, when investigating food-associated anaphylaxis, particularly when reactions occur to previously tolerated foods. This observation also raises awareness of the potential for cutaneous exposure to food-derived proteins in topical products to contribute to sensitization and subsequent systemic allergic reactions.

Categories: Pediatrics, Allergy/Immunology
Keywords: atopic dermatitis, food allergy, goat milk allergy, sheep milk allergy, sheep's rennet

Introduction

Rennet is a mixture of proteolytic enzymes, primarily chymosin and pepsin, used in cheese production. Although rennet is a recognized occupational allergen, IgE-mediated hypersensitivity has predominantly been associated with inhalational exposure, resulting in rhinitis, conjunctivitis, and asthma [1-4]. In contrast, systemic allergic reactions following ingestion of rennet-containing foods have not been well documented. Previously reported cases of anaphylaxis to sheep- and goat-derived cheeses have primarily implicated caseins rather than the enzymes used in cheese production [5-8].

We present a potentially first-reported case of suspected IgE-mediated anaphylaxis associated with ingestion of sheep rennet in a pediatric patient without occupational exposure. The patient developed anaphylaxis after consuming previously tolerated Parmesan cheese, with subsequent allergy testing demonstrating sensitization to sheep rennet. Notably, the patient had a history of prolonged application of a goat milk-containing lotion to eczematous skin, raising the possibility of epicutaneous sensitization through an impaired skin barrier [9-13].

The novelty of this case lies in two distinct findings: the identification of sheep rennet as a potential trigger of food-induced anaphylaxis outside the occupational setting and the possibility of a previously undescribed sensitization pathway involving topical exposure to goat milk proteins. The objective of this report is to highlight rennet as an under-recognized potential food allergen, describe its possible role in pediatric anaphylaxis, and explore epicutaneous sensitization as a potential contributing mechanism. Although the precise allergenic component and proposed sensitization pathway remain unconfirmed, this case broadens the clinical spectrum of suspected rennet hypersensitivity and underscores the importance of considering cheese-processing enzymes when evaluating otherwise unexplained allergic reactions to dairy products.

Case Presentation

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The patient is an 8-year-old boy with a past medical history of atopic dermatitis, currently being treated with as-needed triamcinolone, without known food allergies, who presented to the allergist's office after having symptoms of generalized hives, swelling, throat itching, abdominal cramping, and shortness of breath within a few minutes of consuming a new type of Parmesan cheese. The patient's mother stated that she cooked chicken alfredo pasta with known ingredients, with the exception of a new addition of Parmesan cheese to the recipe. The patient has not reacted previously to this dish and has no known history of food allergy. The patient was given 25 mg of diphenhydramine, and his symptoms did not recur at that time. A week later, the patient consumed the exact same meal with the new Parmesan used the preceding week and had the same reaction. The patient had consumed the pasta and alfredo independently without issue since his two reactions. The patient also consumes milk and cheeses that do not contain sheep's rennet without reaction. Upon review of the food labels, the patient was found to have consumed sheep's rennet. While discussing possible previous exposures to milk proteins and rennet, the patient's mother stated that she had used a goat's milk lotion on him for several months while attempting to control his atopic dermatitis, most recently using it 3 years prior to the current presentation.

Skin prick testing (SPT) and serum IgE (ImmunoCAP; ThermoFisher Scientific, Waltham, USA) were performed on the patient. A positive SPT is defined as a wheal greater than 4 mm, and a positive blood IgE level is defined as 0.35kU/L. In both the SPT and IgE ImmunoCAP, a positive result indicates likely sensitization. Chymosin rennet, "Il Villaggio" brand pecorino romano (the parmesan the mother had newly used; Atalanta Corporation, New Jersey, USA), and WalcoREN milk coagulant (Walcovit Inc., Quebec City, Canada) were tested on the skin as seen in Table *1* below. Commercial rennet is not available for serum IgE immunoCAP testing; as such, sheep milk and goat milk were used for testing, as seen in Table *2* below.

Tested Allergen	Wheal Size (mm)	Interpretation
WalcoREN Milk Coagulant	3	Negative
Il Villaggio Pecorino Romano	12	Positive
Chymosin Rennet	5	Positive

TABLE 1: Skin prick testing results

Reference ranges: Negative: Wheal diameter <4 mm; Positive: Wheal diameter >4 mm

WalcoREN (Walcovit Inc., Quebec City, Canada); Il Villaggio Pecorino Romano (Atalanta Corporation, New Jersey, USA)

Tested Allergen	Serum-Specific IgE (kU/L)	Interpretation
Goat Milk	0.41	Sensitization detected
Sheep Milk	0.27	Low-level detectable IgE

TABLE 2: Serum IgE Testing via ImmunoCAP

Reference ranges: Normal: <0.10 kU/L; Likely sensitization: >0.35 kU/L

ImmunoCAP (ThermoFisher Scientific, Waltham, USA)

The patient was clearly positive to the newly used pecorino romano and chymosin rennet on the SPT. The patient had shown sensitization to goat milk on the serum IgE test, but did not meet criteria for likely sensitization to sheep milk. Upon follow-up with the patient and his parents, he has not had further reactions after eliminating rennet-containing cheese from his diet.

Discussion

Rennet is a mixture of proteolytic enzymes, principally chymosin and pepsin, traditionally derived from the abomasum of young ruminants and used to coagulate milk during cheese production. Although rennet proteins are capable of inducing IgE-mediated sensitization, the published literature has overwhelmingly characterized rennet allergy as an occupational respiratory disease. Studies of workers exposed during rennet and cheese production have documented rhinitis, conjunctivitis, asthma, positive skin-prick testing, and rennet-specific IgE, with sensitization particularly associated with repeated exposure to powdered

enzyme preparations [3]. In one occupational cohort, 14 of 35 rennet-production workers demonstrated positive skin-prick testing to at least one rennet preparation, and sensitization was greatest among workers with regular exposure to rennet powder [5]. Thus, existing evidence establishes rennet as an inhalant occupational allergen but provides considerably less evidence regarding its capacity to cause systemic reactions following ingestion.

Our case is therefore clinically distinct from the predominant phenotype described in the literature. Our patient was a child without occupational rennet exposure who developed anaphylaxis after ingestion of Parmesan cheese that had previously been tolerated. Allergy evaluation demonstrated sensitization to sheep rennet, raising the possibility that an enzymatic component used in cheese production, rather than the major milk proteins alone, contributed to the reaction. This distinction is important because previous reports of severe allergic reactions to sheep- and goat-derived cheeses have predominantly identified caseins as the responsible allergens rather than the enzymes used during cheese production [5, 6, 7].

The sensitivity of food SPT is 85-95%, and the specificity is 87-97%. The sensitivity of food IgE testing ranges from 60-95%, and the specificity ranges from 30-85%. As such, it should be noted that these are diagnostic tools, and the higher the SPT wheal and serum IgE value, the more likely it is that the patient has been sensitized. History and a clinician-supervised in-office food challenge are the gold standard for diagnosis of a food allergy. Sheep and goat milk proteins nevertheless represent an important alternative explanation and a potential component of the sensitization pathway in this patient. Goat and sheep caseins share substantial structural and immunologic similarity, and multiple studies have demonstrated strong IgE cross-reactivity between them [5, 6, 8]. Muñoz Martín et al. demonstrated that sheep casein could be strongly inhibited by goat casein in a patient selectively allergic to sheep and goat dairy products, supporting shared IgE-binding epitopes between these proteins [6]. Similarly, Ah-Leung et al. evaluated 28 children with severe reactions, including anaphylaxis, to goat or sheep milk products despite tolerance of cow's milk and identified the casein fraction as the principal allergenic component [8]. Severe reactions to relatively small quantities of goat or sheep milk proteins have consequently been documented even in patients who tolerate bovine dairy products [6, 9].

In our patient, however, the clinical history argues against sheep milk protein alone as a complete explanation for the reaction. The patient had previously tolerated Parmesan and subsequently demonstrated tolerance of other cheeses, making a generalized clinical allergy to cheese or mammalian milk protein less consistent with the observed phenotype. In conjunction with evidence of sensitization to sheep rennet, this pattern raises the possibility that the specific rennet preparation contained in the implicated Parmesan contributed to the reaction. Given the specificity and sensitivity of our diagnostic tools, it’s important to understand that, while they are clinically useful, they certainly have their limitations. The key to food allergy diagnosis is a thorough history and an allergist-supervised in-office food challenge, if necessary. Nevertheless, without component-resolved testing of the exact cheese and its individual rennet and milk-protein constituents or a controlled oral challenge, causality cannot be established definitively. The possibility of concomitant sheep milk/casein allergy should therefore remain in the differential diagnosis.

A particularly noteworthy feature of this case is the patient's history of prolonged application of a goat milk-containing lotion to skin affected by atopic dermatitis. Increasing evidence supports the concept that disrupted epidermal barrier function in atopic dermatitis facilitates epicutaneous sensitization to food proteins. A systematic review found a strong, severity-dependent association between atopic dermatitis and subsequent food sensitization and food allergy, with evidence that atopic dermatitis may precede the development of food allergy [10].

Subsequent mechanistic and clinical literature has further supported the “dual-allergen exposure” hypothesis, in which exposure to food proteins through an impaired skin barrier can favor allergen-specific IgE production and sensitization, whereas early gastrointestinal exposure may promote oral tolerance [11, 12]. Recent reviews have specifically raised concern that food-derived ingredients incorporated into topical products may provide an unintended source of antigen exposure through compromised skin [12, 13].

These observations provide a biologically plausible framework for our patient's presentation. Repeated application of a goat milk-containing lotion directly to eczematous skin could have provided prolonged epicutaneous exposure to goat milk proteins during a period of impaired barrier integrity. Given the well-established immunologic cross-reactivity between goat and sheep proteins, particularly caseins, such exposure could theoretically have generated an IgE repertoire capable of recognizing homologous sheep-derived proteins [5,6]. Whether this sensitization extended specifically to sheep-derived rennet proteins cannot be determined from the available evidence, and direct cross-reactivity between goat milk proteins and sheep rennet has not, to our knowledge, been established. Accordingly, the proposed sequence of goat milk lotion exposure, epicutaneous sensitization, and subsequent reaction to sheep-derived rennet should be regarded as a mechanistically plausible hypothesis rather than a proven causal pathway.

The significance of this case lies in the intersection of two previously described but largely separate areas of allergy literature: occupational IgE-mediated sensitization to rennet and epicutaneous sensitization to food-derived proteins in patients with atopic dermatitis. Whereas rennet hypersensitivity has

predominantly been associated with repeated inhalational exposure in occupational settings, our findings suggest that clinically significant rennet sensitization may also warrant consideration in nonoccupational pediatric patients presenting with otherwise unexplained reactions to cheese. Furthermore, the history of chronic exposure to a food-derived ingredient through eczematous skin reinforces growing concerns regarding the use of topical products containing potentially allergenic food proteins in patients with impaired skin barriers.

Conclusions

This case describes an unusual pediatric presentation of anaphylaxis associated with sensitization to sheep rennet in the absence of occupational exposure. Clinicians evaluating unexplained anaphylaxis to cheese should therefore consider not only the major milk proteins but also less apparent ingredients and processing agents, including animal-derived rennet. The case additionally underscores the need for further investigation into the allergenic potential of food-derived proteins in topical products used on eczematous skin and whether prolonged exposure to such products can contribute to clinically relevant sensitization. Prospective investigation and molecular characterization of the relevant allergens will be necessary to establish the proposed sensitization pathway and determine its broader clinical significance.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Maribelle Moufawad

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Disclosures

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