

Case Report

Anaphylactic reaction to goat's milk in a cow's milk-allergic infant

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Goat's milk has been used as a substitute for cow's milk in cow's milk-allergic individuals. It is currently advocated for this purpose in writings and internet resources directed at the lay person, and infant formula based on goat's milk is available in many countries. Clinically significant cross-allergenicity between cow's and goat's milk has been noted, but a life-threatening cross-reaction has not been reported. We describe a 4-month-old infant with immunologically documented cow's milk protein allergy but no prior exposure to goat's milk who developed anaphylaxis after the ingestion of commercial goat's milk. Subsequent skin prick testing demonstrated a specific reaction to goat's milk. Thus, the cross-allergenicity between cow's and goat's milk proteins can lead to life-threatening complications. Individuals allergic to cow's milk protein should avoid goat's milk and goat's milk products.

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Individuals with food allergy may exhibit allergic symptoms after the ingestion of foods derived from related plant or animal sources. Cross-reactivity of specific immunoglobulins (Ig) with related antigens likely forms the biochemical basis of this clinical observation. Sera from individuals allergic to cow's milk proteins cross-react extensively *in vitro* with proteins found in milk from the goat (1–3) and other domestic mammals (3). The clinical cross-allergenicity between cow's and goat's milk may be significant (4), although no life-threatening hypersensitivity events have been reported. Here, we present a 4-month-old infant with immunologically documented cow's milk protein allergy, who suffered a life-threatening anaphylactic reaction after the ingestion of a commercial goat's milk preparation. Thus, the immunologic cross-reactivity between cow's and goat's milk proteins may lead to life-threatening clinical complications.

Case report

A 4-month-old Hispanic male infant was brought to the Pediatric Emergency Department of our institution for the treatment of an anaphylactic reaction. After an uncomplicated, full term

pregnancy, he was born at a local hospital, birth weight 3260 g, Apgar scores of 9 and 9. The mother denied the ingestion during the pregnancy of any foods that contained goat's milk or were derived from it. In the newborn nursery, the infant developed a severe feeding intolerance characterized by frequent non-bilious postprandial emesis of the infant formula, which was based on cow's milk protein (Enfamil®, Mead Johnson Nutritionals, Evansville, IN, USA). A postprandial serum glucose level on day 2 was 32 mg/dl. The infant was transferred to the Neonatal Intensive Care Unit. A complete sepsis evaluation was negative. Feeding intolerance secondary to cow's milk protein intolerance was suspected, and he was switched to a formula based on soy protein (Isomil®, Ross Pharmaceuticals, Columbus, OH, USA). The emesis decreased significantly in frequency and volume, and he was discharged home on day of life 7 on the same soy-based formula. At 4 months of age, he presented to a community hospital with an acute onset of watery diarrhea. A stool test was positive for the rotavirus antigen. A diagnosis of acute gastroenteritis was made, and the infant was discharged home on a commercial oral electrolyte maintenance solution. After 2 days

of good tolerance of this solution supplemented with fruit juices, the infant still appeared weak. A relative from the Dominican Republic suggested to feed the infant goat's milk to hasten his recovery. The mother fed him three ounces of reconstituted condensed goat's milk (1:1 diluted with boiled water). Shortly thereafter, he vomited, broke out in hives, developed respiratory distress and became blue and limp, and he was taken to the Pediatric Emergency Department of this institution. On arrival, he was afebrile, the heart rate was approximately 180, the respiratory rate 70–76, with an oxygen saturation of 82% on room air. The blood pressure could not be obtained. The physical examination revealed a well-developed cyanotic, hypotonic infant with facial edema, grossly audible wheezing, deep subcostal and suprasternal retractions, and generalized urticaria. His condition stabilized after the administration of supplemental oxygen, epinephrine, diphenhydramine, nebulized albuterol, and intravenous steroids. He was transferred to the pediatric intensive care unit, where he made an uneventful recovery. Total IgE and a complete blood count with differential were within normal limits. *In vitro* allergy testing by fluorescent enzyme-linked immunoassay (ImmunoCap, Pharmacia Diagnostics, Kalamazoo, MI, USA), performed on serum obtained approximately 12 h after admission, revealed cow's milk protein IgE, 2.16 kU/l [corresponding to Conventional Radio Allergo Sorbent Testing (RAST) Class II (moderate severity), normal value <0.35 kU/l]. Skin prick testing performed 6 weeks after discharge showed the following results: goat's milk (performed with an aliquot of the same commercial product), 4+; cow's milk protein, 3+; and histamine control, 3+ (dermaPIK[®] II skin testing system, Biomedex, Spokane, WA, USA; 0, no reaction; 1+, erythema <10 mm; 2+, wheal <7 mm and erythema <20 mm; 3+, wheal <10 mm and erythema >20 mm; 4+, wheal >10 mm and pseudopodia and erythema >20 mm). The infant was discharged home with a hypoallergenic casein hydrolysate infant formula (Alimentum[®], Ross Pharmaceuticals) and an epinephrine self-injection device (EpiPen Jr, Dey Labs, Napa, CA, USA). At 12 months follow up, he had no further allergic episodes on a diet consisting of the hypoallergenic formula, cereals, and baby and table foods free of milk proteins. He has been growing and developing age-appropriately.

Discussion

This patient's allergy to cow's and goat's milk proteins was demonstrated by immunologic and

clinical criteria. *In vitro* allergy testing and skin prick testing revealed specific reactivity with cow's milk protein. In addition, his feeding intolerance in the neonatal intensive care unit resolved after removal of the presumed offending antigen, i.e., cow's milk protein. Skin prick testing with goat's milk, too, revealed a specific reaction. In addition, the patient suffered a major anaphylactic reaction shortly after the ingestion of goat's milk, and the symptoms did not recur after its removal from his diet. The simplest explanation for this dual allergy is cross-reactivity of this patient's IgE with cow's and goat's milk protein(s). Separate sensitization to cow's and goat's milk proteins is unlikely as neither the infant nor the mother had been exposed to goat's milk proteins before.

Goat's milk has been considered a hypoallergenic milk source for cow's milk-allergic individuals in the agricultural (5, 6) and medical literature (7, 8), as well as in writings directed toward the lay person [e.g., (9)]. It is presently advocated for consumption by cow's milk-allergic individuals on popular health-related internet pages [e.g., <http://www.chiroweb.com> and <http://Ziegenmilch.com>. (in German)], and infant formula based on goat's milk is available in many countries. As illustrated in this case, some cultural groups prefer goat's milk to cow's milk under certain circumstances, especially at times of compromised health. Thus, the likelihood of a cow's milk-allergic individual ingesting goat's milk appears substantial.

Immunologic cross-reactivity among milk proteins from different mammals, including the cow and goat, has been reported previously [e.g., (1, 3)]. Homologies in amino acid sequence that are conserved in evolution likely form the molecular basis of this phenomenon. Indeed, the amino acid sequences of α_{s1} -caseins from cow and goat are 87% homologous (2). As early as 1958, Clein (10) reported that individuals with cow's milk allergy may also be allergic to goat's milk, although no data were presented to support this observation. Significant clinical cross-allergenicity between cow's and goat's milk has been documented by placebo-controlled oral food challenges (4), although a life-threatening reaction has not been reported. In agreement with cautionary statements made by others on the basis of biochemical cross-reactivity (1, 2), these authors suggested that individuals with cow's milk allergy should avoid goat's milk. Consistent with this, the evidence-based literature no longer recommends goat's milk as a milk source for cow's milk-allergic individuals. This case report describes a life-threatening complication resulting

from cross-allergenicity between cow's and goat's milk and thus provides further evidence that individuals with cow's milk allergy would be at high risk if they ingest goat's milk. Considering the high degree of immunologic cross-reactivity among milk proteins from other domestic mammals (3), it may be prudent to recommend that cow's milk-allergic individuals avoid mammalian milk in general. Camel's milk does not cross-react significantly with milk from other domestic mammals and may represent a notable exception (3).

This report illustrates another point of clinical interest. The initial feeding intolerance of the infant progressed to a full anaphylactic reaction by 4 months of age, indicating that mild allergy can escalate to severe anaphylaxis even in infancy. Thus, early diagnosis of milk protein allergy is paramount so that appropriate dietary advice can be given.

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