

This report is intended to alert physicians to the need for an extensive diagnostic approach and a prompt recognition of any unusual localization of non-Hodgkin's lymphoma in order to assure appropriate therapy.

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Anaphylaxis to Cutaneous Exposure to Milk Protein in a Diaper Rash Ointment

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A 12-month-old boy, with a strong history of cow's milk allergy, developed two episodes of anaphylaxis following cutaneous application of a casein containing ointment to an inflamed diaper area. RAST testing showed a significant elevation in specific IgE antibodies to milk and milk proteins. This experience suggests that children who are highly sensitive to milk may have severe allergic reactions on cutaneous exposure to milk or milk products.

THE MANIFESTATIONS of cow's milk allergy range from mild gastrointestinal disturbances, respiratory symptoms, eczema, and urticaria, to anaphylaxis. Most of these reactions occur after oral milk ingestion. Occasionally, similar reactions have been observed following cutaneous exposure to milk.^{1,2} A 12-month-old boy, when exposed to the milk protein casein in a common commercial diaper cream, developed several episodes of anaphylaxis.

Case Report

JR is a 12-month-old boy who was breast-fed until age 5 months, when he was first fed a small amount of cow's milk-based infant formula. Within 15 minutes, he developed a generalized erythematous rash with urticaria, clear rhinorrhea, and sneezing. No wheezing

or gastrointestinal disturbance was noted. The event was self-limited and lasted 10 minutes.

His mother had childhood asthma and atopic dermatitis exacerbated by milk exposure. His father has a history of asthma and animal dander allergy. Advice was given to avoid milk and milk products.

Several months later, JR accidentally drank some milk-based formula from another child's bottle. Within 15 minutes, he developed marked urticaria with wheezing and upper airway stridor requiring hospital admission. At 11 months of age, he was first given whole egg, which produced mild to moderate wheezing within 30 to 40 minutes. This resolved over 2 hours without specific treatment.

At 12 months of age, he developed diarrhea that caused a severe diaper dermatitis. The commonly used diaper cream, Desitin (Leeming Division, Pfizer, Inc., Parsippany, NJ), did not help the rash, so JR's mother switched to another common diaper cream, Diaperene Peri-Anal Ointment (Glenbrook Laboratories, Division Sterling Drug, Inc., New York, NY), which she applied to his very excoriated diaper area. Ten minutes later, he developed marked respiratory distress with wheezing and marked urticaria. On examination, respiratory rate was 80, and he was cyanotic with poor

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air movement. He improved with subcutaneous epinephrine and intramuscular diphenhydramine and was admitted for therapy with intravenous aminophylline and oral metaproterenol.

No ingestion of milk or other new food had occurred nor was there any evidence for intercurrent infection. He improved during the first few hours in hospital and was breathing easily. His mother routinely changed his diaper and again applied the Diaperene Peri-Anal Ointment. Within 5 to 10 minutes, he again developed generalized urticaria, retractions, and mild wheezing and respiratory distress. This reaction was much less severe than the first and resolved with an inhaled metaproterenol treatment.

JR's mother noted the relationship of the reaction to the use of the Diaperene Peri-Anal Ointment. When the labels of the Desitin and Diaperene Peri-Anal Ointment were compared (Table 1), the major difference was the presence of calcium caseinate in the latter. The Diaperene Peri-Anal was no longer used. The child was discharged from the hospital after 2 days without further hypersensitivity reactions.

Several months later, JR was RAST tested for sensitivity to whole milk and its major protein constituents. RAST testing was also performed for egg albumin and to soy protein. Results are listed below as % negative control, where positive is interpreted as 250% negative control and strongly positive is >2,500% negative control:

Whole milk	5,052
Alpha-lactalbumin	2,742
Beta-lactoglobulin	877
Casein	7,002
Egg albumin	7,169
Soy protein	2,122

His total IgE was 1,142 U/ml. The normal mean for a 1-year-old infant is <15 U/ml. RAST and IgE determinations were performed at Mayo Medical Laboratories, Rochester, Minnesota.

Discussion

The close temporal relationship between the exposure to the Diaperene Peri-Anal Ointment and the hypersensitivity reactions suggests a causal relationship. This is strengthened by the disappearance of these episodes since this product has been discontinued. The patient's clear clinical history of cow's milk sensitivity, his strongly positive RAST to casein, and multiple previous usages of Desitin without reactions all strongly suggest that the casein present in the Diaperene Peri-Anal Ointment was the offending antigen. The inflamed denuded skin caused by the diaper dermatitis may have enhanced the absorption of the casein, leading to the anaphylactic episodes in a highly sensitive infant.

RAST testing was performed, since we were reluctant to perform oral challenge or skin testing on the child due to his severe systemic reactions. All of the RAST results obtained were positive, despite the lack

TABLE 1. Comparison of Diaperene Peri-Anal Ointment and Desitin

Diaperene Peri-Anal Ointment	Desitin
Zinc oxide	Zinc oxide
Cod liver oil	Cod liver oil
Petrolatum	Petrolatum
Lanolin	Lanolin
Calcium caseinate (approximately 5%)	Talc
Methylene zethonium chloride	
Starch USP	
Fragrance	
Paraffin	
Mineral oil	
Yellow wax	

of clinical reactions to soy. The presence of lower levels of serum IgE antibodies to foods in young atopic children can be a normal transient phenomenon.³ The strongly positive RAST results, however, were consistent with the child's clinical hypersensitivity, since high concentrations of specific IgE antibodies to food antigens often indicate a clinical sensitivity to these foods.³

We discussed with the boy's parents the option of serial oral challenges with these antigens, because Bock⁴ has reported recently that under very controlled conditions careful oral challenges are feasible and, in his hands, safe. Despite the importance to the family of knowing whether the milk hypersensitivity persists as this boy grows older, they declined this test.

A severe cutaneous and systemic reaction with pallor and hypotonia has been reported in an infant undergoing skin testing with milk and several of its proteins.¹ More commonly, mild patchy erythema or urticarial reactions have occurred in areas such as the mouth, chin, neck, and upper chest where milk may come in contact with the skin.⁵ As the case reported here demonstrates, the small subgroup who show severe systemic reactions to milk must, in some cases, be protected from milk-related substances that come into contact with the body by means other than the oral route.

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