

Brief communication

Food protein-induced enterocolitis to casein hydrolysate formulas

John M. Kelso, MD,^a and Hugh A. Sampson, MD^b *San Diego, Calif., and Baltimore, Md.*

Casein hydrolysate formulas are commonly used as substitutes for milk-based formulas in infants with hypersensitivity reactions to milk. This approach is generally successful, although IgE-mediated reactions to the hydrolysates have been documented. Also, a completely elemental (i.e., amino acid) formula has been reported to be safe for use in children with IgE-mediated reactions to cow's milk.¹ We report an infant with food protein-induced enterocolitis in response to the hydrolysate formulas, which resolved when this elemental formula was used.

CASE REPORT

The patient is a boy who was fed milk-based formula (SMA) from birth and was well until 6 weeks of age, when rotaviral gastroenteritis and guaiac-positive stools developed. He was changed to soy-based formula (Nursoy) with resolution of the diarrhea but persistence of occult blood in the stool. During the third month of life, trials of Nutramigen and Pregestimil both caused diarrhea, whereas Alimentum feeding led to formed stools; however, the stools remained guaiac-positive when any of the three hydrolysate formulas were used. A colon biopsy, performed at age 4 months, revealed chronic inflammation with moderate tissue eosinophilia. An allergy consult was obtained at age 6 months. Skin prick test results were positive to milk and soy-based formu-

las and negative to hydrolysate formulas. At age 7 months he was started on an amino acid formula (Neocate, Scientific Hospital Supplies, Inc., Gaithersburg, Md.), and within 3 days his stools became and remained guaiac-negative. One month later he was challenged twice with Alimentum but had emesis within a few minutes.

DISCUSSION

Several food protein-induced gastroenteropathy syndromes have been described. Benign proctitis is a syndrome of blood-streaked stools in breast-fed infants, which is caused by food antigens in the mother's diet. Food-induced enterocolitis syndrome consists of vomiting, diarrhea with blood, and peripheral and fecal leukocytosis occurring within 2 to 12 hours of milk or soy-protein ingestion. Enteropathy syndrome is similar to gluten-sensitive enteropathy but occurs with other food proteins and is generally more benign and often transient. In some infants the ingestion of cow's milk (but not milk-based formula) may induce an iron-deficiency anemia with occult fecal blood loss or a protein-depleting enteropathy. The pathophysiology of these syndromes is unknown. They are probably immune but not IgE-mediated. The case presented here fits best with the diagnosis of enterocolitis syndrome. This syndrome, however, is generally treated by feeding hydrolysate formulas, an approach not successful in this case.

There are three casein hydrolysate formulas available in the United States (Nutramigen, Pregestimil, and Alimentum). All are extensively hydrolyzed, but a small percentage of larger peptide fragments remain.² These casein hydrolysates are often used successfully for infants with both IgE- and non-IgE-mediated reactions to regular milk and soy-based formulas. Nonetheless, there have been at least 12 patients reported in the literature who demonstrated IgE-mediated reactions to casein hydrolysates, indicating that peptide fragments large enough to cross-link mast cell-bound IgE molecules are present in these formulas. In addition, a few patients have been

From ^athe Departments of Internal Medicine (Allergy Division) and Clinical Investigation, Naval Medical Center, San Diego; and ^bJohns Hopkins University, Baltimore.

Supported in part by AI-24439 from the National Institute of Allergy and Infectious Diseases, National Institutes of Health.

The Chief, Navy Bureau of Medicine and Surgery, Washington, DC, Clinical Investigation Program sponsored this report no. S-92-007, as required by HSETCINST 6000.41. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Reprint requests: LCDR J. M. Kelso, MC, USN, c/o Clinical Investigation Department, Naval Medical Center, San Diego, CA 92134-5000.

J ALLERGY CLIN IMMUNOL 1993;92:909-10
1/54/50448

reported to have blood in the stools while they were fed one hydrolysate, which resolved when they were fed another hydrolysate^{3, 4} or elemental formula.⁵ Neocate formula is a mixture of synthetic amino acids, maltodextrin, fat, minerals, trace elements, and vitamins.

The patient presented here had tolerated milk-based formula for the first 6 weeks of life before his rotaviral infection. This intestinal mucosal insult may have allowed subsequent immunologic reactions to food protein. He had positive skin test results to milk and soy-based formulas, and some of his gastrointestinal symptoms may have been due to IgE-mediated allergic reactions while he was being fed those formulas. However, guaiac-positive stools persisted for 5 months after the acute rotaviral gastroenteritis and for 4 months after the introduction of hydrolysate formula and resolution of the diarrhea. Thus the blood in the stool, as well as the biopsy findings and prompt resolution of the guaiac-positive stools after changing to elemental formula, are very likely the result of food protein-induced enterocolitis syndrome rather than IgE or viral-mediated sequelae.

In conclusion, the patient presented demonstrates that treatment of food protein-induced enterocolitis syndrome with casein hydrolysates is not always successful and that feeding completely elemental (amino acid) formula may lead to resolution of the condition.

REFERENCES

1. Sampson HA, James JM, Bernhisel-Broadbent J. Safety of an amino acid-derived infant formula in children allergic to cow milk. *Pediatrics* 1992;40:463-5.
2. Assadullahi TP, Adler BR, Warner JO. Presence of high molecular weight peptides in protein hydrolysate formulae [Abstract]. *J ALLERGY CLIN IMMUNOL* 1992;89:228.
3. Powell GK. Use of casein hydrolysate formulas in the diagnosis and management of gastrointestinal food sensitivity of infancy. In: Lifshitz F, ed. *Nutrition for special needs in infancy: protein hydrolysates*. New York: Marcel Dekker, 1985:131-43.
4. Pettei MJ. Gastrointestinal milk intolerance of infancy [letter]. *Am J Dis Child* 1990;144:16.
5. Rosenthal E, Schlesinger Y, Birnbaum Y, et al. Intolerance to casein hydrolysate formula. *Acta Paediatr Scand* 1991; 80:958-60.