

PERINATAL/NEONATAL CASE PRESENTATION

Allergic enterocolitis presenting as recurrent necrotizing enterocolitis in preterm neonates

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An uncommon clinical entity mimicking necrotizing enterocolitis (NEC) is allergic enterocolitis secondary to cow's milk protein allergy. Although milk protein allergy is the most common food allergy among infants and young children, the incidence and prevalence of this disease entity presenting as enterocolitis in neonates is not well documented. We report this case of milk protein-associated allergic enterocolitis to highlight the unusual recurrent presentation as NEC, (with recurrent pneumatosis, bloody stools) managed successfully with modification of milk formula.

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Introduction

Necrotizing enterocolitis (NEC) is the most common life-threatening surgical and medical emergency of the intestine encountered in premature infants. Allergic enterocolitis, which is another mucosal inflammatory condition seen mostly in infancy, is less common among preterm neonates. Although this disease is rare in neonates, it can be confused with NEC, particularly in low birth weight infants who are in the neonatal intensive-care unit secondary to other illness. Allergic enterocolitis is relatively benign. We report a case of allergic enterocolitis presenting as a masquerader of recurrent NEC in a 26-week premature baby who recovered completely without any short- or long-term gastrointestinal complications with elimination of milk protein in the diet.

Case

A male preterm baby was born to a 30-year-old, G3P021, African-American mother at 26 weeks gestation. The mother's prenatal screening serological tests were all negative. The baby was delivered through cesarean section with a birth weight of 965 g. The baby was treated for respiratory distress syndrome at birth with conventional mechanical ventilation and weaned to nasal

continuous positive airway pressure on day of life (DOL) 2. Trophic feeds were started on DOL 2 with preterm formula and continued on expressed breast milk (EBM). Feedings were advanced at 20 ml kg⁻¹ day⁻¹ from DOL 8. On DOL 17, the baby developed abdominal fullness with emesis while on full enteral feeds with EBM (24 cal) fortified with human milk fortifier. The abdomen was firmly distended, but not tense, and bowel sounds were sluggish. The complete blood count was significant for marked eosinophilia (40%). The initial abdominal X-ray (AXR) was remarkable for the presence of nonspecific diffusely dilated bowel loops (Figure 1a). The baby was made nil per OS and intravenous antibiotics were started after the sepsis workup. The baby was pale and lethargic, with episodes of bradycardia requiring increased O₂ in the next 12 h, and an AXR at that time showed pneumatosis (Figure 1b) in the right lower quadrant with persistent dilated loops. The baby was managed medically as definitive NEC (stage 2 A) with IV antibiotics, gastrointestinal decompression and parenteral nutrition. Clinical and radiological improvement was noted over the next week with negative blood cultures. Feedings resumed with EBM from the eighth day after initial diagnosis of NEC and tolerated well.

Three days after resuming enteral feeds with fortified EBM (DOL 28), the baby developed diffuse abdominal distension with grossly bloody stools. The eosinophil count rose from 2 to 13%. The AXR showed diffuse pneumatosis (Figure 1c). The baby had a second sepsis workup, was made nil per OS and monitored for clinical progression of the disease. The baby was observed for clinical and radiological signs over the next several days, with return to a normal AXR on DOL 35. After resolution of this episode, the baby was switched to Pregestimil formula. The baby continued on this until DOL 58.

On day 61 of life (post conception age 34 weeks), the baby once again developed abdominal distension with grossly bloody stool. The eosinophil count showed a gradual increase with time (7 to 14%). The C-reactive protein was 2.8. Extensive pneumatosis was seen again (Figure 1d). A repeat sepsis evaluation and stool cultures for bacteria and virus were all negative. Stool examination for leukocytes was positive on Wright's stain. The only interval change was reintroduction of EBM (unfortified) for 3 days before

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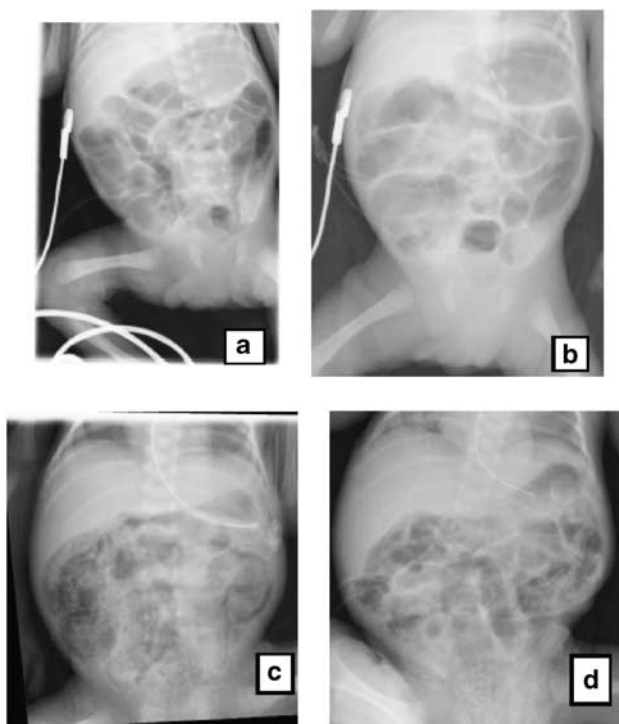


Figure 1 (a) Supine abdominal X-ray showing nonspecific diffuse bowel dilatation upon presentation on day of life (DOL) 17. (b) Diffuse dilatation of bowels with foci of pneumatosis (right upper quadrant and right lower quadrant linear) at 12 h after presentation on DOL 17. (c) Recurrent pneumatosis (extensive) on DOL 28 (second episode) and (d) recurrent pneumatosis (left lower quadrant) on DOL 61 (third episode).

the onset of these clinical symptoms. A change of formula to Neocate (amino acid-based) promptly showed resolution of symptoms with improved radiological findings. Owing to resolution of symptoms with alteration in the formula, an invasive endoscopic evaluation and biopsy was deferred.

This 26-week premature baby developed three clinical episodes of allergic enterocolitis mimicking NEC with definitive pneumatosis on AXR each time. The recovery was complete with conservative management and without progression of the illness with recurrence of clinical signs and symptoms related to milk protein exposure each time. This baby was discharged on Neocate. At 18 months visit the baby is growing well without any intolerance to feeds.

Discussion

Milk protein allergy is the most common food allergy in infants and young children.¹ The incidence and prevalence of this disease entity presenting as enterocolitis in neonates is not well documented and does not seem to affect NEC clinical trials.² This report summarizes a presentation of cow's milk protein allergy in the preterm infant that is not well described in the literature,

in which the infant presented with recurrent episodes of clinical, radiological findings mimicking NEC related to milk protein exposure, which successfully resolved with modification of formula.

Cow's milk induced enterocolitis presenting in the neonate as early as the first week has been reported very rarely in case reports both in term and preterm babies^{3,4} with isolated presentation of profuse rectal bleeding and with no other systemic, abdominal and radiological findings of NEC. This early onset is thought to be secondary to intrauterine sensitization. Our case was novel in that, in addition to early onset, there were recurrences of episodes of enterocolitis associated with increasing systemic eosinophilia, with each episode mimicking NEC clinically and radiologically.

Allergic enterocolitis is relatively benign. A review of literature shows that most infants with this condition are between the age of 1 and 6 months. They are predominantly term infants. The most common presenting symptoms of this disease include bloody stools (often mixed with mucus), abdominal distention (from flatus and third spacing) and irritability. Similar symptoms are sometimes associated with the initial presentation of NEC in preterm neonates. Such symptoms secondary to milk protein allergy rarely develop before 6 weeks of life, making it uncommon in infants weighing <2 kg. The pathogenesis of allergic colitis is driven by dietary antigens, resulting in mucosal inflammation, is relatively well characterized, and its treatment with dietary manipulation is well established.⁵

Symptoms can occur with cow's milk formulas, soy-based formulas and on breast milk fortified with cow's milk-based fortifiers. Suggested diagnostic criteria to diagnose milk protein allergy associated enterocolitis include: (i) cow's milk product exposure; (ii) abdominal distention; (iii) increased stooling, progressing to bloody stools; (iv) pneumatosis in severe cases; (v) resolution of symptoms with bowel rest and/or switch to a non-cow's milk or elemental formula; and (vi) almost never occurs before 6 weeks of life.⁶ Definitive diagnosis of allergic enterocolitis is difficult because there is neither specific laboratory data nor tests.¹ The only hematological abnormality is peripheral eosinophilia. Unique findings on upper and lower gastrointestinal contrast studies with thickened folds of the small intestine such as in spasm, or ribbon-like cords and narrowing, thumb printing in the large bowel has been suggested to be useful in suspecting cases with cow's milk allergic enterocolitis in older infants and children.⁷

Symptoms are also described in exclusively breast milk-fed infants which are attributed to exposure to the maternal dietary milk protein passed into the breast milk in an antigenically intact manner.⁸ The resolution of the symptoms in some infants with strict elimination of dietary cow milk protein in maternal diet has also been described.⁹ In our case, the first two episodes were preceded by exposure to EBM fortified with human milk fortifier. The last episode associated with exposure to unfortified EBM presumably indicates exposure to maternal dietary milk protein allergen passed on through the EBM.

We conclude that the characteristics noted in allergic enterocolitis include rapid onset of abdominal distension associated with grossly bloody stools and acute pneumatosis. Rapid improvement and nonprogression of systemic signs and symptoms after removing milk protein exposure differentiates from NEC and the episodes may be seen with recurrence on exposure to milk protein.

Conflict of interest

The authors declare no conflict of interest.

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