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Eosinophilic enteritis due to cow's milk allergy: Possible cause of anastomosis failure?

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Abstract

Reports of cases of Cow's Milk Allergy [CMA] after neonatal gastrointestinal surgery have recently increased. In recent years it has been suggested that the development of CMA after gastrointestinal surgery in newborn infants is due to an immune function. In addition, the development of CMA might be synergistically exacerbated by congenital abnormalities of the intestinal mucosa, general conditional changes and local damage to the intestine by invasive surgery, and poor pre- or post-surgical nutrition. CMA is manifested by a variety of symptoms, which cause problems such as mild vomiting and bloody stool, decreased activity, poor oral intake, and ileus. CMA may also rarely cause gastrointestinal perforation. Here, we report a case of a newborn infant who developed CMA following repair of focal small intestinal perforation, in which eosinophilic enteritis was suspected to be a possible cause of anastomosis leakage.

Keywords: Cow's milk allergy, Eosinophilic enteritis, Anastomosis leakage.

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Introduction

Several studies have reported an association between infants with surgical gastrointestinal disease and CMA [1-5]. In recent years it has been suggested that the development of CMA after gastrointestinal surgery in newborn infants is due to an immune function. In addition, the development of CMA might be synergistically exacerbated by congenital abnormalities of the intestinal mucosa, general conditional changes and local damage to the intestine by invasive surgery, and poor pre- or post-surgical nutrition [4,5]. CMA is manifested by a variety of symptoms, which cause problems such as mild vomiting and bloody stool, decreased activity, poor oral intake, and ileus [6,7]. CMA may also rarely cause gastrointestinal perforation. Here, we report a case of a newborn infant who developed CMA following repair of focal small intestinal perforation, in which eosinophilic enteritis was suspected to be a possible cause of anastomotic leakage.

Case Report

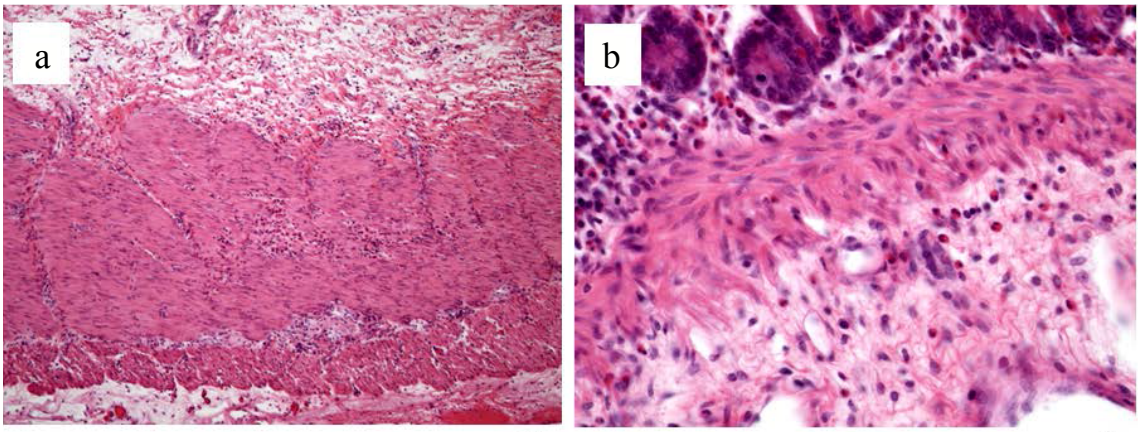
A 20 year old Japanese woman, gravida 2, para 0, was diagnosed with monochorionic diamniotic twins during a first trimester ultrasound examination at a district general hospital at 10 weeks. At 31 weeks and 3 days of gestation, she was referred to our hospital for threatened miscarriage. A baby boy, twin 2 of the monochorionic, diamniotic twins, was delivered at 37 weeks by elective cesarian section. The twin weighed 2300 g and had Apgar scores of 8 at 1 min and 9 at 5 min. Breast feeding was started from birth. On day 1, the baby developed abdominal distension. Free air was evident on plain X-ray. On laparotomy, fecal peritonitis was found. No evidence of Necrotizing Enterocolitis [NEC] was seen. A "punched out" entry and exit perforation was seen on the anti-mesenteric aspect of the ileum 25 cm proximal to the ileocecal valve which was leaking intestinal contents**.** Because the extruded intestine was severely edematous and gross peritoneal contamination was present, primary anastomosis was contraindicated, and ileostomy was performed instead to avoid complications such as anastomosis perforation or stenosis. Histopathology of the intestine around the perforation revealed a well-developed myenteric plexus and ganglion cells, and no evidence of microcirculatory impairment and eosinophilic infiltration. However, the muscle layer was abruptly discontinued**.** Histology of the site of the impending rupture showed an absence of the muscularis, with preservation of the remaining components of the bowel wall.

The postoperative course was uneventful. Breast-feeding supplemented with commercial cow's milk was started. However, the patient showed diarrhea and poor weight gain. Laboratory investigation showed hypereosinophilia

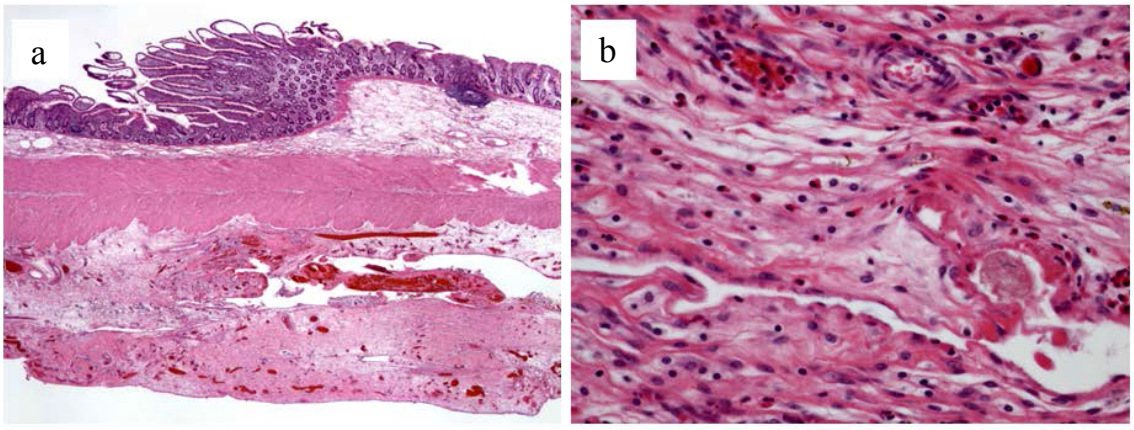
[total white cell count 7800/mm^3 with 6.9% eosinophils]. However, serum allergy investigations revealed no remarkable elevation of non-specific IgE, nor was there evidence of eosinophilia in the stool. Elective stoma closure was planned 6 weeks after the initial operation to maintain adequate fluid and electrolyte balance via the prevention of large-volume enterostomy output. Patency of the distal end of the bowel was confirmed before enterostomy closure by a retrograde contrast study. The intestine was edematous, but there was no evidence of the fragility of intestinal tissue. Although calibers of the small bowels differed [>2.5 times], a one-layer end-to-end anastomosis [monofilament absorbable suture 5-0] was performed using interrupted stitches.

However, the patient required reoperation 7 days after the enterostomy closure operation due to anastomosis failure. No intestinal ischemia was observed at the anastomosis site. Histologic examination of the specimen obtained at the re-ileostomy showed eosinophil and lymphocyte infiltration with intestinal edema (Figures 1a and 1b). Moreover, peripheral blood leukocytosis with hypereosinophilia developed after the operation. The patient was strongly suspected of having CMA, and an allergen-specific lymphocyte stimulation test [ALST] was performed. Lymphocyte response to kappa-casein was markedly increased [8390cpm; stimulation index 1.90, cut-off index 1.2], as was lactoferrin level [31353cpm; stimulation index 7.12, cut-off index 2.7]. Finally, the patient was diagnosed with eosinophilic enteritis due to CMA after the first stoma closure operation. We concluded that this was a case of CMA developing after neonatal intestinal surgery.

After switching to an amino acid formula [Elemental Formula○RR; Meiji, Tokyo, Japan] and casein hydrolysate formula [New MA-1○RR; Morinaga, Tokyo, Japan] from a cow's milk–based formula, his hypereosinophilia disappeared within a few weeks. The digestive symptoms improved and weight gain proceeded satisfactorily. Stoma reclosure was performed 5 weeks after the last operation. Histological findings showed that vessels were dilatated in the transmural region with intestinal edema. Moreover, diffuse fibrosis and increased eosinohilic infiltration of neutrophils, lymhocytes and plasma cells was observed in the subserosal layer and mesenteric regions (Figures 2a and 2b). This finding suggests that eosinophilic infiltration



Figures 1a and 1b. *Histologic examination of the specimen obtained at the re-ileostomy showed eosinophil and lymphocyte infiltration with intestinal edema.*



Figures 2a and 2b. *Histological findings showed that vessels were dilatated in the transmural region with intestinal edema. Moreover, diffuse fibrosis and increased eosinohilic infiltration of neutrophils, lymhocytes and plasma cells was observed in the subserosal layer and mesenteric regions*

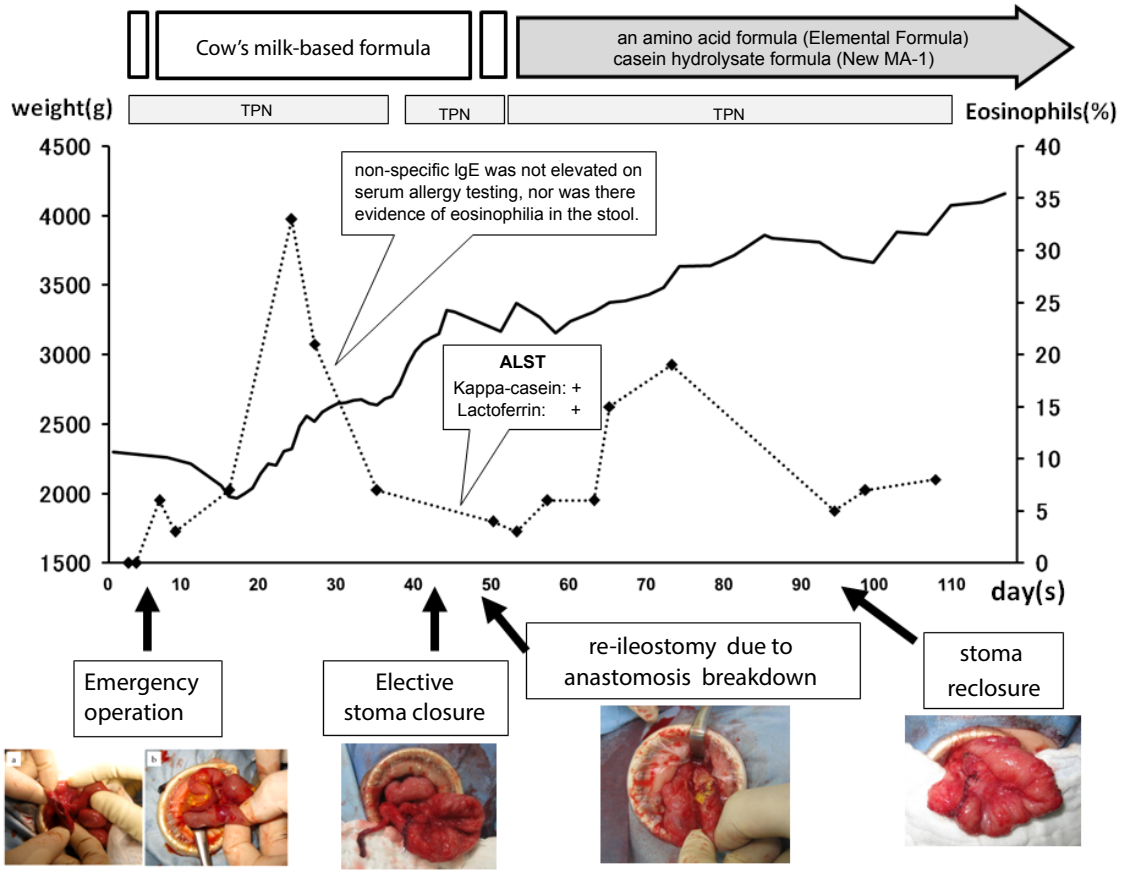


Figure 3. *Clinical course*

extended to the subserosal layer. The postoperative course was uneventful. The patient was discharged three months after the initial perforation, and was doing well on follow-up at 24 months.

Discussion

The course of this case raises an important clinical issue. CMA may occur after neonatal gastrointestinal surgery, and CMA-induced eosinophilic enteritis may be a possible cause of anastomosis leakage.

Several studies have reported an association between surgical gastrointestinal disease and CMA in infants. In recent years it has been suggested that the development of CMA after gastrointestinal surgery in newborn infants is due to an immune function. In addition, development may be synergistically exacerbated by congenital abnormalities of the intestinal mucosa, general conditional changes and local damage to the intestine by invasive surgery, and poor pre- or post-surgical nutrition [1-5].

Allergy to cow's milk is considered the main cause of eosinophilic enterocolitis. Of note, the clinical picture depends on the predominance of eosinophilic infiltration in the different layers of the intestine, namely the mucosal, muscularis, and serosal layers. Moreover, the clinical picture depends on the predominance of eosinophilic infiltration in these different layers. Accordingly, eosinophilic gastroenteritis has been classified as mucosal, submucosal [muscle] and serosal. Mucosal involvement is the most common, and develops with nausea, vomiting, abdominal pain, diarrhea, and weight loss. Involvement of the submucosal layer is accompanied by intestinal obstruction, which may be complicated by intestinal perforation [8,9]. The histological findings are consistent with eosinophilic enteritis and, as mentioned in the manuscript, eosinophilic infiltration extended to the subserosal layer in the present case.

Causes of anastomotic breakdown reported to date include technical errors, infection, and distal obstruction. Although these factors cannot be ruled out in our present case, we strongly suspect the involvement of CMA-induced eosinophilic enteritis. Indeed, eosinophilic enteritis due to CMA may be a possible risk factor for anastomotic failure. To our knowledge, however, no study has reported anastomosis failure related to eosinophilic enteritis due to CMA in an infant.

The development of CMA after neonatal gastrointestinal surgery is not rare. Given that eosinophilic enteritis associated with CMA is a possible factor in anastomosis leakage, stoma closure should be performed with caution in patients who are suspected of having CMA, with symptoms including eosinophilia, watery stools, and poor weight gain after neonatal gastrointestinal surgery.

References

1. Thomas DW, Sinatra FR, Swanson VL, et al. Milk hypersensitivity in an infant with gastroschisis. J Pediatr Surg 1982; 17: 309-310.

2. Snyder JD, Rosenblum N, Wershil B, et al. Pyloric stenosis and eosinophilic gastroenteritis in infants. J Pediatr Gastroenterol Nutr 1987; 6: 543-547.
3. Tsai MJ, Lai NS, Huang YF, et al. Allergic eosinophilic gastroenteritis in a boy with congenital duodenal obstruction. J Microbiol Immunol Infect 2000; 33: 197-201.
4. Kawano T. In: Perinatal medicine. 6. Prinatal medicine editorial committee, editor. Tokyo: Tokyo Igakusya; Milk allergy in neonates 2006: 766-767.
5. Ri S, Ichiba H, Ehara E, et al. Three cases of milk allergy developed after surgical operations of neonatal gastro-intestinal disorders (in Japanese) J Jpn Soc Premature Newborn Med 2006; 18: 35–41.
6. Apps JR, Beattie RM. Cow's milk allergy in children. BMJ. 2009; 339: 343-345.
7. Miyazawa T, Itabashi K, Imai T. Management of neonatal cow's milk allergy in high-risk neonates. Pediatr Int 2009; 51: 544–547.
8. Klein NC, Hargrove RL, Sleisenger MH, Jeffries GH. Eosinophilic gastroenteritis. Medicine (Baltimore) 1970; 49: 299-319.
9. Talley NJ, Shorter RG, Phillips SF, Zinsmeister AR. Eosinophilic gastroenteritis: A clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. Gut 1990; 31: 54-58.

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