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Application of Mitomycin C after dilation of an anastomotic stricture in a newborn with necrotizing enterocolitis



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ABSTRACT

Necrotizing enterocolitis (NEC) is a common life-threatening condition in premature infants. Bacterial translocation, localized inflammation and subsequent perforation often require surgery for source control and definitive treatment. Small and large intestinal strictures may result from either creation of a surgical anastomosis or the disease process itself. Current methods to treat strictures include, balloon dilation and surgical resection with or without anastomosis. We report the diagnosis and surgical management of a premature infant treated for NEC, who developed an anastomotic stricture and was successfully treated with topical Mitomycin C after balloon stricturoplasty.

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Necrotizing enterocolitis occurs 1–3 per 1000 live births and almost exclusively in premature infants. Very low birth weight (VLBW) infants, <1500 g have a 6–7% chance of developing NEC [1]. Medical management consisting of holding enteral feeds, serial abdominal radiographs and antibiotics is initially trialed. However, surgical intervention is often required when necrosis persists or perforation occurs. One of the most frequent complications of NEC is stricture formation, which occurs in 9–36 percent of infants treated medically and surgically [2–5]. Intestinal strictures result from collagen deposition, fibrosis and contraction over time following acute inflammation [6]. Mitomycin C is an antifibrotic agent which has been successfully used after balloon dilation of esophageal and anal strictures to prevent additional procedures [7,8].

We present a case in which an anastomotic stricture was discovered in a neonate after colonic resection for NEC. We also introduce the use of topical Mitomycin C after balloon dilation of an ileo-sigmoid stricture.

1. Case report

A 30 week-old premature male, weighing 1365 g, was delivered via emergent cesarean section secondary to fetal distress and

immediately intubated due to acute respiratory failure. Maternal breast milk feeds were initiated day of life (DOL) 1. However, on DOL 8 the infant became lethargic and was noted to have abdominal distention. Abdominal radiographs revealed widespread pneumatosis intestinalis and he was diagnosed with NEC. Initially,

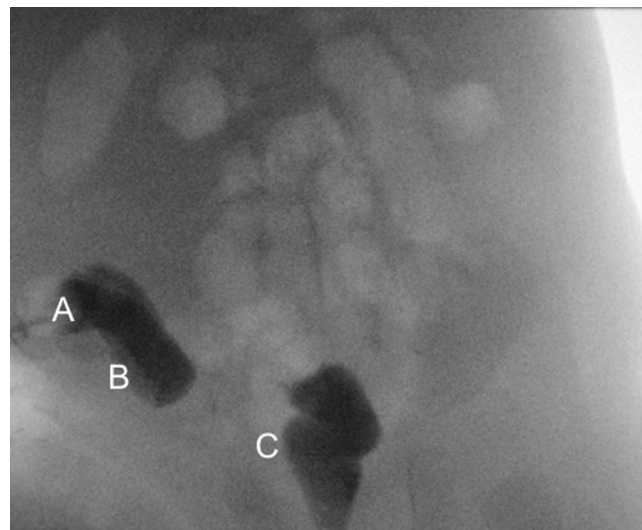


Fig. 1. Contrast enema at age 3 months. A: Mucus fistula, B: Ileum, C: Rectosigmoid.

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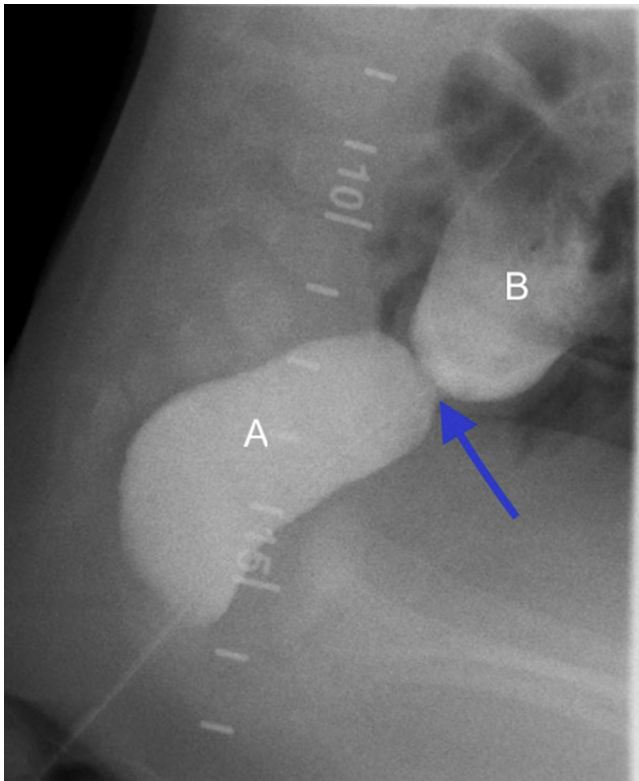


Fig. 2. Contrast enema with ileorectal anastomotic stricture at age 6 months. A: Rectum, B: Ileum, Arrow: Ileorectal anastomosis.

the patient was medically managed by holding enteral feeds held, administering broad-spectrum antibiotics, monitoring serial abdominal exams and radiographs. On DOL 9, lateral abdominal X-ray demonstrated portal-venous gas and free air. An emergent exploratory laparotomy revealed grossly necrotic distal transverse and descending colon, with patchy necrosis of the ascending colon. Sparing of the distal sigmoid and rectum were apparent. A partial transverse and descending colectomy was performed, with end ileostomy and mucous fistula. The procedure was well-tolerated and the patient was extubated on post-operative day 5. Feeds resumed on DOL 22. The patient was discharged home on DOL 45.

The patient was followed closely as an outpatient, tolerating diet and gaining weight. A scheduled water-soluble contrast enema

revealed that distal sigmoid and rectum were patent. Contrast administration at the mucus fistula suggested a small segment of distal ileum. The ileo-cecal valve could not be demonstrated with antegrade or retrograde contrast (Fig. 1). A planned exploratory laparotomy at 3 months of age revealed that the remaining ascending and proximal transverse colon were completely fibrotic and without a patent lumen. After extensive lysis of adhesions, a completion right colectomy and a hand-sewn end-to-end ileo-sigmoid anastomosis were performed. The baby tolerated the procedure well and was discharged home on post-operative day 2.

At 6 months of age, our patient presented to clinic with episodes of extreme discomfort that occurred periodically throughout the day, often prior to bowel movements. Symptom resolution occurred after passing small amounts of stool. Contrast enema study confirmed an anastomotic stricture 7.5 cm from the anal verge, measuring 5.7 mm in width and 2 mm in length (Fig. 2). This site could not be comfortably palpated by physical examination.

The patient was taken to the operating room for exam under anesthesia. Using a rigid sigmoidoscope, we visualized the stricture approximately 10 cm from the anal verge and were unable to traverse it with the scope. Under fluoroscopic guidance, balloon dilation (Boston Scientific CRE™) was performed 3 times to a maximum diameter of 16.5 mm, allowing the area to dilate for at least 5 min each time (Fig. 3). Next, the rigid sigmoidoscope was advanced past the stricture to confirm patency and evaluate for luminal injury. Using a long cotton-tip applicator, Mitomycin C (1.0 mg/ml) was delivered along the length of the stricture. The cotton-tip applicator was allowed to remain in place for approximately 5 min. The patient tolerated the procedure well and was discharged home the same day.

2. Discussion

NEC remains a devastating condition amongst neonates leading to shock, coagulopathy and sometimes death [9]. Although the true etiology of NEC remains elusive, risk factors include VLBW, prematurity and early enteral feeding [10,11]. Medical management is appropriate in some cases [12]. However, infants with advanced NEC and bowel perforation require surgical intervention with the potential of short bowel syndrome postoperatively [9].

Strictures occur in patients managed medically as well as, those who have required surgical intervention [2–5]. Most strictures occur in the colon, however small bowel strictures are also found [13,14]. Our patient developed an anastomotic stricture. We

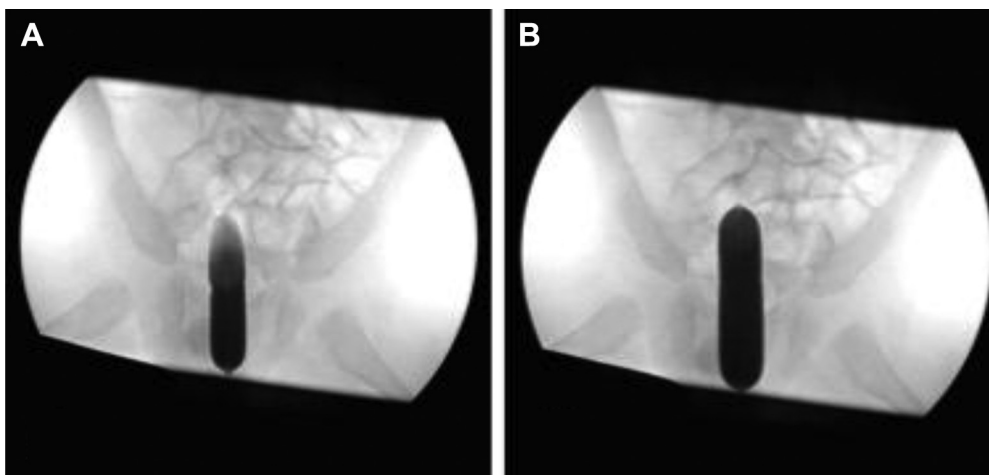


Fig. 3. Balloon dilation of ileorectal anastomotic stricture. A: Partial expansion, B: Complete expansion.

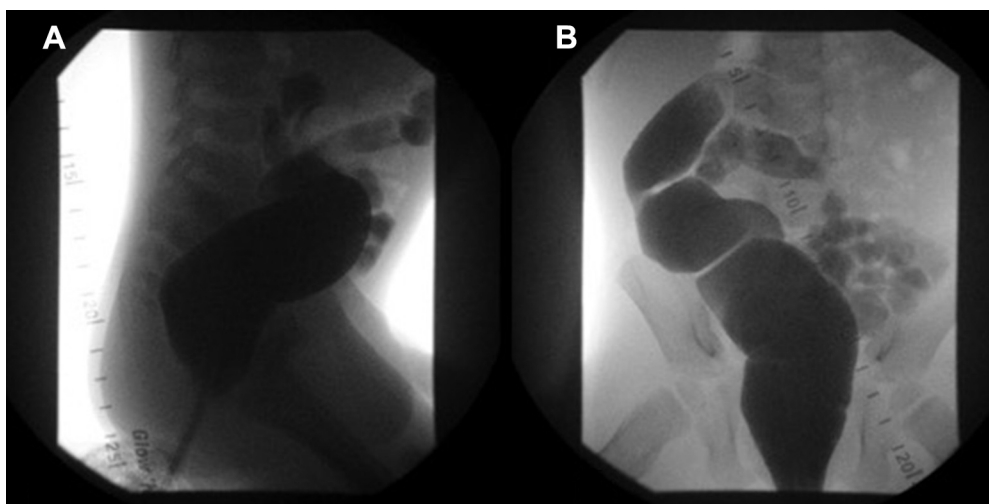


Fig. 4. Contrast enema 2 years post dilation and topical Mitomycin C application. A. Lateral image; B. Anterior/posterior image.

recognize that this stricture may be attributable to the surgical procedure, underlying disease or a combination of the two. After treatment with balloon dilation, Mitomycin C was administered topically in hopes to avoid recurrent stricture and further abdominal surgery including bowel resection and enterostomy, Mitomycin C (MMC) is an antibiotic produced by *Streptomyces caespitosus*. It inhibits DNA-dependent RNA synthesis and suppresses cellular proliferation. In addition to its antibiotic properties, it has been successfully used as an antineoplastic and antifibrotic agent [15]. Although historically most often used to treat ocular conditions, topical administration of Mitomycin C has been effective in treating esophageal and anal strictures [7,8]. Eighty percent of pediatric patients achieved complete resolution of esophageal stricture requiring fewer numbers of dilations with the use of 0.4 mg/ml MMC compared to 35% in the placebo group [7]. Treatment doses vary within the literature. We chose to use a 1.0 mg/ml concentration of topical MMC, as this dose has been successfully used in treatment of pediatric anal stricture [8]. This was safely tolerated by our patient and he has not required any additional dilations or surgical interventions after 2 years of follow-up (Fig. 4).

3. Conclusion

Strictures are a complication of NEC, as well as surgical enterostomy. Low-dose topical Mitomycin C reduces recurrence of esophageal and anal strictures in pediatric patients. Although further investigation is required, our case demonstrates that topical Mitomycin C is safe and may also provide benefit to anastomotic strictures in pediatric patients after balloon dilation. This novel strategy has not been previously reported within the literature.

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