Fatal *Clostridial* necrotizing enterocolitis in a term infant with gastroschisis

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**ABSTRACT**

Necrotizing enterocolitis (NEC) is most often a disease of preterm infants, but can develop in full term infants with gastroschisis. The latter cases typically present later and have a milder clinical course; we present the first case of fatal *Clostridium perfringes*-associated NEC in a full term infant with gastroschisis. Our case highlights the need for a high index of clinical suspicion for *Clostridial* NEC when there is rapid progression of disease and/or evidence of hemolysis. When *Clostridial* NEC is suspected, we recommend treatment with penicillin G and clindamycin, as well as prompt, aggressive surgical intervention.

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Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in neonates and is the leading cause of mortality among pre-term infants. *Clostridium perfringes*-associated NEC has a particularly fulminant course in these babies, with up to mortality [1]. Fewer than 10% of all NEC cases occur in term infants; these babies often have associated with congenital heart disease, gastroschisis, intruterine growth restriction, or sepsis [2]. NEC may develop in up to 18% of infants with gastroschisis and runs a mild course [3]. Here we report the first case of *C. perfringes*-associated NEC in a full term infant with gastroschisis.

1. Case

A 3.7 kg term baby girl with a prenatal diagnosis of gastroschisis was transferred to Seattle Children’s Hospital at 2 h of life. After initial silo placement and intubation for respiratory distress, bedside reduction with umbilical cord closure was completed at 9 h of age [2]. Due to ongoing drainage from her peritoneal cavity around her umbilical cord closure, sutured fascial closure over an inlay aloderm patch was performed on day of life 17. She had an uncomplicated recovery after closure; every 3 h expressed breast milk feeds were initiated on day of life 37 at 10 mL/kg/day and advanced to goal. She was discharged home on day of life 61, but returned 2 days later due to parental concern for feeding intolerance. On readmission there was no distention, vomiting, fever, tenderness, or constipation/obstipation, and it was determined that her gavage feeds may have been administered too quickly at home. Parental education and discharge planning were re-initiated.

On day of life 67, she developed sudden onset emesis, abdominal distension, tachycardia, and tachypnea. Within 1 h, despite fluid resuscitation and broad-spectrum antibiotics (vancomycin and piperacillin-tazobactam), she became hypotensive, bradycardic, and required a bolus of epinephrine. She had a venous lactate of 11.0 and her hematocrit dropped from 38% to 22% within an hour; at that point penicillin G was given. An abdominal radiograph demonstrated markedly distended loops of bowel, pneumatosis intestinalis, and portal venous gas (Fig. 1), raising concern for NEC. She underwent emergent bedside laparotomy 2 h after the onset of symptoms, revealing cloudy ascites, diffuse patchy areas of small bowel ischemia, and a perforation in the ileum. The perforation was resected using the “clip and drop” technique and her abdomen was left open. No signs of intestinal obstruction were noted. Despite ongoing aggressive resuscitation she remained reliant on high dose vasopressors and continuous transfusions; care was transitioned to comfort measures and she died 8 h after the initial onset of her symptoms.

At autopsy, evidence of repaired neonatal gastroschisis was seen, with closure of the abdominal wall and an unfixed mesenteric root. The small bowel was distended with focal gross pneumatosis (Fig. 2A). Microscopic examination showed evidence of diffuse ischemia, with hemorrhagic necrosis of the mucosa from the

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stomach to distal rectum; no intravascular thrombi were identified (Fig. 2B). Pneumatosis of the submucosa and mesenteric soft tissues was present. Tissue gram stain revealed large gram-positive bacilli within the mucosa and the submucosal lymphatic channels (Fig. 2C). Premortem peritoneal fluid cultures grew mixed enteric flora, including *C. perfringes*.

2. Discussion

NEC is an acute inflammatory disease of the intestine that typically affects premature infants in the days to weeks following initiation of enteral feeding. Abnormal colonization of the gut is an established risk factor for the development of NEC; probiotics have shown some benefit in preventing NEC [4]. Premature infants have decreased diversity of their intestinal microbiome, as well as, decreased abundance of the commensal, protective bacterial species *Lactobacillus* and *bifidobacteria* spp. [5]. In term infants, prolonged hospitalization, use of antibiotics, and acid suppressing medications may also alter intestinal flora, allowing for colonization by pathogenic bacteria such as *Clostridium* spp., *Enterobacter cloacae*, and *Escherichia coli* [4]. Gastroschisis is a known risk factor for NEC, with NEC occurring in 2–18% of these patients [3,6–9]. In contrast to NEC in premature neonates, gastroschisis-associated NEC presents later in infancy, with a mean onset 38–80 days after initiating enteral feeds [7]. Infants with gastroschisis-associated NEC tend to have a milder form of the disease, with only two previously reported cases that have required surgical intervention, and no prior reports of perforation in this population [6,7,10–12]. Furthermore, among infants with gastroschisis who develop NEC, only two deaths have been previously reported; both of these patients had the additional risk factor of prematurity [7]. This is the first reported case of *C. perfringes* associated NEC in an infant with gastroschisis, as well as the first reported case of NEC-related death in a term infant with gastroschisis.

*C. perfringes* is a gram positive, anaerobic, gas producing bacterium. Numerous reports linking *C. perfringes* to fulminant cases of NEC in preterm neonates are present in the literature; these cases

![Fig. 1. Supine abdominal plain film taken at 45 min after symptom onset, showing diffuse bowel dilation, pneumatosis intestinalis (arrowheads), and portal venous gas (arrow).](image1)

![Fig. 2. A. Small bowel, in situ, with diffuse distention and dusky discoloration consistent with ischemia; *marks area of perforation. B. Microscopic image with severe mucosal necrosis and ischemic changes; H&E, 500 μm. C. Collections of “rod-shaped” gram-positive bacilli present within the mucosa and submucosa; Brown and Brenn (gram stain), 100 μm.](image2)
tend to present earlier than other patients with NEC, with a mean age of onset between 2 and 8 days of life [1,13]. The hallmark of Clostridial NEC is rapid progression of symptoms with a high incidence of portal venous gas, intestinal perforation, and profound hemolysis, all of which distinguish it from typical NEC. The reported mortality due to Clostridial NEC ranges from 50 to 80%, and often occurs within hours of symptom onset [1].

This case is an unusual presentation of NEC, given the presence of C. perfringes in a term infant with gastroschisis. While the timing of symptom onset was fairly typical for gastroschisis-related NEC, i.e. greater than 30 days after initiation of enteral feeds, the subsequent fulminant course despite aggressive surgical management and the presence of C. perfringes are unusual. Therefore, it is imperative to maintain a high index of suspicion for Clostridial NEC when there is rapid progression of sepsis associated with portal venous gas, even in term infants. Concern for Clostridial infection should be even higher if there is evidence of hemolysis, a known secondary effect of C. perfringes toxin A [1]. In cases where C. perfringes is suspected, high dose penicillin G and clindamycin should be empirically added to the antibiotic regimen [1].

3. Conclusions

C. perfringes-associated NEC may present in term infants with gastroschisis, even months after repair. If Clostridial NEC is suspected, either due to a rapid progression of illness or hemolysis, the antibiotic regimen should be broadened to include penicillin G and clindamycin. In addition, aggressive surgical action should be taken, as this may offer an increased chance at survival in this disease with high mortality.

Conflicts of interest

None.

References