J Ped Surg Case Reports 14 (2016) 29–31

Contents lists available at ScienceDirect

Journal of Pediatric Surgery CASE REPORTS

journal homepage: www.jpscasereports.com

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

Kevin M. Riggle [a], Jessica L. Davis [b], George T. Drugas [a], Kimberly J. Riehle [a,*]

[a] Division of General and Thoracic Surgery, Seattle Children's Hospital and the University of Washington, Seattle, WA, USA
[b] Division of Pathology, Seattle Children's Hospital, Seattle, WA, USA

ARTICLE INFO

Article history:
Received 7 June 2016
Received in revised form
23 August 2016
Accepted 24 August 2016

Key words:
C. perfringes
NEC
Gastroschisis

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.

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, intrauterine 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 alloderm 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

IRB approval: Study # 00000060.

* Corresponding author. Department of Surgery, University of Washington, Seattle Children's Hospital, 4800 Sand Point Way, OA.9.220, Seattle, WA 98105, USA.
E-mail address: Kimberly.riehle@seattlechildrens.org (K.J. Riehle).

http://dx.doi.org/10.1016/j.epsc.2016.08.007

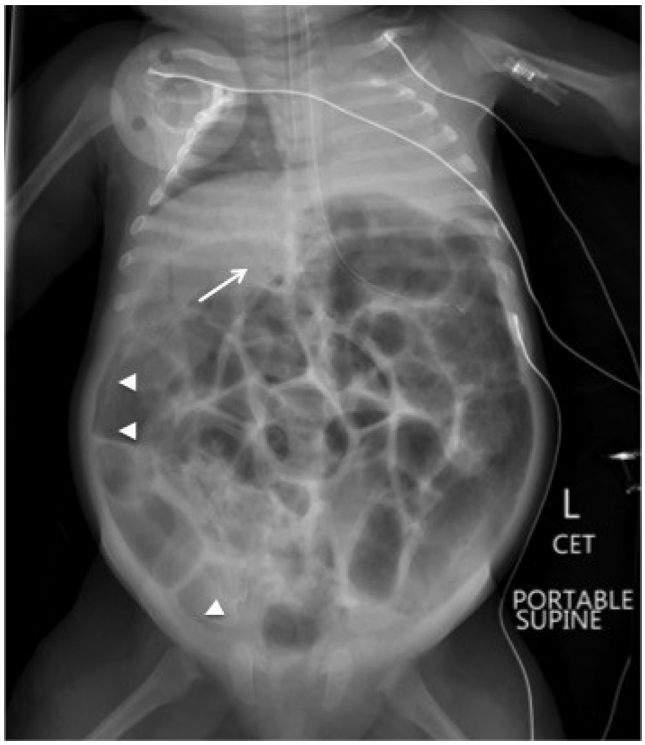

Fig. 1. Supine abdominal plain film taken at 45 min after symptom onset, showing diffuse bowel dilation, pneumatosis intestinalis (arrowheads), and portal venous gas (arrow).

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 *Esherichia 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

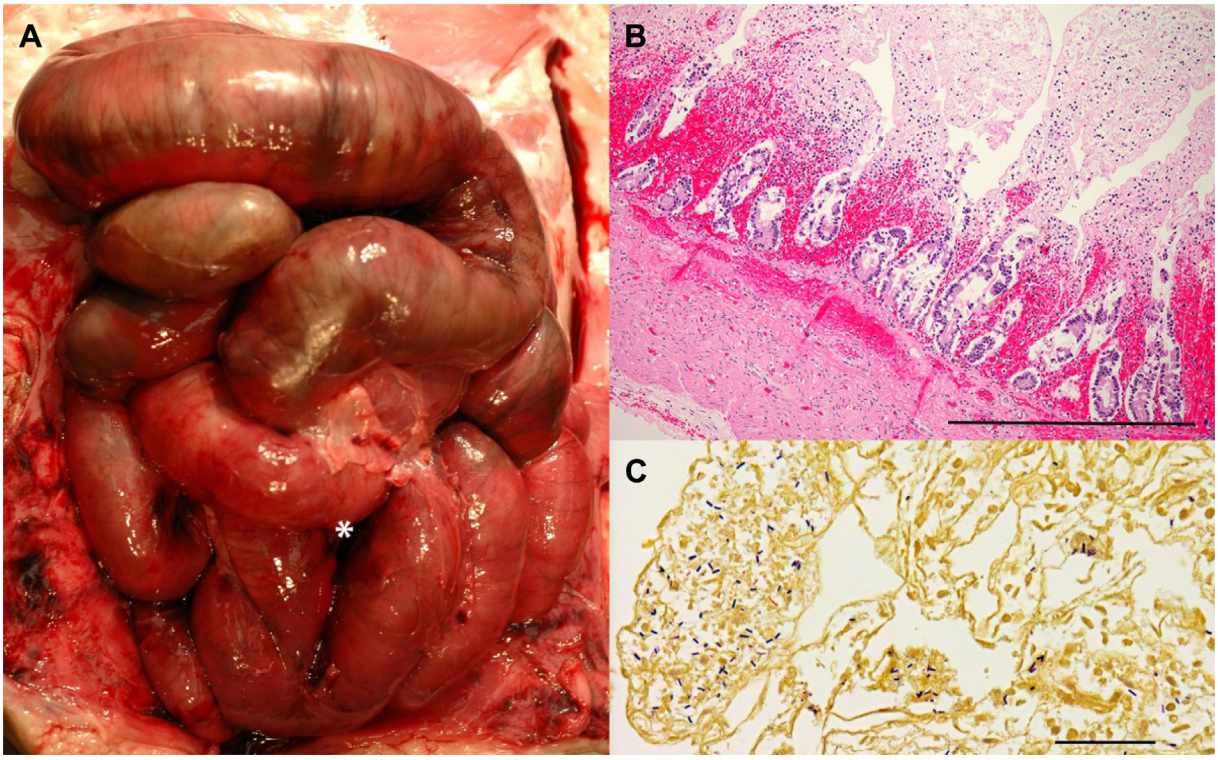

Fig. 2. A. Small bowel, in situ, with diffuse distention and dusky discoloration consistent with ischemia; *marks area of perforation. B. Microscopic image with severe mucosal necrosis and ischemic changes; H&E, 500 μm. C. Collections of "rod-shaped" gram-positive bacilli present within the mucosa and submucosa; Brown and Brenn (gram stain), 100 μm.

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

[1] Dittmar E, Beyer P, Fischer D, Schafer V, Schoepe H, Bauer K, et al. Necrotizing enterocolitis of the neonate with *Clostridium perfringens*: diagnosis, clinical course, and role of alpha toxin. Eur J Pediatr 2008;167:891–5.
[2] Neu J, Walke WA. Necrotizing enterocolitis. N Engl J Med 2011;364:255–64.
[3] Oldham KT. Postoperative necrotizing enterocolitis (NEC) in 10 of 54 (18.5%) infants with gastroschisis. J Pediatr Surg 1989;24:1214.
[4] Neu J. Preterm infant nutrition, gut bacteria, and necrotizing enterocolitis. Curr Opin Clin Nutr Metab Care 2015;18:285–8.
[5] Gewolb IH, Schwalbe RS, Taciak VL, Harrison TS, Panigrahi P. Stool microflora in extremely low birthweight infants. Arch Dis Child Fetal Neonatal Ed 1999;80:F167–73.
[6] Jayanthi S, Seymour P, Puntis JW, Stringer MD. Necrotizing enterocolitis after gastroschisis repair: a preventable complication? J Pediatr Surg 1998; 33:705–7.
[7] Oldham KT, Coran AG, Drongowski RA, Baker PJ, Wesley JR, Polley Jr TZ. The development of necrotizing enterocolitis following repair of gastroschisis: a surprisingly high incidence. J Pediatr Surg 1988;23:945–9.
[8] Shanbhogue LK, Tam PK, Lloyd DA. Necrotizing enterocolitis following operation in the neonatal period. Br J Surg 1991;78:1045–7.
[9] Lusk LA, Brown EG, Overcash RT, Grogan TR, Keller RL, Kim JH, et al. Multiinstitutional practice patterns and outcomes in uncomplicated gastroschisis: a report from the University of California Fetal Consortium (UCfC). J Pediatr Surg 2014;49:1782–6.
[10] Chesley PM, Ledbetter DJ, Meehan JJ, Oron AP, Javid PJ. Contemporary trends in the use of primary repair for gastroschisis in surgical infants. Am J Surg 2015;209:901–5. discussion 905–906.
[11] Snyder CL. Outcome analysis for gastroschisis. J Pediatr Surg 1999;34:1253–6.
[12] van Manen M, Hendson L, Wiley M, Evans M, Taghaddos S, Dinu I. Early childhood outcomes of infants born with gastroschisis. J Pediatr Surg 2013;48: 1682–7.
[13] Kosloske AM, Ball WS, Umland E, Skipper B. Clostridial necrotizing enterocolitis. J Pediatr Surg 1985;20:155–9.