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Case report

Cecal perforation secondary to fungal necrotizing enterocolitis in a premature neonate

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ABSTRACT

Introduction: Necrotizing enterocolitis (NEC) remains one of the most critical gastrointestinal comorbidities associated with neonatal prematurity and low birth weight. Despite extensive research and innovations for successful management, NEC remains the leading cause of morbidity and mortality in premature infants. NEC is commonly appreciated at the level of the small bowel, but in rare instances, it is experienced at the colon. While colonic perforation is rare, cecal perforation, specifically, is seldom reported.

Case report: We report the successful surgical intervention of a preterm African-American infant born at 24-weeks' gestation found to have a cecal perforation due to fungal necrotizing enterocolitis.

Discussion: Perforation is a major cause of morbidity in necrotizing enterocolitis, and even with extensive research in the management of necrotizing enterocolitis, mortality rates have remained unchanged; the treatment option with the most advantageous outcomes is still uncertain.

Conclusion: To our knowledge, there are few reported cases of cecal perforation due to NEC. The pathologic report of our colonic specimen demonstrated mucosal invasion with *Candida Albicans*. This case report is noteworthy due to the unusual location of bowel perforation, fungal sepsis, and successful surgical outcome that is not commonly seen in neonates with intestinal candidiasis. Cecal perforation is rare in necrotizing enterocolitis but should not rule out the pathology.

1. Introduction

Necrotizing enterocolitis (NEC) is one of the most devastating diseases in neonates, with an incidence between 11 and 15% in very-low-birth-weight infants [1]. It is characterized by an inflammation of the intestines with invasion of bacteria or other microbial species. While the cause is still unclear, it is thought to be due to weakened mucosal lining from decreased oxygenation or blood flow. With the progression of necrosis, this can lead to perforation and peritonitis. There are several differential diagnoses of intestinal perforation in neonates including necrotizing enterocolitis, Hirschprung's disease, mechanical obstruction, or idiopathic causes. The small intestines are the most common site of perforation in necrotizing enterocolitis patients [2]. Colonic perforation is rare, but it is associated with a 50% mortality in high-risk patients, specifically underweight, premature infants [3]. Cecal perforation of the colon is scarcely reported in the literature. In this case report, we discuss the rare case of cecal perforation secondary to fungal NEC in a premature infant. This case report has been reported in line with the SCARE Criteria [4].

2. Case report

An 845-gram male of 24 weeks' gestation was born to a 23-year-old gravida two African-American mother by emergent cesarean section. The infant arrived limp, blue, and without cry. The patient's mother notably had bacterial vaginosis and vaginal candidiasis during pregnancy that were pharmacologically treated, but clinical chorioamnionitis was noted during delivery via tachycardia and intermittent maternal fevers. Apgar scores were 1 at 1 min and 6 at 10 min. After intubation, he was subsequently admitted to the neonatal intensive care

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unit (NICU). The patient passed meconium on the first day of life and had an otherwise normal physical exam. On the 13th day of life, feeding intolerance and lethargy were noted. On physical exam, moderate abdominal distention was noted. Sepsis workup was initiated. A complete blood count demonstrated leukocytosis of 41,500/μL along with thrombocytopenia; cultures resulted with *Candida albicans* fungemia. Subsequent abdominal ultrasound showed intra-abdominal fluid as well as an inferior right hepatic lobe abscess. Due to concern for necrotizing enterocolitis, abdominal X-rays (Fig. 1A, B) and a paracentesis were done, which demonstrated brown feculent fluid though X-rays demonstrated a gasless abdomen. Pediatric surgery was then consulted due to a high suspicion of intestinal perforation and grade III necrotizing enterocolitis.

Due to concerns for peritonitis and sepsis, the patient underwent an emergent exploratory laparotomy at the bedside in the NICU. An attending surgeon and 3rd year surgical resident proceeded with the exploration. On exploration, there was a large amount of feculent spillage and necrosed colon identified. More specifically, there was a cecal perforation and necrosis of the ascending and proximal transverse colon. The small bowel was examined from the ligament of Treitz to the terminal ileum and was found to be intact and well-perfused.

Therefore, the abdomen was washed out and the liver was examined

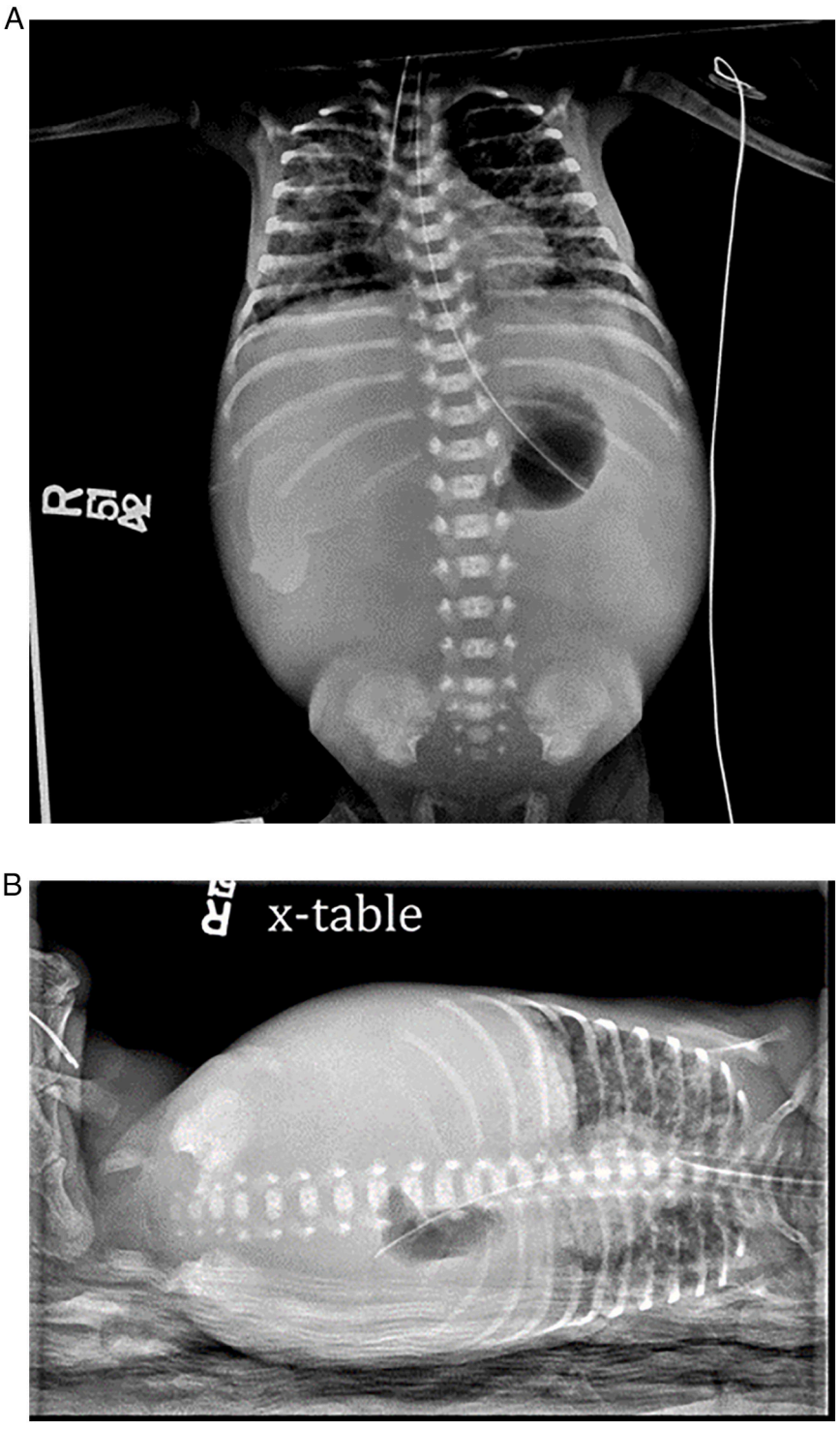

Fig. 1. A. AP X-ray view of patient on the day of operation, prior to paracentesis and operative intervention. The X-ray demonstrates a gasless abdomen with no free air noted.
B. Cross table X-ray view on the day of operation, prior to paracentesis and operative intervention with similar findings of gasless abdomen again with no free air noted.

with no notable abscess, but a subhepatic abscess was opened and evacuated. A right hemicolectomy was performed to remove the necrotic colon and an end ileostomy with mucus fistula was created. At postoperative day 5, the patient developed abdominal distention, increased oxygen requirement, and persistent acidosis, requiring an additional exploratory laparotomy.

At reoperation, a large intraabdominal abscess again in the right upper quadrant was evacuated with placement of a peritoneal drain. Cultures taken at operation demonstrated *Candida albicans* and coagulase negative *Staphylococci*. Pathologic examination of the resected colon noted pseudohyphae on Hematoxylin and Eosin (H&E) as well as Grocott's Methenamine Silver (GMS) staining invading the mucosa. Three months later, the patient's fungemia had resolved and he underwent a successful ostomy takedown. He was later discharged home in good status tolerating enteral feeds.

Due to known systemic *Candida* infection, our patient was already on antifungals 10 days prior to drainage of the intraabdominal abscess. The medications were continued for the next 10 weeks post operation, to ensure complete clearance of the infection. In person follow up in clinic demonstrated excellent recuperation with regular bowel movements and good feeding tolerance.

3. Discussion

Premature neonates that require surgical intervention for necrotizing enterocolitis are among some of the most critically ill infants in pediatric surgery. As a disease with an elusive etiology, it is a multifactorial process due to hypoxic injury causing ischemia, and possibly dysbiosis leading to changes in the microbiota in the immature gastrointestinal tract [5]. The pathophysiology of NEC is an inflammatory response in the intestines leading to loosening of cellular tight junctions and subsequent microbial invasion that results in cellular damage and necrosis, with possible perforation and peritonitis [6].

Perforations in preterm and full-term infants have several different etiologies including NEC, Hirschprung's disease, mechanical bowel obstruction, or an idiopathic, spontaneous rupture. The most common site of perforation secondary to necrotizing enterocolitis is the small bowel, with colonic perforation being less common [2].

Patients with necrotizing enterocolitis and consequent perforation may present with nonspecific symptoms including lethargy, poor feeding, and abdominal distention [7]. Additional clinical findings include significant respiratory complications, increased oxygen demand, and the presence of various types of microbiological infection in the peritoneal fluid or blood. On imaging, portal venous air is a classic diagnostic finding [8]. Portal venous air is an indicator of poor prognosis in the right clinical setting, with morality in up to 90% of patients [1]. In premature patients with a nonspecific presentation, NEC should always be considered in a differential diagnosis because of its critical nature and high-risk of mortality. Diagnosis is mostly clinical, but paracentesis has been used to assist if the clinical picture remains unclear [9,10]. One must keep in mind that paracentesis has its own risks in premature neonates if this is to be used.

In the presented case, the patient's perforation was complicated by a post-operative intraabdominal fungal abscess likely secondary to the initial systemic candidiasis. *Candida albicans* most commonly colonizes the genitourinary tract and is seldom seen as a predominate species in the colon or small bowel. Typically, gram-negative or anaerobic bacteria are the most likely etiology of abdominal abscesses, but fungal infections should still be considered despite its low likelihood. Risk factors of neonatal candidiasis with subsequent colonic seeding include prematurity with very-low-birth-weight, use of broad-spectrum antibiotics, surgical procedures, and long-term parenteral feeding [11,12]. In cases of necrotizing enterocolitis with pathologic intestinal candidiasis, one retrospective review noted an incidence of intestinal candidiasis in overall perforated NEC cases of 7.5%, with a 100% mortality rate when this was found on pathology review of surgical specimens [13]. H&E stains and GMS stains of resected colon on our patient both demonstrated pseudo hyphae and spores (Fig. 2A, B).

Additionally, the infant's mother had vaginal candidiasis during pregnancy. This raises the question if the colonization seen in the patient could be attributed to the initial infection by the mother and if a mother presenting with vaginal candidiasis should be considered at risk of transmitting the infection to the neonate. Vertical transmission of fungal candida is typically seen within the first week of life, but the sites of infection are most commonly the oral cavity, rectum, or groin, and usually do not cause fungemia [14].

Once present systemically, *Candida* species have the ability to spread via hematogenous route to almost any organ tissue, most commonly the retina, kidneys, liver, brain, and heart, and is known to cause extensive neurological disease and developmental abnormalities. Due to its rapid invasion, investigation of fungal seeding to these areas is highly recommended in neonates with an initial presentation of fungemia, with or without gastrointestinal tract involvement.

Perforation is a major cause of morbidity, and even with extensive research in the management of necrotizing enterocolitis, mortality rates have remained unchanged; the treatment option with the most advantageous outcomes is still uncertain. Although many cases can be managed medically, some cases require surgical intervention. Surgical intervention is indicated in infants with evidence of perforation and/or clinical deterioration, abdominal distention, portal venous gas, abdominal discoloration with worsening clinic status, and positive paracentesis with presence of brown/turbid fluid [7]. Laparotomy effectively resects ischemic or perforated bowel and stops feculent spillage while peritoneal drainage has similar overall outcomes [15–18]. The goals of surgery are to remove necrotic tissue, preserve as much bowel length as possible, control sepsis, and reduce post-surgical complications [19]. Prevention may be key with necrotizing enterocolitis, with probiotic administration, and colostrum administration both showing promise in decreasing incidence rates.

4. Conclusion

To our knowledge, there are few reported cases of cecal perforation due to NEC. Additionally, the patient's postoperative intraabdominal abscess is unique in the fact that the source of infection was due to *Candida albicans*, and not the usual gram-negative or anaerobic microbes. In addition, the pathologic report of our colonic specimen demonstrated mucosal invasion with *Candida Albicans*. This case report is noteworthy due to the unusual location of bowel perforation, fungal sepsis, and successful surgical outcome that is not commonly seen in neonates with intestinal candidiasis.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet current ICMJE criteria for Authorship.

Ethical approval

This study is exempt from ethical approval as no identifying factors are used in the case report itself or any of its images.

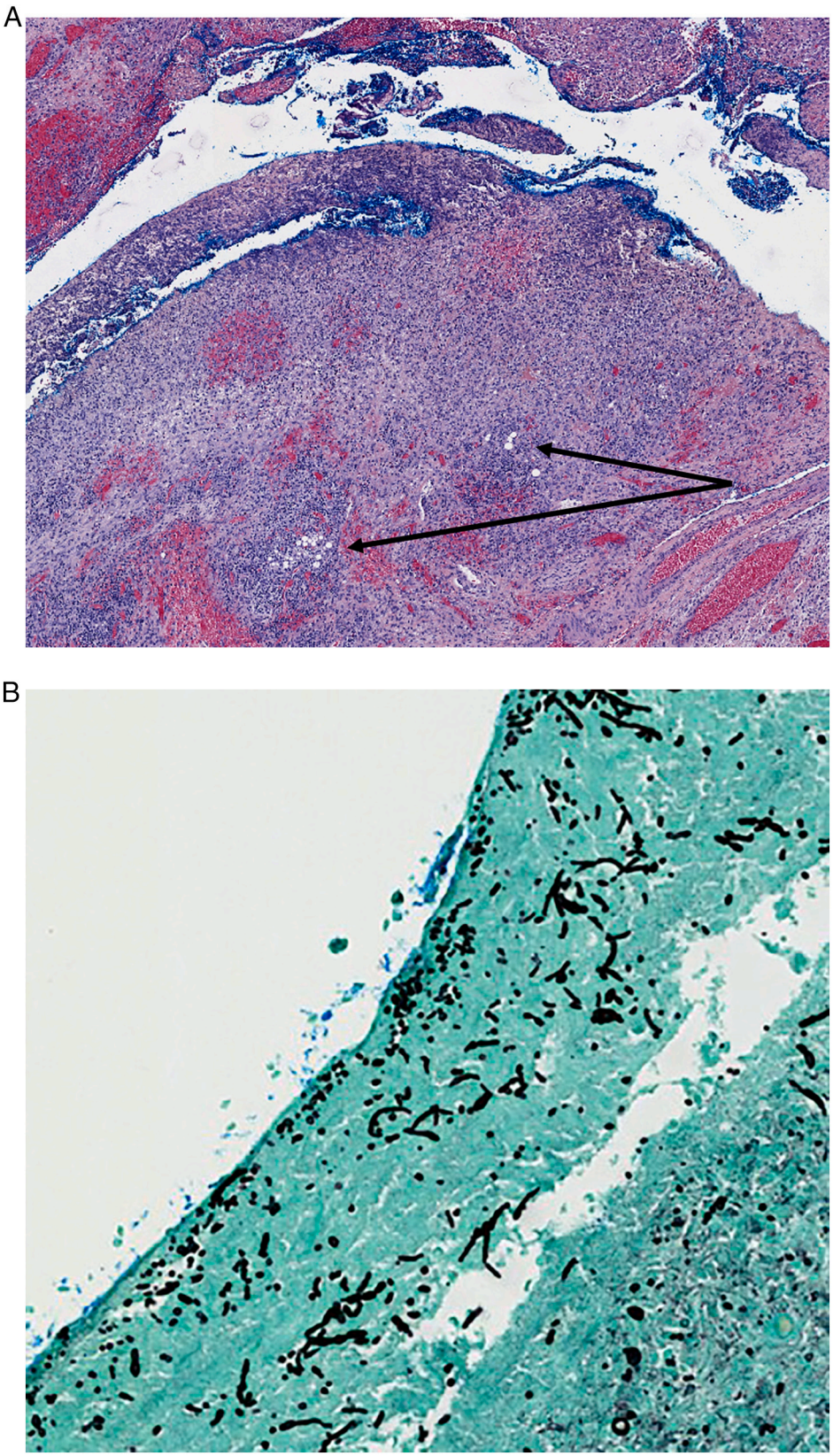

Fig. 2. A. H&E stained Cecal (colonic) specimen - hyperemia and necrosis of the mucosa, submucosa, and muscularis. Intramural gas is seen as rounded bubbles in the submucosa along with lymphocytic/neutrophilic infiltration demonstrated by arrows (×20 - zoomed).
B. Small bowel wall infiltrated with fungal spores and pseudohyphae (Grocott's Methenamine Silver stain, ×20 - zoomed).

Consent

No identifying features are given in the paper or images and therefore informed consent was not required.

Author contribution

Christina Onyebuchi: data collection, writing the paper, proofing the paper, background research

Christian Sommerhalder: data collection, writing the paper, proofing the paper, background research

Sifrance Tran: Proofing the paper

Ravi Radhakrishnan: Proofing the paper

Aijan Ukudeyeva: Proofing the paper, pathological studies

Suimmin Qiu: Proofing the paper, pathological studies

Kanika A. Bowen-Jallow: Proofing the paper, oversight of literature review

Registration of research studies

Not applicable.

Guarantor

Christina Onyebuchi, Christian Sommerhalder, Kanika A Bowen-Jallow.

Declaration of competing interest

The following authors have no financial disclosures: CO, CS, KABJ, ST, AU, RR.

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