CASE REPORTS

Perforated appendicitis in a preterm neonate: A case report with literature review

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ABSTRACT

Neonatal appendicitis is a rare entity, with a mortality rate that has decreased in past decades but remained high. Of cases reported in the literature, more than 50% occur in preterm neonates, and none have been diagnosed preoperatively. Here, we report the case of a female infant of 27-4/7 weeks' gestational age, who presented with perforated appendicitis on day of life (DOL) 30. She was thought to have medically refractory necrotizing enterocolitis (NEC), but was found, instead, to have perforated appendicitis during an exploratory laparotomy. A thorough literature search indicates she is the second youngest neonate to survive perforated appendicitis to date.

Key Words: Perforated appendicitis, Neonatal appendicitis, Preterm, Neonate

1. INTRODUCTION

Appendicitis is the most common surgical cause of acute abdomen in pediatric patients.[1] Thus, it is regularly considered in the differential diagnosis of children with abdominal pain and vomiting. However, in the youngest pediatric patients—newborn infants—appendicitis is extremely rare and a preoperative diagnosis has yet to be reported.[2] Necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP) are considered more frequently due to NEC appearing in 5%-10% of all very low birth-weight (VLBW) infants (< 1,500 g),[3] and SIP in 1.1% of VLBW infants and 7.4% of extremely low birth-weight (ELBW) infants (< 1,000 g).[4] Meanwhile, the incidence of acute appendicitis is as low as 0.04% to 0.2% in neonates.[5] Here, we present the second youngest preterm neonate diagnosed with perforated appendicitis to date.

2. CASE PRESENTATION

A female infant was born at 27-4/7 weeks' estimated gestational age to a 22-year-old mother by cesarean section, prompted by severe preeclampsia. The neonate's birth weight was 670 g (10^{th} percentile) due to intrauterine growth restriction. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The newborn was transferred to the neonatal intensive care unit in good condition and placed on non-invasive ventilatory support.

On day of life (DOL) 11, our pediatric surgical team was consulted due to persistently increased abdominal girth and dilated bowel loops on plain abdominal *x*-rays (AXR). At the time, there was no evidence of pneumatosis intestinalis. A barium enema showed no narrowing or obstruction along the colon. No surgical interventions were indicated at this time. On DOL 14, she began spontaneously stooling with the

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aid of glycerin shave suppositories for stimulation. On DOL 19, the newborn was started on 1 ml/hr of Pedialyte. The next day, her *x*-ray demonstrated that all contrast had been evacuated. She was transitioned from Pedialyte to breast milk on DOL 21. By DOL 28, she was receiving 4 ml/hr of continuous breast milk fortified with Enfamil Premature to 24 kcal/oz.

On DOL 29, the patient passed a bloody stool, and subsequently underwent respiratory decompensation, requiring intubation and ventilation. AXR suggested pneumatosis intestinalis and management for NEC was started (see Figure 1). Management included bowel rest, gastric decompression, and administration of broad-spectrum antibiotics.

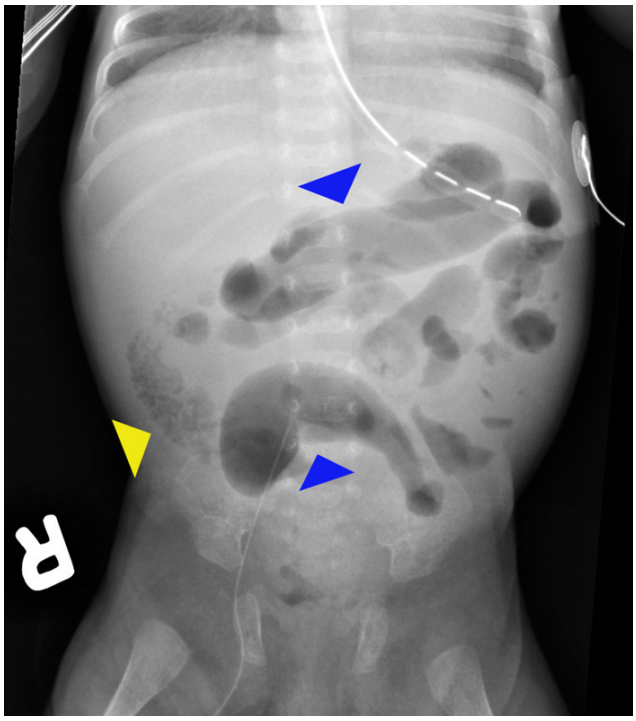

Figure 1. A supine abdominal radiograph of our patient on DOL 29

The yellow arrowhead denotes suspected pneumatosis intestinalis in the right colon. The blue arrowheads demonstrate dilated abnormal bowel loops indicative of the patient's intra-abdominal illness

On DOL 30, the pediatric surgical team was consulted again when the newborn became neutropenic (WBC 3.4) and thrombocytopenic (platelet count 106). Her blood counts continued to decrease despite medical management, prompting a laparotomy. She was taken to the operating room, where an exploratory laparotomy was performed on the now 1,175 g neonate. Surprisingly, her small bowel appeared viable without evidence of any necrotizing process. However, there was fibrinous exudate in the right lower quadrant, originating from her appendix. The appendix was indurated, hyperemic, and perforated distally (see Figure 2). The right colon appeared normal, without clear evidence of NEC. Due to inflammation and perforation of the appendix, an appendectomy was performed. On further abdominal exploration, no other cause for the sepsis and decompensation were found. Pathologic examination demonstrated necrotizing appendicitis with perforation.

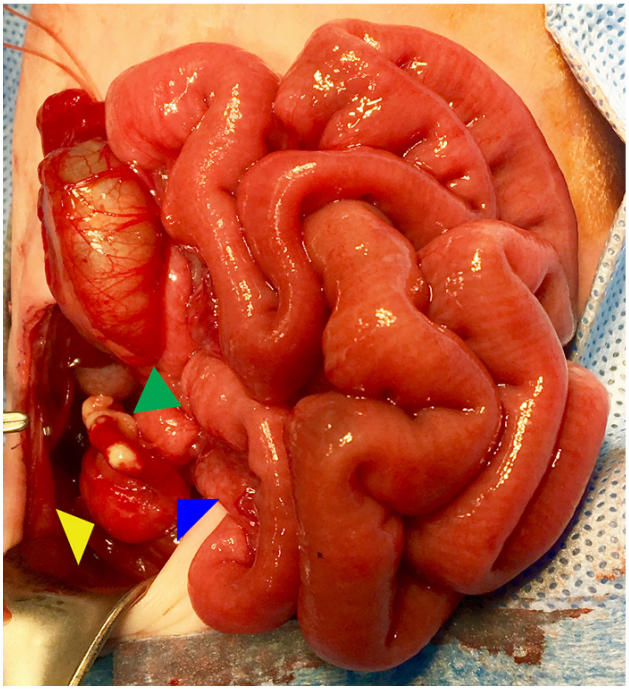

Figure 2. Our patient's intra-abdominal contents during an exploratory laparotomy

The green arrowhead identifies the perforated distal portion of the appendix. The blue arrowhead shows the viable base of the appendix, with fibrinous exudate between the two ends. The yellow arrowhead marks the right colon, which also appeared viable, without overt evidence of NEC

Postoperatively, the infant improved clinically. She was weaned from ventilatory support and extubated on post-operative day 3. Her laboratory values and AXRs normalized. Later, her feeds were advanced until she reached goal enteral feeds on post-operative day 25. At gestational age of 40 weeks, on post-operative day 61, our patient was discharged home. Other than developing a left inguinal hernia at 3 months of age, which was repaired without incident, she had an uneventful recovery.

3. Discussion

Neonatal appendicitis is most common in males and is associated with prematurity and comorbidities, such as Hirschsprung's disease, cystic fibrosis, cardiopulmonary de-

fects, and inguinal hernias.[6,7] Our female newborn was extremely premature at 27-4/7 weeks' gestational age, and presented with perforated appendicitis by DOL 30, with no other comorbidities. We conducted a literature search for neonatal and infant appendicitis and appendectomy on PubMed and Google Scholar, with no restrictions on publication date. The articles were then cross-referenced with those that were cited. International publications were included when an English abstract was provided, but foreign language publications were excluded. Cases where appendicitis was discovered after death; the neonate failed to survive an appendectomy; or reports that specified no gestational age were also excluded. After thoroughly reviewing the existing literature, we believe our patient is the second youngest case to present with perforated appendicitis and survive without complications (see Table 1).

Table 1. The 15 youngest neonates who have survived perforated appendicitis

#	Author (s)	Year of Publication	Estimated Gestational Age at Birth (wk)	Postnatal Age at Surgery (d)	Corrected Gestational Age (d)
1	Schorlemmer & Herbst[8]	1983	26	12	194
2	Bose & Wakeman	2017	27-4/7	30	223
3	Mammou et al.[5]	2015	32	2	226
4	Beluffi & Alberici[9]	2002	30	18	228
5	Mathew et al.[10]	2015	33	4	235
6	El-Gohary & Al Jubouri[11]	2014	33	5	236
6	Narasimharao et al.[12]	1987	32	12	236
8	Nichol et al.[13]	2004	32	15	239
9	López-Valdés & Escarcega-Serv ín[14]	2016	34-2/7	0	240
10	Jahangiri et al.[15]	2013	32	20	244
11	Arias-Llorente et al.[16]	2014	33	14	245
12	Vakrilova et al.[17]	2014	31-4/7	25	246
13	Barbosa et al.[18]	2000	34	9	247
14	Semerci et al.[19]	2017	35	5	250
15	Haider et al.[20]	2017	29	54	257

As shown in Table 1, our patient was the second youngest preterm neonate to present with perforated appendicitis and survive, according to published literature. The corrected gestational age in days is the estimated gestational age at birth (in days) plus the postnatal age at surgery.

In cases of neonatal appendicitis, the most commonly presenting sign is abdominal distension, which appears in 75% of patients. Other signs and symptoms include vomiting, anorexia, leukocytosis or left shift, abdominal tenderness, temperature instability, sepsis, skin changes, irritability, lethargy, free air on AXR, respiratory symptoms, abdominal mass, and hematochezia, in decreasing order of frequency.[2] Our patient presented with six of these signs and symptoms. It is believed that neonates who are not septic and those that present with free intraperitoneal air on AXR—resulting in speedier surgical intervention—are more likely to survive from appendicitis.[2] Of note, our patient was both septic and without free air on AXR at the time of successful surgical intervention.

Due to the rarity of appendicitis in newborns, the spectrum of signs is often mistaken for NEC or SIP, both of which occur more frequently in premature infants. NEC affects 5%-10% of all VLBW neonates, and 90%-95% of all cases occur in newborns of 36 weeks' gestational age or younger.[3] The bowel inflammation and bacterial infection can cause feeding intolerance, emesis, bloody stools, abdominal distension, and abdominal tenderness.[3] Our premature ELBW infant presented with one episode of bilious emesis, a bloody stool, increasing abdominal distension, and suspected pneumatosis intestinalis on AXR, suggesting NEC. The absence of free intraperitoneal air suggested against SIP.[21] Medical management is often sufficient to treat NEC,[22] but failed to improve our patient's condition. Surgical exploration revealed only a perforated appendix, with no bowel resection indicated. An appendectomy and excellent neonatal intensive care resulted in a prompt and full recovery.

Given our patient's presentation, peritoneal drainage could have been an alternate treatment to consider. A multi-center randomized trial of 117 preterm infants found no significant difference in survival or other clinically important early outcomes when preterm neonates with NEC or SIP are treated with a peritoneal drain versus a laparotomy.[23] In our case, a peritoneal drain may have been successful, but a laparotomy allowed us to specifically diagnose isolated perforated acute appendicitis, and to more conclusively determine that no

bowel resection was necessary.

With regard to diagnostic imaging for perforated appendicitis, cross-sectional imaging with either computer tomographic scan (CT) or magnetic resonance imaging (MRI) is the most sensitive and specific diagnostic test for appendicitis. However, abdominal ultrasound (AUS) is often used as first-line imaging for younger pediatric patients to decrease cost, expedite the diagnostic evaluation, and ameliorate the cancer risk associated with CT imaging.[2] While no studies have been conducted on the efficacy of AUS in detecting neonatal appendicitis, AUS has been used in detecting NEC. AUS imaging can be considered superior to plain radiography in depicting portal venous gas, free or focal fluid collection, bowel wall thinning, and free air, which could allow for earlier detection and earlier surgical intervention.[24] However, the usage of AUS in detecting NEC has rarely influenced therapeutic decisions.[25] Thus, it is unlikely to have altered the course of our patient's treatment. AUS would also be unlikely to visualize the neonatal appendix, even if dilated and perforated, due to its small size.

Acute appendicitis typically remains undetected in neonates until perforation occurs, and mortality rates have remained as high as 28% in recent decades.[2] Due to its rarity and varying presentation, neonatal appendicitis has yet to be diagnosed preoperatively. Our extremely premature neonate of 27-4/7 weeks' gestational age was diagnosed with perforated appendicitis by laparotomy on her 30^{th} DOL, making her the second youngest patient with perforated appendicitis to survive in the reported literature. She was initially thought to have NEC, but clinically deteriorated despite maximal medical therapy. Subsequent surgical exploration revealed perforated appendicitis. While a preoperative diagnosis likely would not have altered our patient's treatment course, acute appendicitis should be considered in the differential diagnosis of neonates presenting with abdominal symptoms in order to decrease morbidity and mortality. In this case, quick surgical intervention in response to our patient's deteriorating condition led to her successful recovery.

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CONFLICTS OF INTEREST DISCLOSURE

The authors declare they have no conflicts of interest.

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