

Recurrent focal intestinal perforation in extremely-low-birth-weight infant

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Abstract

In recent years, the incidence of focal intestinal perforation (FIP) has been increasing, as the survival rate of extremely-low-birth-weight (ELBW) infants has been rising. We present a case of an ELBW infant who suffered three recurrences of FIP in a very short period of time. The patient was a female infant who was born at 24 weeks and 2 days of gestation, with a birth weight of 579 g. On her 22nd day of life, abdominal X-rays revealed free air, which suggested intestinal perforation, and an intraperitoneal drainage tube was placed. Intraperitoneal lavage was performed on day 28 of life, and the drained fluid was turbid with feces, suggesting a recurrence of perforation. On day

30 of life, laparotomy revealed a perforation of approximately 1 cm in diameter located at 6 cm from the ileocecum on the oral side. The X-ray taken on day 34 again revealed free air, and, through another laparotomy, a new perforation was found at about 15 cm from the stoma on the oral side. This case provides suggestions that may shed light on our approach to determine the pathogenesis of FIP, especially since no other case of FIP recurring three times has ever been reported.

Key words : intestinal perforation, extremely-low-birth-weight infant, necrotizing enterocolitis

Introduction

Focal intestinal perforation (FIP) is defined as follows: a localized perforation that develops in the digestive tract, showing no association with histological or clinical necrotizing enterocolitis (NEC), presents no signs of inflammation on blood tests in the early stage, and causes no inflammatory cell infiltration macroscopically or histologically in the region of perforation.¹ Different from NEC, FIP is sometimes referred to as spontaneous or local intestinal perforation. The incidence has been increasing with the improved survival rate of ELBW infants.² Although it affects the survival of ELBW infants and their development,³ the pathogenesis of FIP

has not yet been elucidated, and a preventive strategy is yet to be established. We report an ELBW infant who was considered to suffer three recurrences of FIP. This report may provide important suggestions for clarifying the pathogenesis of FIP.

Case report

The patient was a girl born at 24 weeks and 2 days of gestation to a 38-year-old primigravida, who was admitted to Kinki University Hospital for threatened premature delivery. Since the mother presented a fever and a blood test revealed signs of inflammatory response such as a white blood cell count (WBC) of 24,100/ μ l

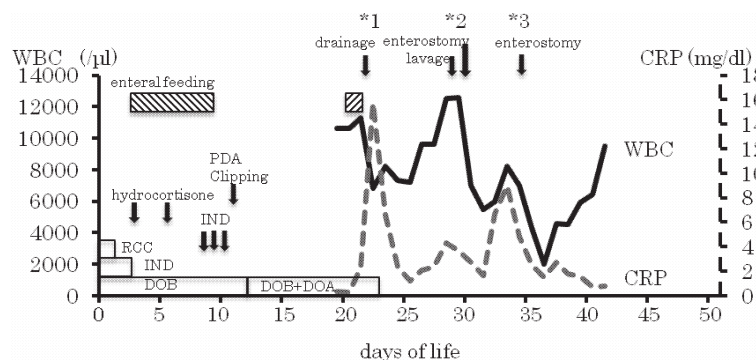


Fig. 1 Clinical course
WBC: white blood cell count, CRP: C-reactive protein, RCC: red cell concentrate, IND: indomethacin, DOB: dobutamine, DOA: dopamine, *: perforation

and C-reactive protein (CRP) of 3.1 mg/dl, an emergency C-section was performed 8 hours after 12 mg of intramuscular betamethasone, and she delivered a girl. The baby was an appropriate-for-dates infant with a birth weight of 579 g. The Apgar score was 2 at 1 minute, and 5 at 5 minutes. Since she had respiratory distress syndrome, pulmonary surfactant was administered followed by mechanical ventilation. Glucose was administered via peripherally inserted central catheters placed at the right atrium and inferior vena cava. Figure 1 shows the clinical course. She received intravenous indomethacin (0.1 mg/kg/day) for three days starting after birth to prevent intraventricular hemorrhage. The continuous intravenous infusion of dobutamine hydrochloride was also started at 4.6 μ g/kg/min to maintain a mean blood pressure range of 25-30 mmHg. The dobutamine hydrochloride dosage was increased to 8 μ g/kg/min on day 11 of life, and to 9.6 μ g/kg/min on day 12. Dopamine hydrochloride was also added thereafter. The blood pressure stabilized, and then the dosage was tapered and discontinued on day 23 of life. Also, concentrated red cells were transfused at 15 ml/kg over 24 hours on day 1 of life, and hydrocortisone sodium succinate was administered at 30 mg/kg as a vasopressor on days 3 and 6. On day 3 of life, enteral breast milk feeding was started via a nasogastric tube (three times a day, 0.5 ml per dose); however, gastric residual fluid was bilious and copious. Therefore, feeding was discontinued on day 10 of life. Three doses of indomethacin were administered at 0.2 mg/kg with 8-hour intervals over days 9 through 10 of life for symptomatic patent ductus arteriosus (PDA). Nevertheless, the ductus arteriosus was not closed, and so clipping was performed on day 12 of life, with an uneventful postoperative course. Enteral breast milk feeding was resumed on day 20 of life after

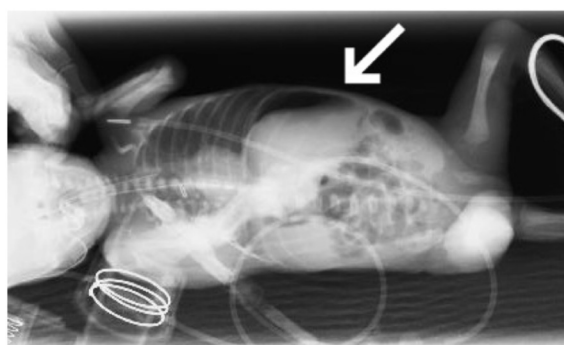


Fig. 2 decubitus X-ray showing intraperitoneal air (arrow).

defecation was observed. On day 22 of life, findings of abdominal X-rays indicated gastrointestinal perforation (Fig. 2). An intraperitoneal Penrose drain was placed, and continuous drainage was started. A small amount of serous ascites was discharged. Blood examinations demonstrated a reduction of inflammatory signs (CRP: 15.7 mg/dl, WBC: 6,800/ μ l) after the drain was applied; however, the serum concentration of CRP rose to 4.3 mg/dl, associated with leukocytosis (12,500/ μ l), on day 28 of life. Although no free air was observed on X-rays, the pattern of intestinal gas indicated distention. The intraperitoneal lavage fluid was turbid with feces, suggesting a recurrence of perforation. Since feeding could not be resumed, enterostomy and intraperitoneal drainage with Penrose drain were conducted on day 30 of life. Based on laparotomic findings, a perforation with a diameter of approximately 1 cm was demonstrated at about 6 cm from the ileocecum on the oral side. The locus surrounding the perforation point showed redness; however, no necrosis was noted (Fig. 3). The X-ray findings on day 34 of life again revealed free air, and a new perforation (longitudinal laceration-like perforation) was found at about 15 cm from the stoma on the oral side on additional laparotomy. An additional

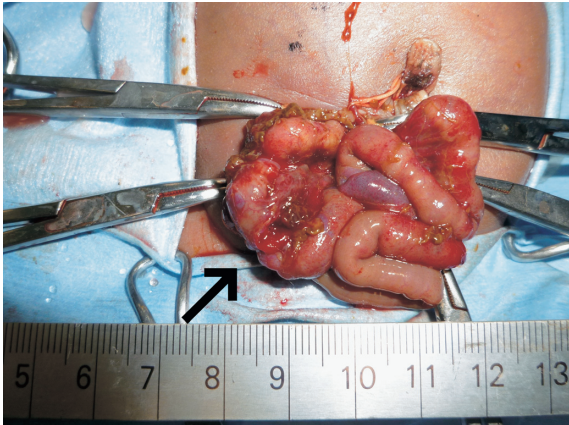


Fig. 3 Perforation of the intestine. An approx. 1-cm perforation was found during the first laparotomy at 6 cm from the ileocecum on the oral side (arrow).



Fig. 4 Perforation of the intestine. A new perforation was found in the second laparotomy at 15 cm from the stoma on the oral side. Forceps are being inserted into the perforation.

stoma was constructed at the site. Although the intestinal wall was thin and reddish, no signs of necrosis were seen this time either (Fig. 4). There was no other perforation in the 30-cm area from the stoma to oral side. No perforation developed thereafter, and feeding was resumed on day 49 of life. Stomas were closed on day 169 of life, and she was discharged from the hospital

on day 194.

Histopathologic examination of the tissue specimen of the small intestine obtained on day 52 of life revealed the presence of normal ganglia, ruling out Hirschsprung disease. *Staphylococcus epidermidis* was isolated repeatedly from feces and the nasal cavity by bacteriologic culture on and after day 16 of life.

Discussion

In the ELBW population, causal associations have been established between FIP and early postnatal steroids (use within the first week of life), early use of indomethacin (use within the first 3 postnatal days), and the synergistic combination of the two.⁴ These two risk factors are considered to play a causal role in the etiology of FIP through their negative influences on intestinal haemodynamics that affect ileal trophism and motility. Other reported risk factors include two common pathogens (*Candida* and *Staphylococcus epidermidis*), early neonatal hypotension, umbilical artery catheters, and dehydration.⁴ Chorioamnionitis is also thought to be a risk factor for FIP, as is the stress and elevated cortisol accompanying it.⁵ In this report, both steroid and indomethacin were administered in the early postnatal stage, and the patient presented with early neonatal hypotension. She was also a carrier of *Staphylococcus epidermidis*. While indomethacin is not associated with the occurrence of FIP in ELBW infants when used for intraventricular hemorrhage prophylaxis, it is thought to be associated with an increased risk of FIP when used as a treatment for symptomatic PDA.³ Therefore, in this case, indomethacin used on days 9 and 10 of life as a treatment for symptomatic PDA may have affected the occurrence of perforation, not the early use of indomethacin. Also, while a pathologic diagnosis of the placenta was not made, the mother's onset of fever and inflammatory response clinically suggested the presence of chorioamnionitis, which may have contributed to the perforation.

All the risk factors mentioned above are commonly seen in ELBW infants, and, when more of these factors are involved, the risk of FIP increases. While a few cases of FIP recurring two times have been reported in the past,^{2,6,7} this is the only case of FIP recurring three times as far as we know. Although only one perforation was

revealed by the first laparotomy, we believe that the intestine perforated twice before the operation; one suggested by the free air found in X-rays, and the other by the presence of feces in the intraperitoneal cavity. However, perforation recurring in the same region is possible. Blood examinations showed that significant inflammatory signs in a relatively early stage are not consistent with the FIP definition.¹ However, the facts that the perforations were observed only focally during the laparotomy, and no necrosis was macroscopically observed, suggesting no presence of NEC, strongly support the diagnosis of FIP.

Although the pathological conditions responsible for the onset of FIP are not yet fully defined, it has been speculated that immature bowel movement and congenital muscle defects may be involved in the pathogenesis of FIP.^{2,8} Kubota et al.² clarified that 27% of FIP cases showed intestinal musculature abnormalities. Although pathological examination of the lesions was not performed in this case, congenital structural abnormalities may have been one of the factors causing the recurrence of perforation.

Risk factors of FIP onset range widely from the ones believed to be effective methods for improving the prognosis of the development of ELBW infants to the ones that could cause extremely preterm birth. It is not possible to eliminate all factors, but when a treatment is suspected to increase the risk of FIP, we must strictly examine its necessity so as to limit its

occurrence.

References

1. Advanced Medical Care Review Committee (2005-2006, 2007-2008) Japanese Society of Pediatric Surgeons; Neonatal Nutrition Forum (2010), Survey on intestinal perforation in extremely-low birth weight infants. *JJSPS* 46: 791-796
2. Kubota A, et al. (2007) Focal intestinal perforation in extremely-low-birth-weight neonates: etiological consideration from histological findings. *Pediatr Surg Int* 10: 997-1000
3. Wadhawan R, Oh W, Vohr BR (2013) Spontaneous intestinal perforation in extremely low birth weight infants: association with indometacin therapy and effects on neurodevelopmental outcomes at 18-22 months corrected age. *Arch Dis Child Fetal Neonatal Ed* 98: F127-132
4. Shah TA, et al. (2012) Hospital and neurodevelopmental outcomes of extremely low-birth-weight infants with necrotizing enterocolitis and spontaneous intestinal perforation. *J Perinatol* 32: 552-558
5. Gordon PV, Attridge JT (2009) Understanding clinical literature relevant to spontaneous intestinal perforations. *Am J Perinatol* 26: 309-316
6. Drewett MS, Burge DM (2007) Recurrent neonatal gastro-intestinal problems after spontaneous intestinal perforation. *Pediatr Surg Int* 23: 1081-1804
7. Giacoia GP, Azubuikie K, Taylor JR (1993) Indomethacin and recurrent ileal perforations in a preterm infant. *J Perinatol* 13: 297-299
8. Oretti C, Bussani R, Janes A, Demarini S (2010) Multiple segmental absence of intestinal musculature presenting as spontaneous isolated perforation in an extremely low-birth-weight infant. *J Pediatr Surg* 45: E25-27