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## Case Report

# Necrotizing enterocolitis in preterm newborn with a history of maternal COVID-19: a case report<sup>☆,☆☆</sup>

Rennilia Nita, MD<sup>a</sup>, Aryati, MD<sup>b,\*</sup>, Fendy Matulatan, MD<sup>c</sup>

<sup>a</sup>Clinical Pathology Specialist Medicine Academic Program, Department of Clinical Pathology, Faculty of Medicine, Airlangga University/Dr. Soetomo General Regional Hospital, Surabaya, Indonesia

<sup>b</sup>Department of Clinical Pathology, Faculty of Medicine, Airlangga University/Dr. Soetomo General Regional Hospital, Surabaya, Indonesia

<sup>c</sup>Department of Pediatric Surgery, Faculty of Medicine, Airlangga University/ Dr. Soetomo General Regional Hospital, Surabaya, Indonesia

## ARTICLE INFO

## Article history:

Received 25 March 2022

Revised 25 April 2022

Accepted 28 April 2022

## Keywords:

NEC

COVID-19

Sepsis

Klebsiella pneumoniae

## ABSTRACT

A 6-day-old newborn male presented with a primary complaint of abdominal distension for 3 days before hospital admission. The newborn was delivered from a confirmed COVID-19–positive mother through caesarean section at 38–39 weeks with a birth weight of 2800 grams. Various tests, including blood tests, cultures, and radiography were performed. The patient was diagnosed with necrotizing enterocolitis and sepsis; the prevalence of necrotizing enterocolitis in at-term newborns with >36 weeks of gestational age is 10%. In this case, NEC was suggested to be due to maternal infection during the prenatal phase, as the mother was a confirmed COVID-19 patient. Further exploration is needed to illustrate neonatal outcomes following necrotizing enterocolitis diagnosis in correlation with maternal intrauterine COVID-19 infection.

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## Introduction

Necrotizing enterocolitis (NEC) is an inflammatory gastrointestinal disease in newborns. It is an acquired and multifactorial disease that is most frequently reported in newborns delivered preterm. The pathogenesis of NEC includes inflammation, ischemia, and necrosis in the bowel walls due to infec-

tions by various pathogens. The signs and symptoms manifest predominantly in the second to eight weeks postpartum, and the morbidity and mortality rate is 50%, with most fatalities occurring in preterm infants. Thus, NEC is an emergency condition and immediate management is required, including the performance of surgical procedures to prevent the extension of bowel perforations and gangrene gases [1–4].

NEC can be diagnosed clinically or with supporting workup. NEC commonly manifests as abdominal distension, decreased

<sup>☆</sup> Competing Interests: The authors have no conflict of interest to declare.

<sup>☆☆</sup> Acknowledgments: Highest appreciation for peers in supporting data collection, proofreading, and translation, and to all the institutes involved.

\* Corresponding author.

E-mail address: [aryati@fk.unair.ac.id](mailto:aryati@fk.unair.ac.id) (Aryati).

<https://doi.org/10.1016/j.radcr.2022.04.056>

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bowel sounds, vomiting, shortness of breath, and lethargy. Laboratory assessments in patients with NEC may reveal increased C-reactive protein (CRP), leucocytosis, thrombocytopenia, hyponatremia, and neutropenia. NEC on radiology examination may appear as pneumatosis intestinalis due to the production of gangrene gases [1–4].

Preterm birth, gestational age of <32 weeks and birth weight of <1500 grams are the primary risk factors for NEC. Additional risk factors are classified as prepartum, intrapartum, and postpartum factors. Prepartum factors include a history of medications, maternal hypertension, infection and placental issues during pregnancy. Exposures to pathogens and hypoxic-ischemic disturbances are risk factors that occur during the delivery process. Enteral feeding during the postpartum period is also a risk factor for NEC [1–4].

NEC can occur in full-term and normal-weight newborns of >36 weeks and >1500 grams, despite the higher prevalence in preterm newborns. Risk factors for NEC in full-term newborns include a history of intrauterine growth retardation, polycythemia, hypoglycemia, gestational diabetes, sepsis, exchange transfusion, umbilical line procedure, and chorioamnionitis. In full-term infants, NEC can occur as soon as 1 week postpartum [1–4].

Despite the predominant prevalence of NEC in preterm newborns, our patient demonstrated an infrequent case of NEC in a full-term newborn, which was presumed to be caused by maternal COVID-19 infection. We explored neonatal outcomes following NEC diagnosis in an effort to prevent and mitigate future cases of NEC due to maternal COVID-19 infection.

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## Case report

### Medical history

A 6-day-old newborn male was referred from a secondary regional hospital to the emergency center of the tertiary Soetomo General Regional Hospital with a chief complaint of abdominal distension for 3 days before hospital admission. A history of late meconium was present; the first and last defecation was 3 days before hospital admission after an enema procedure was performed. Following the enema, no spontaneous defecation occurred and the distention worsened. There was a history of non-projectile bilious vomiting at 3 days old after ingestion of  $\pm$  10 mL of fluid. The volume of the vomit was greater than the volume of fluid intake.

An orogastric tube and rectal tube were then inserted, and the patient was kept nil per oral (NPO). Approximately 10 mL of bilious gastrointestinal retention was obtained via the orogastric tube. Minimal defecation was collected via the rectal tube. The infant's vital signs were stable. No icterus or shortness of breath was present. Micturition was spontaneous, clear, and with sufficient urine output.

Routine antenatal care was performed by a midwife, and the antenatal history was insignificant. The patient was delivered from a G3P1A1 mother with a birth weight of 2800 grams at 38–39 weeks gestation via caesarean section due to confirmed maternal COVID-19. The APGAR score was 7 at 0' and 8 at 5' after birth.

### Physical examination

Upon hospital admission, the patient was *compos mentis* with a Glasgow Coma Scale of E4V5M6. There were sufficient movements and normal work of breathing. Vital signs were stable, with a heart rate of 140 beats per minute, respiratory rate of 40 breaths per minute, temperature of 36.5°C, and oxygen saturation of 98%. The head and neck examination showed no anemia or icterus. Breathing was vesicular with no rhonchi or wheezing. Cor was within normal limits. The extremities were warm, CRT was less than 2 seconds and no edema was found.

Abnormalities were found during the abdominal examination. The abdomen was distended with venectasis. There was no visible darm contour. Bowel movements were present but weak. Abdominal percussion elicited a tympanic sound, although the liver was difficult to evaluate. Rectal toucher examination showed a normal anal sphincter with minimal feces and mucus. The rectal ampulla and rectal mucous were normal.

### Laboratory findings

Hematology analysis showed a persistent decrease in hemoglobin, hematocrit, and red blood cell counts during care, indicating the presence of anemia. White blood cell counts were within normal ranges, although a consistent increase in white blood cell count was evident on day-to-day comparisons. Increases were also found in neutrophil, lymphocyte, and monocyte percentages throughout hospitalization. Platelet counts were exceedingly low during the first 2 days of care, although the count subsequently recovered favorably.

Increased CRP persisted on clinical biochemistry and immunology examination during the first week of care. Albumin levels were initially low but rebounded following treatment. Electrolyte levels remained within reference values throughout hospitalization.

Coagulation function examination revealed prolonged PT and APTT, suggesting an abnormal coagulation function.

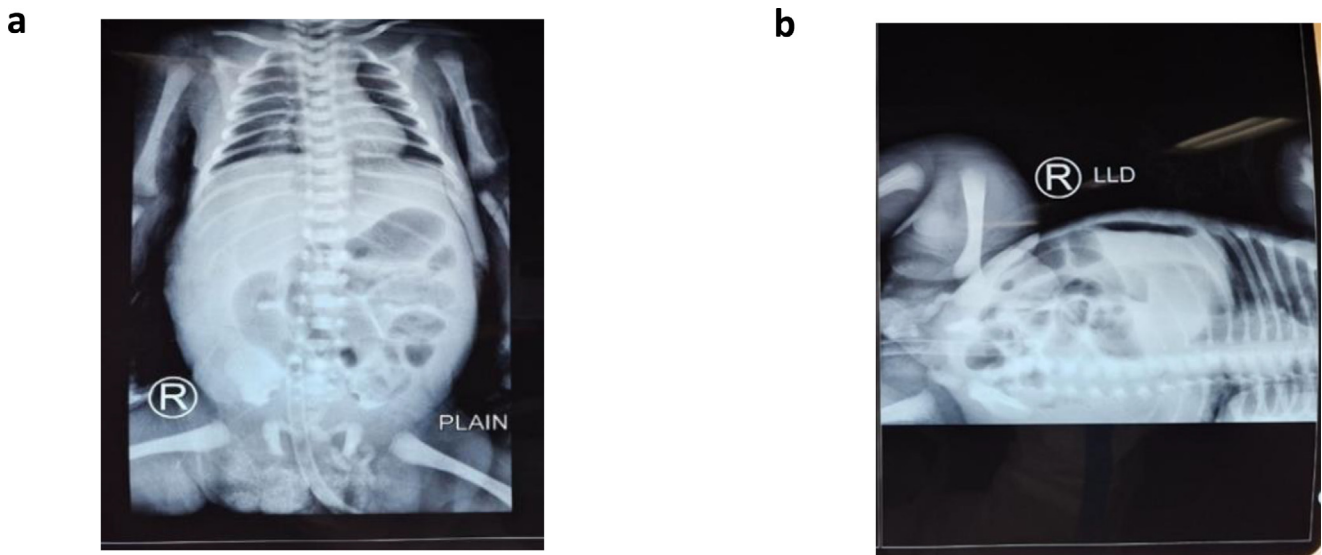
The SARS-CoV-2 antibody test revealed reactive IgG and IgM. However, 2 negative results were found on 2 distinct SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction examinations (Fig. 1).

### Radiology findings

The babygram visualized opacities on the right side of the abdomen, indicating the presence of free fluids in the peritoneal space. Gases were limitedly present in the gaster and small intestines. No gas was found in the intestinal lumen in the pelvic region. The colon was not visible in the radiograph. These findings indicated a collapse of the distal gastrointestinal tract, including the colon and rectum. On the left lateral decubitus radiograph, an air-fluid level was seen in the upper region, indicating the presence of pneumoperitoneum. No pneumatosis intestinalis was seen (Fig. 2).



**Fig. 1** – Clinical presentation of a 6-day-old newborn referred to the emergency room, with chief complaint of abdominal distension.

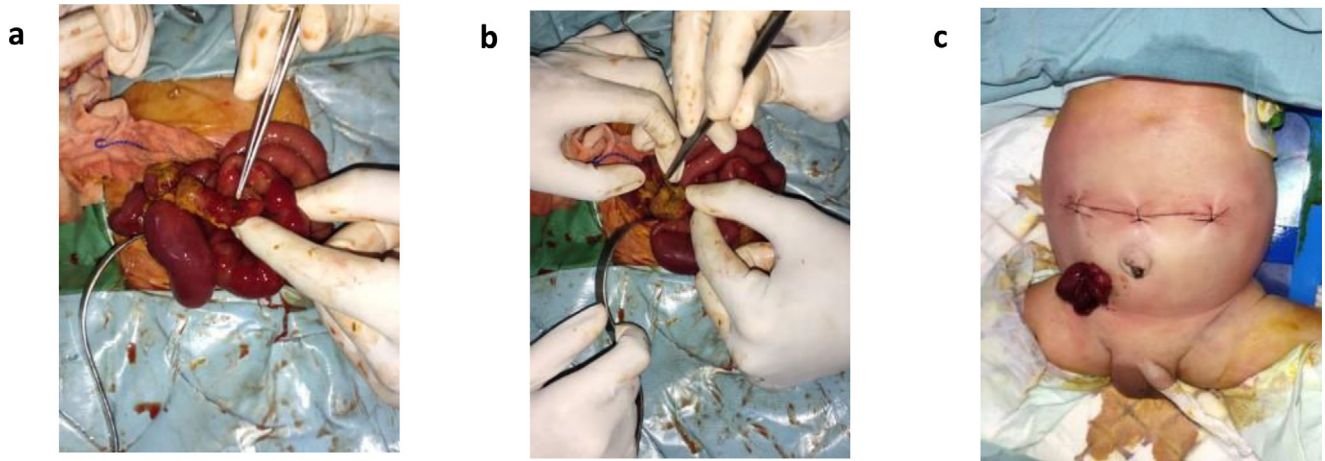


**Fig. 2** – Plain radiograph of the newborn in the (a) AP position showing chest, abdomen, and pelvic area (babygram) and in the (b) LLD position showing the abdomen area.

#### *Preoperative and intraoperative management*

A primary diagnosis of neonatal NEC with the complications of hollow organ perforation and generalized peritonitis was suspected. Operative management was then proposed and the pediatric and anesthesia departments were consulted for surgical clearance. An emergency explorative laparotomy with a

stoma insertion was arranged and performed with duration of 4 hours. The locus minoris resistentiae was found in the ileum. The perforation had occurred 150 cm and 170 cm distal to the ligament of Treitz. Approximately 25 cm of ileum was then resected to remove any other potential vulnerable tissues, and a full-thickness biopsy of the sigmoid and double-barrel ileostomy was performed. The tissue collected was sent



**Fig. 3 – Intraoperative images showing perforations at a) 150 cm distal and b) 180 cm distal from Treitz ligament. Postoperative images showing c) a doublebarrel ileostomy stoma on the right lower quadrant of the abdomen and a closed horizontal incisional wound above the umbilicus.**

to the pathological anatomy laboratories for histopathological examination.

#### Postoperative management

The infant was transferred to the neonatal intensive care unit with a backup ventilator following the surgery. Medications administered included the following: intravenous D10 0.18 NS 400 mL once per day, intravenous metronidazole 30 mg thrice per day, intravenous ampicillin 140 mg twice per day, intravenous gentamycin 14 mg twice per day and intravenous paracetamol 40 mg thrice per day. The patient was kept NPO for 24 hours with an orogastric tube. Transfusion of thrombocyte concentrate and fresh frozen plasma was performed. The postoperative evaluation included stoma viability and any presentations of peritonitis. In addition, blood cultures were carried out.

#### Discussion

NEC is an emergent condition in newborns. The majority of newborns with NEC are preterm due to their immature organ functions and ineffective metabolisms. NEC has a high rate of morbidity and mortality. Therefore, adequate intensive care in the neonatal intensive care unit is necessary for the management of patients with NEC. In this case, the patient was not preterm. The occurrence of NEC in normal-weight, full-term newborns is low but possible. Several risk factors predispose infants to the condition, including prenatal, natal and postnatal factors. The antenatal care history, delivery process and postnatal findings in our patient were found to be unremarkable. Thus, maternal COVID-19 was thought to be the primary predisposing factor of NEC in the patient. The risk of intrauterine transmission of COVID-19 is still unclear, though vascular abnormalities and chorioamnionitis of the placenta have been found in COVID-19-positive pregnancies [1,3,5,6].

The diagnosis of NEC is established based on clinical presentation and supportive workup. In this case, NEC was suspected due to the newborn's progressive abdominal distention, shortness of breath and lethargy. Pneumatosis intestinalis on plain radiographs is a pathognomonic finding for NEC; however, this radiographic finding was not seen in our patient. As the initial workup was not able to confirm the diagnosis of NEC, further management had to be carried out to establish the diagnosis. Management plans for NEC are proposed based on the clinical presentation and severity classification using Bell's staging. Our patient was classified as definitely and moderately ill (stage IIB) according to the modified Bell's staging criteria for NEC in neonates [4,7].

Treatment options for NEC are classified as surgical and nonsurgical. Nonsurgical treatments are preferred as initial strategies as they are less invasive, considering the vulnerability of patients with NEC. Nonsurgical treatments include rest and decompression of the bowel, parenteral nutrition, support of the respiratory, and cardiovascular systems, further laboratory and radiological examinations, and administration of antibiotics, fluids, and other supportive medications. The goal of conservative treatment is centered around disease limitation. Surgical strategies are commonly arranged if nonsurgical treatment fails to limit the extent of the disease. Surgical treatments, however, may be the primary strategy in the presence of bowel perforation, peritonitis, or any metabolic disturbances, such as metabolic acidosis, CRP elevation, hyponatremia, hyperglycemia, thrombocytopenia, neutropenia and leucocytosis. Peritonitis was found in our patient as an advancement of the hollow organ perforations that occurred due to NEC; thus, surgical actions were taken. The surgical strategies, in this case, were not only utilized as a treatment plan but also to confirm the diagnosis of NEC through histopathological examination. We found that the findings in the histopathological examination were consistent with NEC [4,8,9].

The differential diagnoses of NEC include Hirschsprung disease, volvulus and ileal atresia [4]. These diagnoses should be thoroughly differentiated from NEC through examination

and workup to enable early diagnosis of NEC and implementation of prompt treatment, given that NEC is an emergent condition.

NEC gives rise to numerous complications. Acute complications include sepsis, meningitis, peritonitis, and intra-abdominal abscesses. Several NEC complications may occur weeks or months after the onset of NEC, as primary effects of the disease itself or secondary effects of the disease management. These late complications can manifest as short bowel syndrome, gastrointestinal failure or bowel stricture due to the surgical procedures. Our patient presented with an acute complication of peritonitis, which caused shifts in laboratory parameters, including anemia, thrombocytopenia and elevated CRP. These shifts were suspected to be due to infection, inflammation, and occult bleeding following the NEC peritonitis [2,4].

Following the intensive management and treatment, our patient has been progressing toward a better prognosis. Although not all parameters in the most recent examinations were within normal limits, they were trending toward normal levels. These improvements are consistent with previous findings that mortalities in newborns with NEC are primarily due to preterm or low-birth-weight conditions rather than the NEC itself [5].

In conclusion, the impacts of COVID-19 on pregnancy and neonatal outcomes are still being investigated; thus, comprehensive assessments should be implemented in newborns, particularly when maternal COVID-19 has been identified.

## Conclusion

Maternal COVID-19 was suspected to be the predisposing factor in the diagnosis of NEC in a 6-day-old newborn. NEC was suspected due to significant clinical presentations, including progressive abdomen distention, venectasis, peritoneal free fluids and uneven bowel gas distribution. Laboratory results were indicative of neonatal sepsis due to the presence of anemia, thrombocytopenia, elevated CRP, prolonged PT and APTT, and a positive ESBL *Klebsiella pneumonia* on blood culture. No remarkable history was found in the patient's antenatal care, delivery process or postnatal findings except for maternal COVID-19. Further studies are required to explore the correlation between maternal COVID-19 and NEC in both preterm and full-term newborns.

## Patient consent statement

Written informed consent was obtained from patients for the publication of this case report.

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