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CASE REPORT

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# A case of necrotizing enterocolitis in full-term infant on his first day of life—Early presentation with multifactorial etiology

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**Abstract**

We aimed to show the complexity of NEC in the full-term newborns. Additionally, we wanted to underline the importance of breastfeeding from the first day of life and show how deteriorating effect the antibiotics can have on gastrointestinal tract.

**KEYWORDS**

formula milk, full-term, necrotizing enterocolitis, total parenteral feeding

## 1 | INTRODUCTION

Necrotizing enterocolitis (NEC) is a severe disease of the gastrointestinal tract occurring in neonates, that ultimately can lead to bowel perforation or death. We present a case of a full-term neonate who developed NEC on the first day of life and multiple factors that may have contributed to its advancement.

The course of necrotizing enterocolitis (NEC) in premature infants differ from the one in full-term infants. Premature infants manifest symptoms later and, what is more, other risk factors are connected with NEC development. NEC in preterms is mainly associated with digestive system immaturity and low birth weight—lower weight indicates higher risk of NEC development. On the contrary, NEC in full-term infants is linked with various congenital malformations, such as Hirschsprung's disease or heart diseases, but also with perinatal risk factors, such as hypoxia, hypoglycemia, hyperglycemia or maternal factors, like preeclampsia, diabetes, and PROM.[1] NEC incidence in full-term newborn is much lower than in premature newborn. Precise pathophysiology is not known in both cases; however, it is believed to be connected with hypoxia and secondary inflammation due to intestinal damage. This article shows how various factors in full-term newborns contribute to the development of NEC and the importance of fast reaction that may prevent disease development and long-term complications.[1,2]

## 2 | CASE

Male newborn in the first day of life due to NEC was admitted to our unit for diagnosis and treatment. The baby

boy was born by emergency C-section in the 40th week of pregnancy (second pregnancy and second labor). Clear amniotic fluid drained 5 h before labor. Wait and see attitude was adopted, but due to the risk of asphyxia C-section was performed. The infant received 10 points in Apgar scale at 5 and 10 min of life, respectively. The birth weight was of 3600 g (75 centile) and body length of 53 cm (75 centile). The course of pregnancy was complicated by bleeding in the 14th and 18th week of pregnancy and did not require intervention–no other complications were observed. In primary hospital, the umbilical cord blood for gasometry was not taken; however, blood for morphology and culture was. The tests revealed CRP at the level of 0.10 mg/dL (norm of 0.5 mg/dL) and elevated leukocytes at 34660/μL for which patient received empirical antibiotic treatment—ampicillin 2 × 270 mg iv with gentamicin 1 × 14 mg iv. Other parameters were within normal range. Intensified sucking reflex was observed in the patient within first few hours after birth. Due to lack of mother's own milk, the newborn was fed several times with formula.

In the 18th hour of life the newborn started to be restless, his abdomen was bloated, rigid, and tender. Moreover, bowel sounds upon auscultation were absent. Enteral feeding was stopped and total parenteral nutrition was introduced.

Post-admission imaging examinations (Figure 1A,B) showed large intestine pneumatosis and its emphysema. In addition, ultrasound examination presented small hyperechoic lesions in portal vein system that indicate the presence of gas bubbles and peristalsis was absent. However, there were no signs of perforation. At that time, CRP amounted to 2.5 mg/dL and it caused the change in antibiotic treatment—from ampicillin with gentamicin to merapenem 3 × 40 mg/kg/dose iv for 4 h with 4-hour break and vancomycin 10 mg/kg/dose iv every 12 h. Fluconazole, in preventive dose, was added next day.

Echocardiography in the second day of life showed wide ductus arteriosus—5.7 mm with large left-to-right shunt. Due to massive leak through ductus Botalli, there was a significant decrease in mesenteric and renal perfusion. Additionally, ECHO presented the signs of pulmonary hypertension with increased pulmonary vascular resistance (PVR). Wide ductus arteriosus in the patient was treated with paracetamol in the dosage of 15 mg/kg four times a day until clinical improvement. In the third day of life; however, the patient was administered with dobutamine in the dose of 5 mcg/kg/min and dopamine in the dose of 10 mcg/kg/min due to heart failure.

Despite broad-spectrum antibiotic treatment, the patient's general health condition deteriorated and inflammatory parameters increased–CRP increased from 2.5 to 7.5 mg/dL in the second day of life and there was a rapid increase to 20.6 mg/dL in the third day of life. Due to high inflammatory parameters and poor general condition, it was decided to perform laparotomy. Caecum perforation, as well as sigmoid colon perforation with a large stool leakage to abdominal cavity was observed during operation. Up to 30 cm of ileum, whole colon till the rectum connection were necrotic, then removed and colostomy was performed.

The samples were taken for histopathological examination. The results confirmed the diagnosis of NEC–bleeding and necrosis in the intestinal wall. Additional histopathological examinations showed proper large intestine innervation that excluded Hirschsprung's disease as NEC comorbidity.

Cefotaxime was included into the antibiotic treatment after the surgery and it finally lowered the inflammatory parameters within few following days. Echocardiography was performed 1 day after the surgery presented decreased PDA–from 5.7 to 3.5 mm. In the sixth day of life, 3 days after the surgery, PDA closed completely due to the treatment.

On the 10th day of life, enteral feeding with mother's own milk or with milk from human milk banks was introduced. The portions were increased gradually under the control of tolerance. However, despite enteral feeding

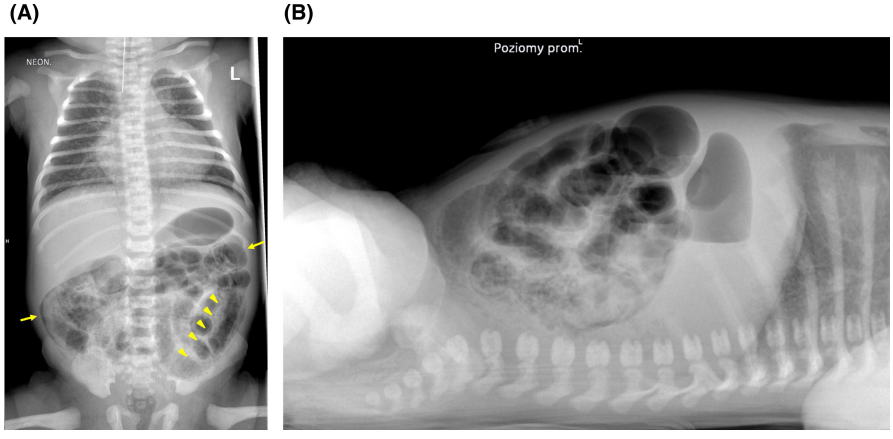


**FIGURE 1** (A) X-ray of chest and abdomen reveals distended large bowel (arrows) with pneumatosis intestinalis (arrowheads). (B) There is no free peritoneal gas-assessed on lateral projection taken with horizontal beam technique.

of volume up to 8 × 20–25 mL (44 mL/kg/day), the stoma losses reached almost 86% of enteral supply.

Additionally, lower albumin concentration and decreased diuresis, which are the prerenal renal failure factors, were observed. Due to this fact, total parenteral nutrition was maintained and short bowel syndrome (caused by massive intestines' resection due to NEC) was diagnosed. The patient in fair to good condition at 47th day of life was transferred to The Department of Paediatrics, Nutrition and Metabolic Diseases for further short bowel syndrome treatment.

## 3 | DISCUSSION

According to the available literature reports, the time of NEC onset varies between full-term newborn and the premature one. Usually, the preterm infants present the first symptoms after first 2- or 3 weeks after delivery, while full-time newborns may present the symptoms within the first week of life. If a preterm presents NEC symptoms within first days of life, it is usually connected to spontaneous intestinal perforation (SIP).[1,3] Our patient manifested the symptoms within the first 24 h of life and then we confirmed them in abdominal x-ray and ultrasound examination. Such early outcome of symptoms is untypical, even for full-time newborns, and it shows the number of factors influencing such severe NEC in our patient.

NEC pathophysiology is not fully understood. There are a lot of hypotheses that suggest the cause of this disease. What is important, they vary between full-term newborns and preterms. In preterms we may observe imbalance between vasoconstrictive factors, such as endotelin-1, and vasodilation factors, such as nitric oxide (NO), which promote vasoconstriction to vasodilatation and lead to hypoxia and furthermore to intestinal damage. On the other hand, in full-term newborns, especially with heart diseases, the main cause is ischemia and hypoxia, which leads to intestinal damage.[4-7] Due to wide PDA of 5.7 mm, our patient had decreased perfusion of mesentery and intestinal wall and intestine itself. This all lead to chain reaction–local hypoxia, then damage and finally necrosis.[8] Essentially, NEC caused by CHD is more common in full-term newborns, rather than in preterms who do not often suffer from heart diseases with decreased intestinal vessels perfusion.[3]

According to the literature, intestinal necrosis in full-time newborns with heart disease includes mainly colon and is rare in small intestine or ileocecal area, which is characteristic for preterms. It is due to the fact that colon is more prone to damage caused by ischemia than other parts of the intestine.[8] In case of our patient, the necrotic area was from ilea, through colon to the connection with sigmoid. It suggests that the ischemic component was one of the main causes of the disease.

Martin van der Heide proved that low Apgar score, especially in children with CHD, correlates with ischemic and hypoxic episodes which are later the underlying etiology for NEC. Although having high Apgar score after birth and no need for respiratory support, our patient developed NEC in the first day of life. It may suggest that wide PDA was not the only inflammatory factor in the case of our patient.[7]

Despite the proper Apgar score, we cannot fully exclude the intrauterine hypoxia episode caused by impending asphyxia. The Apgar score is a subjective measuring tool of child's well-being. In order to fully evaluate the newborn, it is necessary to consider biochemical markers such as cord blood gasometry.[9]

What is crucial in case of our patient is the fact of being fed with formula immediately after birth. Necrotizing enterocolitis is more common in newborns fed with formula in comparison to breastfed newborns or newborns fed with milk from human milk bank.[2,10] It is because formula has pro-inflammatory effect on the intestine and it may negatively influence intestinal microbiome in comparison to mother's own milk.[11,12] It suggests that in spite of wide PDA, enteral feeding might have accelerated NEC or worsen it by starting inflammatory reaction, which constitutes to the NEC pathophysiology (Figure 2).

Moderately elevated leukocytes and increasing inflammation markers within first 24 h of life suggest starting or ongoing inflammation. It may be speculated that it might have been caused by beginning of intrauterine inflammation, which is an additional NEC risk factor.[2] These divagations are uncertain to some extent.

It is important to mention that our patient got broad-spectrum antibiotic treatment in the first 24 h after birth. The treatment was necessary due to deteriorating clinical condition and positive inflammatory markers. Moreover, administration of empirical antibiotic treatment within first 3 days of life and its prolonged use, are associated with higher risk of NEC, it is because antibiotics delay the maturity of the intestinal microbiome and its colonization, which impairs intestinal homeostasis.[11,13,14]

Early antibiotic administration and delayed enternal feeding with maternal milk had a synergic aggravating effect on the gastrointestinal tract in our patient. The abovementioned factors alongside with formula, that induces mucosal hypoxia and inflammatory response, have led to such an extensive clinical manifestation of NEC.[15]

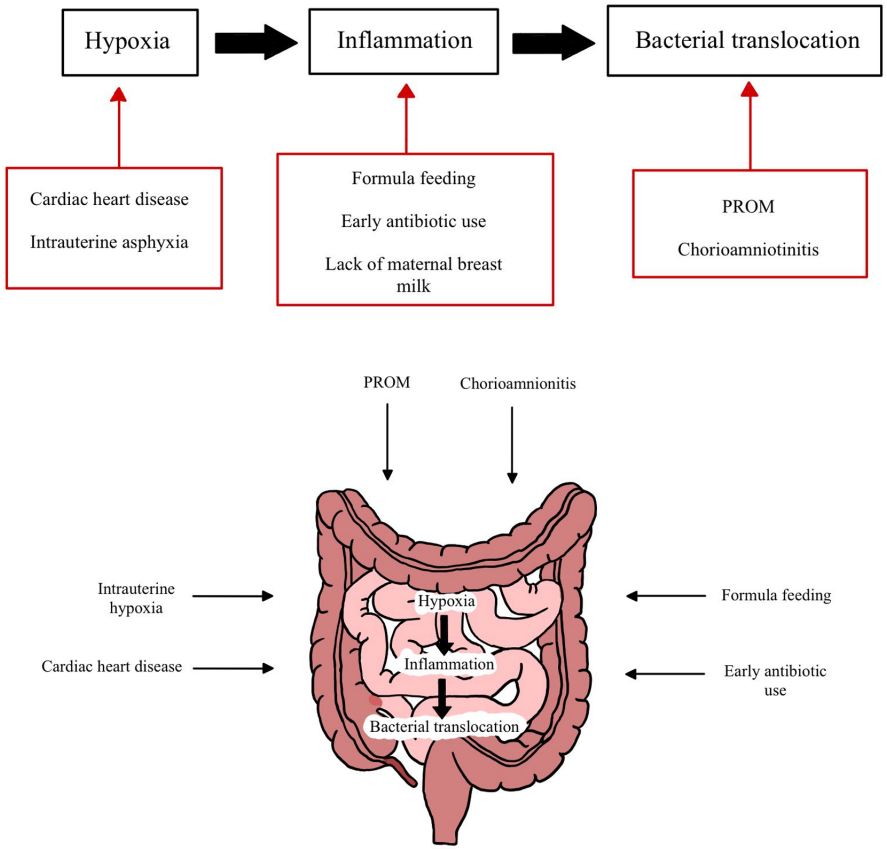


**FIGURE 2** The most common risk factors of necrotizing enterocolitis in full-term infants.

## 4 | CONCLUSION

The patient described in this study developed NEC in the first day of life. A lot of factors might have influenced the appearance of disease symptoms, such as: wide PDA, formula feeding in the first day of life, delayed maternal feeding, the risk of intrauterine hypoxia or empirical antibiotic treatment. It is difficult to state the factor which was the most prominent.

We suppose that in case of our patient, formula, lack of human milk and antibiotics might have accelerated the onset of NEC. However, we do believe that the overlap of all negative factors contributed to such severe and tragic manifestation of necrotizing enterocolitis. We aimed to show the complexity and severity of this particular disease in full-term newborns. Additionally, we wanted to underline the importance of breastfeeding from the first day of life, as human milk protects intestinal microbiome. It may be speculated that unless formula feeding, the disease course might have been less severe.

### AUTHOR CONTRIBUTIONS

**Bożena Kociszewska-Najman:** Validation; writing – review and editing. **Ewa Głuszczak-Idziakowska:** Supervision; validation; writing – review and editing. **Joanna Schreiber-Zamora:** Writing – review and editing. **Mariusz Furmanek:** Visualization. **Olga Żelazna:** Conceptualization; writing – original draft. **Malgorzata Maria Bednarczyk:** Conceptualization; formal analysis; investigation; writing – original draft.

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### CONFLICT OF INTEREST STATEMENT

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### DATA AVAILABILITY STATEMENT

All relevant data are included in the report and the associated images. Further inquiries can be directed to the corresponding author.

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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