

Colonic Stenosis Post-Necrotizing Enterocolitis in Term Newborn with Acquired Cytomegalovirus Infection

L. Marseglia¹, S. Manti¹, G. D'Angelo¹, M. Lima², P. Impellizzeri³, C. Romeo³, E. Gitto¹

¹Neonatal Intensive Care Unit, Department of Pediatrics, University of Messina, Italy

²Department of Pediatric Surgery, S. Orsola-Malpighi Hospital, University of Bologna, Italy

³Department of Pediatric Surgery, University of Messina, Italy

Rezumat

Stenoză colonică post-enterocolită necrotizantă la un nou-născut la termen cu infecție dobândită cu Citomegalovirus

Enterocolita necrotizantă este o urgență gastrointestinală ce apare în mod tipic la nou-născuții prematuri. Stricturnile intestinale complică rareori tratamentul medical sau chirurgical al enterocolitei necrotizante. Infecția postnatală cu citomegalovirus cu afectare digestivă a fost ocazional descrisă la subiecți cu enterocolită necrotizantă. Prezentăm cazul unui nou-născut la termen, cu enterocolită necrotizantă, infecție dobândită cu citomegalovirus și stricture colonică post-enterocolită necrotizantă.

Cuvinte cheie: enterocolită necrotizantă, nou-născut la termen, sepsis, citomegalovirus, stricture intestinală

Abstract

Necrotizing enterocolitis is a gastrointestinal emergency typical of premature infants. Intestinal strictures infrequently complicate medical or surgical treatment of necrotizing enterocolitis. Postnatal cytomegalovirus infection with gastrointestinal involvement has occasionally been described in subjects with necrotizing enterocolitis. We report the case of a

full term infant presenting necrotizing enterocolitis, acquired cytomegalovirus infection and post necrotizing enterocolitis colonic stricture.

List of abbreviations: necrotizing enterocolitis = NEC, cytomegalovirus = CMV

Key words: necrotizing enterocolitis, term newborn, sepsis, cytomegalovirus, intestinal stricture

Introduction

Only very few cases of post necrotizing enterocolitis (NEC) colonic stricture in term neonates have been reported. Postnatal cytomegalovirus (CMV) infection with gastrointestinal involvement is also extremely rare in immunocompetent term newborns, and has occasionally been described in subjects with NEC.

We describe the case of a full term infant presenting NEC and postnatal CMV infection, who developed a post NEC colonic stricture.

Case report

Postnatal cytomegalovirus (CMV) infection with gastrointestinal involvement is extremely rare in immunocompetent term newborns.

We describe the case of a full term infant presenting NEC and postnatal CMV infection, who developed a post necrotizing enterocolitis (NEC) colonic stricture.

An Italian male infant from non-consanguineous parents

Corresponding author: Lucia Marseglia, MD
Neonatal and Pediatric Intensive Care Unit
Department of Paediatrics, University of Messina
Via Consolare Valeria, 1, 98125 Messina, Italy
E-mail address: lmarseglia@unime.it

was born full-term via caesarean delivery, due to gestosis. There was no known maternal exposure to teratogens or infections. The infant's Apgar score was 9 at both 1 and 5 minutes. Birth weight was 2780 g. Three hours after birth, the infant developed respiratory distress and required intubation, exogenous surfactant administration and mechanical ventilation, for three days. Ecocardiocolordoppler showed patent ductus arteriosus, treated successfully with a course of intravenous ibuprofen. The infant passed meconium 18 hours after birth. Enteral feeding was started after 4 days with maternal milk. On day 8 of life he presented frequent vomiting and regurgitation, gastric residuals, abdominal distension, feedings withheld due to intolerance, passing dark green loose stool. Abdominal X-ray showed diffuse dilated bowel loops, without evidence of pneumatosis; this condition was listed as NEC (Bell's stage ≥ 1) (1).

Therefore, the patient was kept nil by mouth, total parenteral nutrition was administered, and Metronidazole added to the antibiotic therapy started at birth, with temporary beneficial effects.

After 15 days, the patient showed new onset of feeding intolerance due to recurrent infections; blood culture, urine culture and copro-culture were positive for Gram positive and Gram negative bacteria (*Pseudomonas aeruginosa*; *Enterococcus Faecalis*; *Klebsiella Pneumoniae*; *Staphylococcus Warneri*; *Staphylococcus Haemolyticus*). A series of abdominal X-rays were performed showing severe colonic distension. Sweat chloride test for cystic fibrosis was normal.

Viral investigations were positive for CMV infection. Positive IgM CMV antibodies with low IgG tittle, low avidity IgG, presence of CMV DNA in blood and urine, and absence

of CMV IgM and CMV DNA in maternal blood allowed exclusion of congenital CMV infection. We hypothesized that the patient had contracted CMV infection through blood transfusions performed for anemia.

Abdominal distension was considered due to CMV-related gastroparesis, and specific therapy with Ganciclovir was started, but the infant showed no benefit. An immunodeficiency was supposed because of repeatedly acquired infections, but specific investigations excluded such condition.

Six weeks after the episode of NEC, a barium enema study was performed confirming marked colonic dilatation (transverse colon > 5 cm), showing the presence of colonic strictures of 1.2 cm from descending to sigmoid colon with severe degree of upstream bowel dilation (Fig. 1, 2).

Hirschsprung Disease was excluded by negative rectal biopsies.

Therefore, a post-NEC colonic stricture was suspected and the patient underwent surgery with resection of a sigmoid stricture and primary anastomosis, followed by complete recovery.

Discussion

NEC is the most common gastrointestinal emergency of preterm neonates involving about 7% of infants with a birth weight between 500 and 1500 g (2). Since the early 1970's some reports have described its occurrence also in term neonates (2); however, the incidence of NEC in term infants is still controversial. For Ayala et al., only 10% of neonates developing NEC are full term infants (3). Recently Christensen et al. evaluated the incidence of NEC among

Figure 1. Colonic strictures in barium enema study

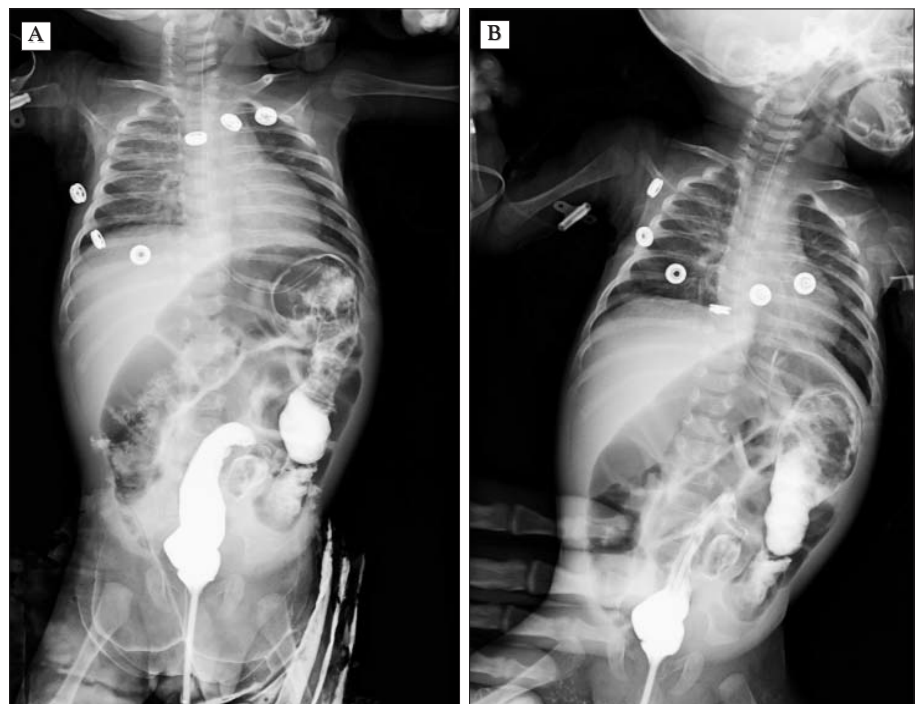




Figure 2. Marked colonic dilatation in barium enema study

full term neonates admitted to a Neonatal Intensive Care Unit over a period of 11 years, and identified this condition in 52 cases out of 11,596 admitted term infants (4). NEC appeared to occur earlier in full-term infants than preterms (8.56 days vs 12.78 days) and frequency of complications was less common (3).

Risk factors for NEC in term infants include intrauterine growth retardation, birth asphyxia, congenital heart disease, gastroschisis, hypoglycemia, sepsis, milk allergy, premature rupture of membranes with and without chorioamnionitis, and gestational diabetes (4). Early onset of NEC suggests a pathogenic mechanism related to a perinatal ischemic insult that might act independently from any risk factor (4) and oxidative stress is known to play a critical role in both premature and term neonates (5).

Several studies have confirmed the hypothesis that occurrence of NEC in full-term infants is usually associated with predisposing events, such as sepsis (6). Bacterial colonization has been hypothesized to play a major role in the onset and extension of disease, and infection is also a common, underappreciated complication of NEC that may develop at onset of the disease or at a later stage (6). Enterobacteriaceae species, Staphylococcus species and Clostridium species are most commonly associated with NEC. Several enteric viruses (rotavirus, echovirus, coronavirus, torovirus, norovirus, CMV) and Candida species have also been described (6). In our case, cultures were positive for Gram positive and Gram negative bacteria, and 4 weeks after the acute episode of NEC an acquired CMV infection was diagnosed, manifesting with abdominal distension and feeding intolerance. Postnatal CMV

infection with gastrointestinal involvement has been reported in a small number of premature infants (7), but is extremely rare in term infants. NEC has been reported to be associated with CMV infection in very few cases. However, specific antiviral therapy did not resolve the intestinal symptoms in this case, and thereafter a colonic stricture was diagnosed. In previous reports, CMV was detected during the acute phase of NEC (7) as well as during the proliferative stage of stricture development after NEC (7).

Fung et al. reported a case of an infant with post-NEC stenosis, resolved with operative measures. CMV was detected at histological analysis of the resected sigmoid colon, raising the question if the intestinal stricture was the true consequence of a primary enteric viral infection or a superinfection due to a transitory immunodeficiency after the acute phase of NEC (8).

Unfortunately, histological investigation on the resected colon was not performed in our case, not permitting us to ascribe a role to CMV in the development of the intestinal strictures.

Conclusions

We report a rare case of an immunocompetent term newborn with post-NEC stenosis requiring surgical intervention, associated with CMV infection. We underline the role of bacterial and viral infections in the pathogenesis of post NEC-stenosis, either as directly responsible for the enterocolitis or as a secondary colonization after the initial acute phase (6).

Acknowledgements

The authors would like to acknowledge the Division of Radiology at University of Messina for its support in the performance of diagnosis.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images.

Authors' contributions

LM: Study conception and design of the manuscript
SM: Writing up of the first draft of the paper
GD: Conceived the case and helped draft the manuscript.
ML: Critical revision of the article.
PI: Conceived the study and participated in its design
CR: Conceived the study and participated in its coordination
EG: Approved the final manuscript.

All authors read and approved the final manuscript.

Author Disclosure Statement

The authors declare that they have no competing interests.

References

1. Bell MJ, Shackelford P, Feigin RD. Epidemiologic and bacteriologic evaluation of neonatal necrotizing enterocolitis. *J Pediatr Surg.* 1997;14:1-4.
2. Rodin AE, Nichols NM, Hsu FL. Necrotizing enterocolitis occurring in full-term neonates at birth. *Arch Pathol.* 1973;96:335-338.
3. Maayan-Metzger A, Itzhak A, Mazkereth R, Kuint J. Necrotizing Enterocolitis in Full-Term Infants: Case-Control Study and Review of the Literature. *J Perinatol.* 2004;24:494-499.
4. Christensen RD, Lambert DK, Baer VL, Gordon PV. Necrotizing Enterocolitis in Term Infants. *Clin Perinatol.* 2013;40:69-78.
5. Gitto E, Marseglia L, Manti S, D'Angelo G, Barberi I, Salpietro C, and Reiter RJ. Protective Role of Melatonin in Neonatal Diseases. *Oxid Med Cell Longev.* 2013;2013: 980374.
6. Bizzarro MJ, Ehrehkranz RA, Gallagher PG. Concurrent Bloodstream Infections in Infants with Necrotizing Enterocolitis. *J Pediatr.* 2014;164:61-66.
7. Hamprecht K, Maschmann J, Vochem M, Dietz K, Speer CP, Jahn G. Epidemiology of transmission of cytomegalovirus from mother to preterm infant by breastfeeding. *Lancet.* 2001;357:513-518.
8. Fung GPG, Leung W, Chan LM, Ho YC, Wong BPY, Hui Y, et al. A rare case of Cytomegalovirus enteritis transmitted through breast milk in an immunocompetent term infant after gastrointestinal surgery. *HK J Paediatr.* 2009;14:205-208.