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Rotavirus infection in newborn: A rare case of necrotizing enterocolitis

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ABSTRACT

Rotavirus infections in neonates are often asymptomatic, but they can become complicated, up to Necrotizing Enterocolitis.

Aim of the study is to resume the history of a rare case of NEC due to Rotavirus infection comparing clinical features, lab tests and development of Rotavirus-NEC to bacterial-NEC in order to identify the correct management and the best therapeutical strategy for this group of patients.

Our case report described the complicated story of a preterm female affected by Rotavirus-NEC who underwent surgery three times, but at least with good outcome.

Different risks factors predispose to NEC due to Rotavirus such as prematurity, seasonality and formula feeding. Associated symptoms are abdominal distention, tenderness, bloody stools and fever. Development of NEC in newborns affected by Rotavirus is pathognomonic: only a very small percentage of newborns affected by Rotavirus infections develop NEC, but all of them need surgery which is resolutive most of time. The average hospital stay of surgical newborns affected by Rotavirus infection was longer than that of newborns surgically treated for bacterial gastrointestinal infections.

Prevention of Rotavirus infections may be important to decrease the incidence of NEC, the morbidity and the mortality rate in neonatal period.

1. Introduction

Necrotizing enterocolitis is a severe and potentially fatal disease of newborns [1]. Despite of all advances in the management of preterm infants, NEC is still associated to a high perinatal morbidity and mortality rate [2,3]. Even if the causes of NEC are not fully understood, it is universally accepted that it is a multifactorial disease due to both infective and non-infective factors [4]. Infective agents are more and more implicated in the etiological pathway of NEC. Among these pathogens E. Coli, Klebsiella, Clostridia and Staphilococcus species are the most frequently involved [4]. Otherwise more recent studies [5–10] have demonstrated the active role of viral agents in the pathogenesis of this disease too, in particular the Rotavirus one.

Even if Rotavirus infections are usually community – acquired, nosocomial ones are not uncommon [11], especially those acquired in Neonatal Intensive Care Units [12,13]. Rotavirus infections in neonates are often asymptomatic, but, in case of bacterial co-infections, they can become complicated, and, at worst, they can cause necrotizing enterocolitis [4].

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1.1. Aim

Aim of this study is to describe a rare case of NEC due to Rotavirus infections. In particular, we want to highlight incidence, risk factors, presenting features and development of viral NEC in order to identify the best management of neonates affected by Rotavirus infections.

2. Case report

A 1090 g preterm female patient was born from spontaneous vaginal delivery at 27 + 4 gestational weeks from a 36-year-old secondi-gravida. Her mother had been hospitalized because of a high risk of prenatal delivery due to E. coli corioamniositis treated with Ampicillin, Clindamicin and Ceftriaxon. At birth, the baby had Apgar scores of 6, 8 and 9 at 1, 5 and 10 minutes, respectively. She required positive pressure ventilation with 100% oxygen. Furthermore, she was empirically treated with Ampicillin, Gentamicin and Fluconazole which were administered for 13 days and then switched to Vancomicine and continued for seven days Amikacine due to the positive blood cultures for E. Coli. At day 1 the baby started a parenteral nutrition continued until day 4 when Minimal Enteral Feeding (MEF) was introduced. A regular abdominal US was performed at her 12th day of life. Formula feeding was tolerated up to her 17th day of life when, because of her abdominal distention and general discomfort, an abdominal RX was performed, and it was negative for pneumatosis. Feeding was interrupted for some days, after which it was started again gradually. In her 49th day of life, the first episode of rectorrhagia was reported. A stool sample was collected and fecal cultures resulted positive for Rotavirus. The day after, she had marbled skin, she was hypo reactive and she had an important abdominal distention with presence of mucus and blood in her diaper. A second abdominal RX showed important bowel loops distention with pneumatosis and air-fluid levels **[**Fig. 1**]**. Because of her clinical features and radiological images, pediatric surgeons decided for explorative laparotomy, in the suspicious of necrotizing enterocolitis. **[**Fig. 2**]** At the surgical exploration, colon loops were inflamed with intestinal pneumatosis. There were suffering loops up to the descending colon. A Mickulitz ileostomy was packed. During the surgical procedure mucous membrane was

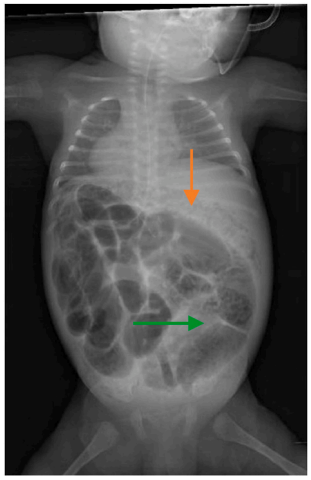

Fig. 1. Abdominal RX made on the day of the first surgery. It shows meteoric distension of colic loops (green arrow) with air-fluid levels. Free air in the abdomen and intestinal pneumatosis can be seen (orange arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

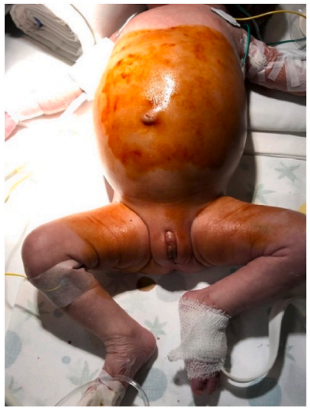

Fig. 2. Abdominal distention before the first surgical procedure.

taken for the histological exam, which demonstrated edema and venous stasis. [Fig. 3] Her postoperative course was regular. She evacuated semi-formed feces on post-operative day 3. On post-operative day 9, NGS was removed. Six days later oral feeding was gradually started and the parenteral nutrition was contemporarily gradually interrupted. On her 25th post-operative day, fecal recycling was started and continued until the subsequent surgical procedure of recanalization. The second surgery was done one month and twenty days after the first one, after the performation of colostogram, which was negative for obstruction. [Fig. 4] During the second surgery, an ileal term-terminal anastomosis was done, resecting the exposed parts of the bowel in the ostomy. On post-operative day 2, she was canalized at feces and gas. On post-operative day 4th, oral feeding was gradually started and the parenteral nutrition was gradually decreased and then stopped on her 11th post-operative day. On her 17th post-operative day she was discharge in optimums general clinical condition. The day after, the baby was driven to emergency room for lack of appetite, associated with vomit episodes and no air and feces in the last two days. An abdominal Rx was performed and it showed "Absence of pneumoperitoneus and of air-fluid levels". The day after, because of white stools, abdominal US was performed, resulting regular. Nine days later, after a further worsening of her abdomen condition, an RX with contrast medium was done, showing "Multiple permanent air-fluid levels and distended small bowel loops were identified, in particular there was a distended loop in right hypochondrium and minimum air in the rectal tract without any signs of pneumoperitoneum". [Fig. 5] The day after, because of a significant and rapid deterioration of her clinical conditions, she underwent a second explorative laparotomy. [Fig. 6] An important colic distention, associated to the presence of two stenosis, one located in the transversal colic segment and the other located in the splenic flexure of the colon, were found. [Fig. 7] The two stenotic segments were resected and the histological examination was asked. Anastomosis was performed after tailoring of the distal segment. A protective ileostomy was created at the same site of the first surgical procedure. [Fig. 8] The post-operative course was regular. Gradually oral feeding was administrated 3 days after surgery. Ileostomy started to produce feces on her second post-operative day. On her 13th post-operative day, she was discharged from the hospital in good general

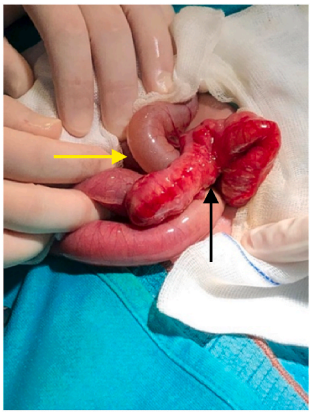

Fig. 3. Intra-operative images of the first surgical procedure. It shows the differences between the regular ileal intestinal tract (yellow arrow) and the necrotic colon, which appears inflamed (black arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

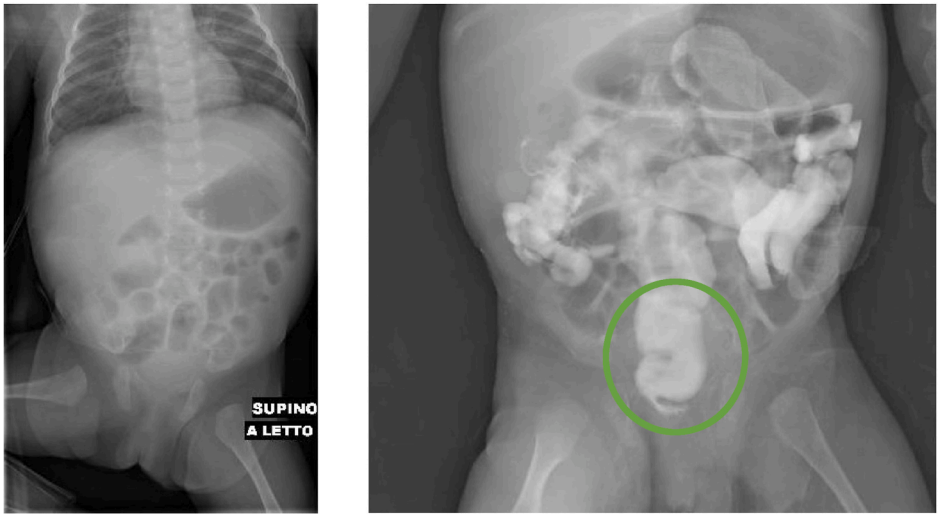

Fig. 4. Pre-surgical recanalization images. 4a) Abdominal RX 4b) Distal cologram (contrast medium inserted in the distal ostomy). The contrast arrived in the rectal ampoule (green circle) in 2 h after the somministration. It didn't show free air in the abdomen. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

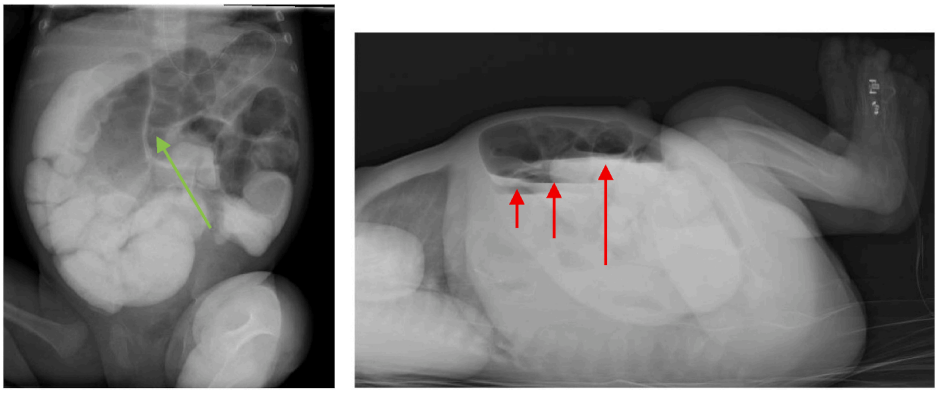

Fig. 5. Pre-surgical third laparotomy images. 5a) Frontal proiection of abdominal RX of the day before the third operation. It shows general loops distension. In particular, there is a distended loop in right hypochondrium (green arrow). Multiple air-fluid levels can be seen. Not visible free air in the abdomen. 5b) Lateral proiection. It shows multiple air-fluid levels (red arrows) and distended loops. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Fig. 6. Image of the pre-operative time during the third surgical procedure.

condition. [Fig. 9] Lab tests were regular, the ostomy was good-working and the baby ate 110 ml of artificial milk for 6 time a day, with the adding of rice cream, due to thickened feces. 3 months later she was recanalized with optimums results. Now she eats regularly with good tolerance and she evacuates normal consistency feces. Her vital auxological parameters were on range according to her age.

3. Discussion

Rotavirus is the most common pathogen involved in nonbacterial gastroenteritis in childhood [1–7]. Rotavirus infections in newborns are usually mild or asymptomatic [1]. However, literature reports rotavirus could be associated with sever condition such as NEC, which can also cause infantile death [7–14]. The incidence of gastrointestinal infection by Rotavirus in children is higher than 100 million cases and the associated mortality rate is about half a million deaths per year [14]. Generally, Rotavirus affects children younger than 5 years old [15]. Literature Review showed different risk factors associated to Rotavirus' severe infections such as prematurity due to biological immaturity typical of preterm infants [11], congenital malformations and both maternal and neonatal prior infections medically treated [13]. The incidence of Rotavirus infection is higher in low – weight for their gestational age infants and in formula – fed ones [5], even if this difference was no statistically significant. There are two main theories about the role of Rotaviruses in the pathogenesis of NEC. The first one sustains that NEC occurs when the pathogen is transmitted orofecally among newborns, particularly susceptible such as premature ones. The second hypothesis sustains that the onset of NEC depends on the level of virulence of the microorganism or on the consequence of the synergic action of two microorganism (most of times K. Pneumoniae and Rotavirus) [4].

Our case report presents the story of low-weight of her gestational age preterm infant. Because of the low levels of maternal antibodies and the severe immaturity of immune system, preterm newborns are at higher risk for Rotavirus infections and complications such as Necrotizing Enterocolitis [5]. Different cases of gastrointestinal infections by Rotavirus have been identified in newborns es-

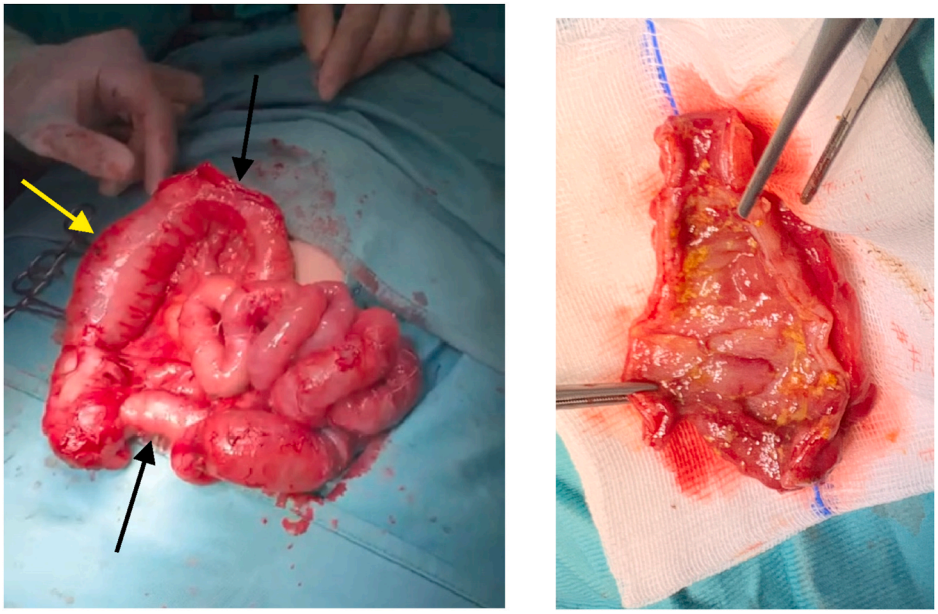

Fig. 7. Intraoperative images of the third surgical act. A) It shows two stenosis located in the colon, distal to the ostomy (black arrows). Between the two stenosis an important dilatation can be seen (yellow arrow). B) It shows the internal view of the stenotic bowel tract, compatible with macroscopic signs of NEC. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

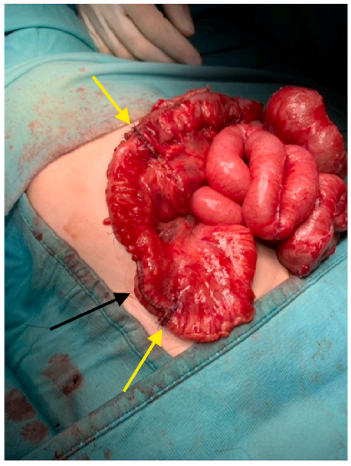

Fig. 8. Intraoperative image of the third surgical act. It shows the anastomosis distal to the ostomy (yellow arrows), made in the stenotic tract after the tapering of the dilatated bowel (black arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

pecially in preterm ones recovered in Neonatal Intensive Care Units [11,16]. Parenteral feeding was administered and then enteral feeding introduced, mixing mother's milk and the artificial one, adding a new risk factor for the onset of NEC.

Generally multiple infective agents and different risk factors are involved in the pathogenesis of NEC [1]. In the case described in our study, the girl had an important hematic infection, treated with antibiotics therapy, associated with hemoculture positive for E. Coli and viral gastroenteritis. The role of Rotavirus in the pathogenesis of enterocolitis has not been established yet. Probably it may play a synergic role with other microorganisms and worsen the gastrointestinal infection causing Necrotizing Enterocolitis [17].

Most of Rotavirus infections in newborns occurred in the first months of the year, especially in March and April because of the seasonal variation of Rotavirus [6]. Our case occurred in April according to Literature data. Despite of the prevalence of this infection in Spring, no statistically significant difference was evidenced with other seasons ($P = 0.657$) [5]. Furthermore, the RV + NEC infants developed symptoms later and more insidiously than RV- NEC babies. Radiological examination revealed less severe and more distal colon involvement [18]. This is fully compatible with the history of the case described in our study. Significant symptoms occurred on her 49th day of life, with rectorhaggia and abdominal distention. In Herruzo et al. newborns underwent surgery for Rotavirus infections started to present signs and symptoms later than those babies affected by bacterial NEC, most of them were 20 days-old newborns. 50% of symptomatic patients affected by Rotavirus progressed to full recovery, only 7% of them developed NEC (bell stages I, II and III) [6].

Fig. 9. Ostomy after the last surgical procedure.

In our experience, the development of NEC in newborns affected by Rotavirus infections was very similar to that proposed in Literature. In Herrero et all study, 1.5% of patients affected by Rotavirus gastrointestinal infection needed surgery, all the others babies had good prognosis without any complications [6]. Several studies tried to evaluate the differences between Rotavirus and non-Rotavirus Necrotizing Enterocolitis. Keller et al. and Schmidt et al. reported that left-sided pneumatosis was more common among infants with Rotavirus infections. It is well known that the most commonly afflicted regions of the gastrointestinal tract with NEC include terminal ileum, ileocolic region and ascending colon. Rotavirus-associated NEC disproportionately seems to involve the descending colon and rectum. Most of these cases is generally confined to descending colon and rectum and was a milder disease [8]. According to these data, the case of our study presented at the first surgical procedure a Necrotizing Enterocolitis involving the bowel until the descendant colon. A particular detail of the development of this baby's story was the finding of two stenosis distal to the ileostomy, showing the infection due to Rotavirus involves the last part of the bowel. The average hospital stay of surgical newborns affected by Rotavirus infection was longer than the ones of newborns surgically treated for bacterial gastrointestinal infections [6]. This data was confirmed by our experience. Even if Rotavirus infection increased the duration of hospitalization, this difference was no statistically significant [5]. Surgery seems to be the best therapeutic strategy for newborns affected by complicated Rotavirus infections. Despite of our experience, general good prognosis was described for this group of patients after surgery. Maybe prevention of Rotavirus infections should be promoted. The first measure should be taken was to improve hygiene protocols such as alcohol base hand-washing solutions [19,20]. Even if there are no enough studies, the role of maternal vaccination with RV vaccine should be considered, to improve neonatal immunity against Rotavirus infections. Other measures could include increased awareness of RV season in the community, use of strict isolation precautions, and maternal milk feeding [8].

4. Conclusion

In conclusion RV infection may precipitate the development of NEC in susceptible infants, and it can be considerate a risk factor in the pathogenesis of severe NEC in newborns.

The symptoms due to NEC related to RV infections occurred later than in NEC related to bacterial agents and they are less evident. An early diagnosis is essential for a correct management of these infants to avoid serious complications. It is important not to underestimate the symptoms and to perform surgery immediately, when it is necessary. This fragile group of patients has to be long-term followed-up in order to prevent tardively complications, such as stenosis.

The best way to decrease the incidence and the mortality of this disease is to prevent the infections by Rotavirus, through maternal vaccination, maternal milk feeding and normal hygiene measures, especially in the RV infection's seasons.

Ethics approval and consent

Not applicable.

Consent for publication

The consent for publication has been obtained from parents' children involved in the study through the fill in of our consent form.

Availability of data and materials

Please contact authors for data requests.

Funding sources

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Authors contributions

FM and GB carried out the surgical procedures, FN and GB participated in the design of the study and helped to draft the manuscript. RA, MM, TC, GV, GF helped to draft the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

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