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Case Report

Necrotizing enterocolitis associated *Klebsiella pneumoniae* sepsis

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ABSTRACT

Necrotizing enterocolitis (NEC) is a common multifactorial illness of the gastrointestinal tract with life threatening complications affecting mostly premature infants. NEC associated sepsis often cause high mortality and severe morbidity in newborns. The present paper reports a severe form of necrotizing enterocolitis in a preterm infant with *Klebsiella pneumoniae* sepsis.

Keywords: Necrotizing enterocolitis, Disseminated intravascular coagulation, Primary peritoneal drainage, Premature infants

INTRODUCTION

Necrotizing enterocolitis (NEC) is a life-threatening gastrointestinal illness among newborns particularly preterm babies or low birthweight babies. It is a multifactorial disease.[1] Neonatal sepsis is considered as a risk factor for NEC. NEC associated sepsis has high inflammatory response results in severe disease with significant immediate and late complications.[2]

CASE REPORT

A late preterm female baby of gestational age 36 weeks, second of twins was born to a G2P1L1 mother with no significant antenatal history. She was delivered by lower segment caesarean section (LSCS) with a birth weight of 2 kilogram and Apgar 9 at 1 minute. Baby was on formula feeds since birth. She developed poor activity and poor sucking on third day of life with abdominal distension and greenish nasogastric aspirate. She was then referred to our hospital for further management.

On admission to neonatal intensive care unit (NICU) baby was sick with gross abdominal distension, tachycardia and poor perfusion. Her investigations on admission revealed leukopenia, thrombocytopenia, metabolic acidosis, hypoglycemia, hyponatremia and elevated C-reactive protein (CRP). Her initial abdominal X-ray showed asymmetrically dilated bowel loops. Stool occult blood was positive. She was kept nil per oral and gastric decompression. Fluid resuscitation along with broad spectrum intravenous antibiotics and inotropes was started. In view of clinical worsening of shock, increasing abdominal distension and respiratory distress, she was ventilated and cardio respiratory support was initiated. Serial monitoring figured out increasing abdominal distension with abdominal wall edema and erythema. Repeat blood investigations disclosed severe thrombocytopenia with a platelet count of 4000/mm^3, persistent metabolic acidosis and increasing CRP. Her initial blood culture showed growth of *Klebsiella pneumonia* and meropenem injection was added to the treatment according to the sensitivity pattern. Baby was being provided with parenteral nutrition. Sequential abdominal X rays showed fixed bowel loop with suggestive signs of peritonitis. In addition, ultrasound abdomen marked multiple prominent bowel loops with no appreciable peristalsis and ascites with echogenic debris.

Immediate laparotomy under high risk was planned and discussed with parents, however deferred as no consent for surgery was obtained from caregivers. She also developed

features of disseminated intravascular coagulation (DIC) on day 5 of life with prolonged prothrombin time and international normalized ratio (PT-INR) and abnormal activated partial thromboplastin time (APTT). Hence baby received multiple fresh frozen plasma and platelet transfusions. Computed tomography (CT) abdomen taken on day 6 showed pneumoperitoneum confirmed bowel perforation (Figure 1). As laparotomy was not feasible due to lack of consent, a corrugated drain was inserted initially over left flank as a temporalizing procedure on day 7 of life and cloudy peritoneal fluid was drained which grew *Klebsiella pneumoniae* on culture. Baby started to improve gradually after peritoneal drainage, but abdominal distension and high inflammatory markers persisted. After obtaining parents' consent on day 9, laparotomy was done. Laparotomy pointed out ischemic enteritis with colonic perforation at transverse colon near sigmoid flexure and peritonitis. Perforation was repaired and colostomy was done proximal to the perforation site. Baby improved clinically after laparotomy. She was extubated on second post-operative day. Nil per orally was continued for few more days. Enteral feed was started after reappearance of bowel sounds and improved to full feeds slowly. Thrombocytopenia and coagulopathy resolved with treatment. IV antibiotics were given for a total period of 21 days. Repeat blood culture was found to be sterile. Cerebrospinal fluid (CSF) analysis ruled out meningitis.

She was later discharged on day 25th of life on breast feed with functioning colostomy.

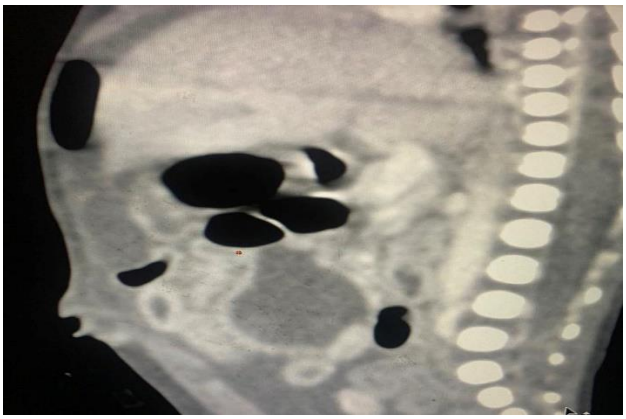

Figure 1: CT abdomen sagittal view showing pneumoperitoneum suggestive of bowel perforation.

DISCUSSION

NEC affects 10-15% of preterm who weigh less than 1500 g at birth.[3] The overall mortality rate of NEC in newborns is as high as 20-40%, and 50% mortality precisely for those who require surgical intervention.[4] To boot, of those who survive, 25% develop long term sequelae. Even though NEC survival rate improves over time, still high mortality and morbidity are associated with babies with advanced NEC, who require surgical intervention. Early diagnosis and prompt treatment are essential to improve outcome of NEC. The primary and most promising method of reducing morbidity and mortality lies in NEC prevention.

NEC occurs in preterm during the first few weeks of life. The reported median age of onset is one to three days in term infants, but it can appear as late as age 1 month also.[5] The exact etiology is unknown.[6] Research suggests that it is multifactorial. Prematurity and low birth weight are the main risk factors, in which the contributing factors are immaturity of gastrointestinal system, the intestinal barrier function and immune defenses. Notably, anaemia, red blood cell transfusions and formula feeding have been associated with NEC. Therewithal, gut bacterial dysbiosis has also been proposed as one of the main risk factors for the development of NEC.[7] Perinatal asphyxia leading to intestinal hypoxia and ischemia could be another reason for NEC in term newborns. Bunch of cases in epidemics suggest an infectious etiology such as specific bacteria, viruses and fungi. *Klebsiella* species have been described in NEC outbreaks with nosocomial origin.[8]

Inflammation of the intestines leading to bacterial invasion and intestinal necrosis contribute to the pathophysiology of NEC.[9] This leads to perforation ultimately, which may be either micro-perforation or a frank perforation. Gastrointestinal involvement may be unifocal, multifocal or pan intestinal.

Early signs and symptoms of NEC are nonspecific. A high index of suspicion is crucial for the diagnosis of NEC. Poor feeding, vomiting, feed intolerance, lethargy, abdominal distension are the initial manifestations of NEC observed so far. Behind time, apnea, abdominal tenderness, abdominal wall erythema, blood in stool can occur. The classic triad of NEC consists of abdominal distension, bloody stool and pneumatosis intestinalis. If the disease progresses unrecognized, intestinal perforation, sepsis, disseminated intravascular coagulation, shock and multi organ failure ensue.

It was in 1978 the first classification system for NEC was released. It was proposed by Bell and colleagues.[10] According to Bell staging NEC is classified into 3 stages. This is considered as the most commonly utilized case definition for NEC worldwide. Bells staging criteria was modified in 1986 by Walsh and to guide therapeutic decisions based on the severity of illness.[11]

Newer scoring criteria or diagnostic definitions like Vermont oxford Network (VON) definition, Center for Disease control and Prevention (CDC) definition, gestational age specific case definition of NEC (UK) have been proposed to classify NEC, however limited studies have compared the diagnostic validity of these definitions against a gold standard diagnosis of NEC.[12-14]

Abdominal radiography remains the main stay of diagnosis.[15] Supine X-ray, if there is a suspected perforation, cross table lateral or left lateral decubitus X-rays have been used to diagnosis NEC. Serial X-rays can

be done depending upon the clinical course as well as disease progression. X rays can show dilated bowel loops, thickened bowel walls, fixed bowel loop and absent bowel gas. Pneumatosis intestinalis, which is nothing but air in bowel wall is pathognomonic of NEC. Portal venous gas is a late sign. Abdominal free air is suggestive of pneumoperitoneum. Disease severity can be assessed using Duke abdominal assessment scale score of X rays which has values ranging from 0 (normal gas pattern) to 10 (pneumoperitoneum).[16,17]

Ultrasound seems to be an alternative to current standard usage of radiography. Ultrasound is a non-invasive, easily available, and frequently usable bedside investigation, albeit plain radiology remains the gold standard imaging modality for diagnosing NEC. It offers some potential advantages over plain X-ray films as it can depict bowel wall thickness and echogenicity, free and focal fluid collections, peristalsis, and the presence or absence of bowel wall perfusion using Doppler imaging.[18,19] To demonstrate pneumatosis or a site of perforation computed tomography (CT) scanning may be used.

Early treatment includes bowel rest, nasogastric decompression of dilated bowels, intravenous antibiotics, fluids and parenteral nutrition by keeping the baby nil per orally.[20] Duration of treatment depends on clinical condition of baby. Breast milk feeding, restrictive use of antibiotics, supplementation with probiotics and standardized feeding protocols (SFPs) are recommended to reduce NEC.[21]

When medical management fails or the condition of the baby deteriorates surgical intervention is necessary instantly. Nam et al mentions that pneumoperitoneum, clinical deterioration and abdominal mass are the indications for surgery in the acute phase of NEC.[22] The most frequently used surgical strategies for perforated NEC are laparotomy and primary peritoneal drainage (PPD). Resection of the involved intestine warrants enterostomy, primary anastomosis [resection and anastomosis (RA)] or delayed anastomosis in infants undergoing laparotomy. Primary anastomosis is not generally advocated because of the risk of complications like ischemia at the anastomosis site. Peritoneal drain is used in sick and unstable babies or extreme preterm who are not supposed to tolerate the surgery. Peritoneal drain can be inserted in neonatal ICU under local anaesthesia. It may be followed by subsequent laparotomy.

Primary peritoneal drainage was introduced for the first time by Ein and colleagues. It is described as an interval procedure for the treatment of neonates with very low birth weight babies who might not tolerate traditional laparotomy.[23] Presently many surgeons recommend PPD as the initial treatment in extremely LBW infants with perforated NEC to allow resuscitation and stabilisation before definitive laparotomy.[4] Nevertheless, some reports do not see advantages of PPD over laparotomy. On top of that, a meta-analysis of three prospective observational studies and 2 randomised controlled trials (RCTs) showed a significant excess mortality of 55% associated with PPD.[24] Few other studies bring out no significant benefits or harms of PPD over laparotomy.[25] Thus, controversies exist in performing PPD for stabilisation before laparotomy.[2] All in all, optimal surgical procedure must be decided upon clinical condition of individual patient. Researches are ongoing on the role of Toll-like receptor 4 (TLR4) signalling within the intestinal epithelium, intestinal stem cells, modulation of the genetics and intestinal microbiome.[26]

There are many complications which can arise as a sequalae in necrotizing enterocolitis survivors. These include recurrent episodes of necrotizing enterocolitis, development of intestinal strictures, short bowel syndrome, intestinal failure, parenteral nutrition-related complications, and neurodevelopmental disabilities.

In our case we opted for peritoneal drainage first as relatives were not willing for laparotomy. *Klebsiella pneumoniae* was isolated from blood and peritoneal fluid cultures of our baby. We report a more serious form of NEC with *Klebsiella pneumoniae* sepsis and severe thrombocytopenia and DIC. It is supported by the articles which states that the onset of NEC in the patients with *Klebsiella* sepsis is earlier, more rapid and more severe than usual with severe thrombocytopenia.[27]

CONCLUSION

NEC continues to be one of the most fulminating diseases affecting premature infants. The main challenge in the management of this disease is an early diagnosis, which can reduce mortality and morbidity rate. NEC with *Klebsiella pneumoniae* sepsis remains a disease of high morbidity and mortality with adverse long-term outcomes.

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