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Case Report

Necrotizing Enterocolitis and Anasarca: Unusual Presentation of Multisystem Inflammatory Syndrome in Neonates – A Case Report

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Abstract

Multisystem inflammatory syndrome in neonates (MIS-N) is a rare complication of COVID-19, characterized by immune dysregulation leading to various systemic manifestations. We present a case of a preterm neonate with MIS-N who developed necrotizing enterocolitis (NEC) and anasarca. Despite initial challenges in diagnosis, MIS-N was suspected based on clinical presentation and confirmed by laboratory findings, including elevated inflammatory markers and positive SARS-CoV-2 antibodies in the infant and the mother. Management involved immunomodulatory therapy with IVIG and methylprednisolone, resulting in clinical improvement. This case underscores the importance of considering MIS-N in symptomatic neonates born to mothers with a history of COVID-19, particularly in the post-pandemic era.

Introduction

COVID-19 is a viral respiratory infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), capable of infecting individuals of all ages. SARS-CoV-2 infections in neonates appear to be less common, likely because neonatal nasal epithelium expresses fewer SARS-CoV-2 entry receptors compared to adults.[1] Neonatal cases primarily stem from horizontal transmission within familial clusters, although isolated instances of maternal-fetal transmission have been documented.[2] An expanding body of literature reports critically ill children with SARS-CoV-2 infection developing a severe inflammatory condition known as multisystem inflammatory syndrome in children (MIS-C) due to immune dysregulation post-infection.[3] MIS-C is a significant COVID-19-related complication affecting neonates and infants as well. Multisystem inflammatory syndrome in neonates (MIS-N), unlike MIS-C, is thought to result from antibodies passed from the mother to the fetus through the placenta or from antibodies developing in the neonate after acquiring SARS-CoV-2 horizontally.[4] Pawar et al have proposed criteria for defining cases of MIS-N.[5] Common organ involvement in MIS-N encompasses cardiovascular dysfunctions, respiratory distress, gastrointestinal symptoms, neurological impairment, mucocutaneous abnormalities, and acute kidney injury.[6] NEC is a severe multifactorial disease caused by interactions between immaturity, mucosal injury, and bacterial dysbiosis, leading to a dysregulated host response. It has significant long- and short-term consequences. Early diagnosis, which relies on high suspicion and careful clinical and radiographic observation, is crucial for improving outcomes.[7]

We hereby present a case necrotizing enterocolitis accompanied by anasarca in a preterm neonate with MIS-N.

Case report

A 17-day-old male preterm infant was referred to our hospital with a 6-day history of feed intolerance and anasarca. The infant, born at 30 weeks of gestation weighing 1400 grams, was delivered by LSCS and cried after 30 seconds of positive pressure ventilation. The infant was placed on continuous positive airway pressure (CPAP), and a chest X-ray suggested respiratory distress syndrome (RDS). A single dose of surfactant was administered using the INSURE technique. Orogastric feeding was initiated on third day of life. The infant had multiple episodes of bilious vomiting on the 11th day of life, followed by abdominal distension and several episodes of apnoea.

At admission, the infant presented with hypothermic (35.1°C), tachycardia (HR 210 / min), tachypnea (RR 75 / min) with chest indrawing, and SpO_2 85% at room air. Systemic examination showed a distended, tense, and shiny abdomen, as well as peripheral oedema including periorbital and sacral oedema. The infant appeared irritable, with spontaneous movements of all four limbs. Initially, the clinical possibilities considered were late-onset neonatal sepsis and NEC. The infant was placed on nasal CPAP, fluids and antibiotics. Laboratory tests showed elevated total leukocyte count, thrombocytopenia, and high CRP. Abdominal x-ray revealed dilated bowel loops with mild bowel wall thickening. Abdominal ultrasound revealed increased bowel wall thickness and echogenicity, absent peristalsis, and free abdominal fluid. Cerebrospinal fluid testing was normal, and blood and urine cultures were sterile. Despite 72 hours of treatment initiation, the infant persisted with vomiting, abdominal distension, and elevated inflammatory markers. Considering temperature instability, ileus, abdominal distension, bilious vomiting, absent bowel sounds, and dilated bowel loops on abdominal radiograph, NEC stage IIA was diagnosed. Total parenteral nutrition was initiated, and standard monitoring protocols were followed.

The infant experienced progressive deterioration, necessitating the transition from CPAP to non-invasive positive pressure ventilation (NIPPV). In the context of the recent COVID-19 pandemic, we considered MIS-N. The infant tested positive for anti-SARS-COV-2 antibodies IgM and IgG. Laboratory results showed elevated serum ferritin (> 2000 micrograms / L), CRP (318 mg / L), procalcitonin (33.8 ng / mL), IL-6 (2900 pg / mL), and D-dimer (10.75 micrograms feu / mL). Echocardiography revealed no coronary vessel dilatations. These findings supported the diagnosis of MIS-N. We initiated Intravenous Immunoglobulin (IVIG) at a dose of 2 gm / kg on 33rd day of life. However, due to a poor clinical response, a pulse dose of methylprednisolone was administered along with fresh frozen plasma (FFP) therapy. After three doses of methylprednisolone, there was noticeable clinical improvement, including reduced respiratory support, decreased anasarca, and improved feeding tolerance. Methylprednisolone was stopped after five days, and oral dexamethasone was started with a tapering dosage. Repeat tests on day 5 and day 12 of steroid therapy showed decreasing inflammatory markers, and the baby achieved full feeds by the 56th day of life.

Discussion

The pathophysiology of MIS-N is not fully understood. One proposed pathway suggests that MIS-N occurs following maternal SARS-CoV-2 infection in late pregnancy, leading to the transfer of pathological autoantibodies from the pregnant mother to the fetus, even in the absence of active infection in the neonate.[8] While clinical criteria for MIS-C in children are well-defined, there is no consensus on the definition of MIS-N. MIS-N is primarily a diagnosis made by excluding other conditions. Symptoms observed in neonates diagnosed with MIS-N include cardiac involvement (67%), respiratory issues (64%), fever (52%), CNS symptoms (22%), gastrointestinal symptoms (11%), skin issues (4%), and haematological abnormalities (6%).[9]

While the development of NEC secondary to COVID infection has been documented, the potential association of NEC and anasarca with MIS-N has been rarely reported. Unlike older children with MIS-C, where gastrointestinal symptoms were the most common manifestation (87.3%), neonates with MIS-N predominantly exhibit cardiovascular dysfunction and respiratory distress.[10] In our case, the infant had NEC and anasarca. It is uncertain whether the NEC and anasarca were related to prematurity or resulted from intestinal injury triggered by the inflammatory cascade associated with the immune dysregulation seen in MIS-N.

Management of MIS-N is primarily supportive, focusing on respiratory and hemodynamic interventions. Specific therapy may include immunomodulatory treatments such as IVIG and methylprednisolone.[8] For severe or refractory cases, anakinra (IL-1 receptor antagonist) could be considered, although its safety and efficacy in MIS-N have not been established. Heparin and low-dose aspirin may be used in the presence of thrombus, particularly large intracardiac thrombi. Close follow-up with monitoring of neurodevelopment, electrocardiogram (for conduction abnormalities), and echocardiogram (to assess ventricular function and coronary dilation) is recommended for affected neonates.

Conclusion

Diagnosing MIS-N in the neonatal period poses several challenges due to the lack of uniform diagnostic criteria and overlapping symptoms. Many neonatal conditions are associated with elevated inflammatory and cardiac enzymes, potentially mimicking or co-existing with MIS-N. Maintaining a high suspicion for MIS-N in the post-COVID pandemic is crucial.

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