


Case Report

Dramatic Response of Multi-System Inflammatory Involvement (Mis-N) in Neonates Treated with IvIg and Methylprednisolone

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Introduction

Severe acute respiratory coronavirus-2 (SARS-CoV2) has shown its impending impact by causing multisystem inflammatory syndrome in children. MIS-N is an evolving entity with a skeptical presentation. Its progression is very unforeseeable and fatal. Recent studies have speculated vertical transmission of immunoglobulins (IgG) to the fetus. Along with the antibodies, some cytokines might cross the placenta and induce a systemic-inflammatory response in the newborn. Infection and subsequent hyper-inflammatory process appears to have occurred in two different individuals (i.e. infection in mother and Mis-N in neonates). It typically occurs 2-6 weeks after acute SARS-CoV-2 infection. Angiotensin-converting enzyme II (ACE2) was known to be the cell receptor for SARS-CoV. It is speculated that children were less sensitive to 2019-nCoV than adults due to the immaturity and binding ability of ACE2 in children.² Additionally, children have a higher levels of antibody against virus than adults. Furthermore, children's immune systems are still developing and may respond to pathogens differently from adult immune systems. However, it has been found that the proportion of severe and critical cases was 10.6%, 7.3%, 4.2%, 4.1%, and 3.0% for the age groups <1, 1 to 5, 6 to 10, 11 to 15, and >15 years, respectively.³ These results suggest that young children, particularly infants, were vulnerable to 2019-nCoV infection. Therefore, the mechanism for the difference in clinical manifestations between children and adults remains to be determined.

CASE-1

A preterm 36 week, 2.7 kg, was admitted in our setup on DOL-1 with increased work of breathing. On admission, child was provided with continuous positive airway pressure. But, within 12 hours, distress got increased and child was put on ventilator. Inotropic support and antibiotic cover was provided. Blood investigations were sent on DOL-2 which was near normal, then on dol-4 the blood reports got deteriorated. Platelet count got decreased with markedly raised CRP and deranged coagulation profile. Blood culture was negative. Child continued to have oxygen requirement despite full treatment and empirical antibiotics. There was a constant requirement of inotropes and high ventilatory support.

One unit of platelet concentrate and FFP was also given. Empirical antibiotics were started. Child also had complaint of polyuria and abdominal distension, for which USG was done which showed minimal ascites. 2D-ECHO was normal.

So, a COVID IgG was done in view of MIS-N, which was markedly raised i.e. >250 U/ml. Then in view of SARS, child was given IV Methylprednisolone 1mg /kg for 5 days and IvIg 1gram/kg (5gram) in a span of 2 days. Child showed drastic improvement clinically as well biochemically within 2 days. Child was gradually weaned off from ventilator to CPAP to nasal prongs.

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Citation: Ashutosh Singh Rathore, Harshita Jain, Mayur Shah, Karthik Surabhi. Dramatic Response of Multi-System Inflammatory Involvement (Mis-N) in Neonates Treated with IvIg and Methylprednisolone. Journal of Pediatrics, Perinatology and Child Health 6 (2022): 429-431.

Received: June 04, 2022

Accepted: June 12, 2022

Published: October 01, 2022

Child was then active on room air, taking & tolerating feeds and got discharged on DOL-15.

CASE-2

A preterm 32 week, 1.78 kg was admitted in our setup on DOL-1 with increased work of breathing. Child was put on ventilator.

Xray showed B/l reticulo-granular pattern. So, child was given 8ml surfactant at 4 hours of life and inotropes were given. Empirical antibiotics were started.

Blood investigations were done on dol-2 which was normal. Child was gradually weaned off and put on High flow nasal cannula.

But, during the course of treatment, child got deteriorated and was again put on ventilator. Blood reports showed raised CRP, raised total leucocyte count and decreased haemoglobin and platelet.

Blood culture was sent which was negative. Antibiotics were upgraded to meropenem, colistin and levofloxacin. One unit of PCV and FFP was given. Anti-fungal was also added since oral thrush developed.

Baby's mother was covid positive before conception, so baby's COVID IgG was sent which was raised.

Other MIS-N markers were also sent like serum ferritin - >1177, serum Pro-BNP >35000, Prolactin 38.33, D-dimer -1580. All were markedly raised. 2D-echo was normal.

So IVIg was given 1gram/kg in a span of 2 days. Patient showed drastic improvement and was weaned off within 12 hours.

Septic part was still there. So culture was sent again which showed growth. Antibiotics were upgraded and were given for 14 day. Inj MPS was also given for 5 days.

Patient improved gradually, weaned off and put on o2 via nasal prongs feed was started eventually and was taking and tolerating feeds and got discharged on DOL-26. CASE-3

A preterm 32 week old, 2.03 kg birth weight child got admitted on DOL-1 in our set up with complaint of increased work of breathing and prematurity. Child was kept on o2 via hood.

Feed was started on DOL-2 and antibiotics were started empirically. Oxygen support was omitted.

On DOL-6, child deteriorated and had 2 e/o apnea and went in shock. Inotropes were started and investigation were repeated which were suggestive of sepsis.

2D-ECHO was normal.

On DOL-9 culture report came negative and since there was no improvement, antibiotics was upgraded. Patient required ventilatory support. Due to sudden deterioration, COVID IgG was sent which was markedly raised.

So IvIg was given and Inj MPS was given with a dose of 1mg/kg for 5 days.

Child got drastically improved in one day clinically as well as biochemically.

Child was weaned off and put on CPAP and thereby nasal prongs. Feeds were gradually increased and reached full feed. Child was gaining weight and was discharged successfully (Table 1).

Table 1: Demographic and Clinical Characteristics of Three Infants with Sars-Cov-2.

PATIENT CHARACTERISTICS	PATIENT 1	PATIENT 2	PATIENT 3
Age at admission	DOL-1	DOL-1	DOL-1
Sex	Male	Male	Female
Exposure			
Contact with individual with confirmed SARS-CoV-2 infection or individual with fever and/or symptoms	No	No	Yes
Haemoglobin	Decreased	Decreased	Decreased
TLC	Raised	Raised	Raised
Platelet count	Decreased	Decreased	Decreased
CRP	Raised	Raised	Raised
Coagulation profile	Deranged	Deranged	Deranged
Polyuria	Yes	Yes	Yes
Inotropic requirement	Yes	Yes	Yes
Respiratory distress	Yes	Yes	Yes
Supplemental oxygen support	Yes	Yes	Yes
COVID IgG	250 IU		
Serum ferritin , Pro-BNP, Lactate		Raised	
Length of stay, h	15 days	26	40

Discussion

In the short case series reported here, all the mothers were asymptomatic and despite that all the babies developed MIS-N. It suggests that even asymptomatic mothers can cause MIS. Ofcourse, it is a diagnosis of exclusion as all the babies with minimal oxygen requirement had an increased demand of oxygen with sudden deterioration showing no improvement with antibiotic upgradation and ventilatory support.

We speculated that MIS-N involves not only respiratory but all other system simultaneously. However, the unusually high frequency of findings such as atrioventricular conduction abnormalities and the phenomonal response to immunomodulatory therapy with intravenous immunoglobulin (IVIg) and steroids suggests that it is a disease of immune dysregulation which requires further study.

Based on our case series, we recommend that among neonates born to mother with a history of COVID-19 or contact, neonatal MIS must be considered in the differential diagnosis after excluding common causes.

References

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