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Multisystem inflammatory syndrome in a neonate, temporally associated with prenatal exposure to SARS-COV-2: Case series

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Abstract

COVID-19 associated MIS-C like the disease has not been well described in neonates. So this study aimed to alert the neonatal community to the possibility of the multisystem inflammatory syndrome in children (MIS-C) like disease in critically ill neonates born to mothers with or without a history of SARS-CoV-2 infection or exposure. It's a retrospective study of four neonatal cases admitted in Dr. DY Patil Medical College NICU. All four cases are from different localities with sharing of common antepartum, intrapartum and postpartum period. All are preterm with meconium aspiration syndrome. All are presented on day three of life with dark red color vomiting and respiratory distress. All Babies were normal initial three days. Early treatment with IVIG and surfactant were showed rapid clinical improvement in all four cases. SARS-CoV-2 associated MIS-C like the disease has not been well described in neonates. Even though WHO defined criteria for MIS-N, that typical features may be conspicuously absent. Therefore a high index of suspicion is warranted in critically ill neonates who presented after a period of normality about three days with the above symptoms.

Keywords: multisystem inflammatory, syndrome, sars-cov-2

Introduction

In worldwide, SARS-CoV-2 infection in children accounts for about 1–8%. Almost all of them are asymptomatic or mildly symptomatic. Neonatal infection is rare and usually asymptomatic. Since April 2020, severe manifestations were seen in children. Which are presenting as Kawasaki disease-like illnesses involving multiple organs. This multisystem inflammatory syndrome in children (MIS-C) was given a name and a case definition by the Centers for Disease Control and Prevention. A case definition comparable to this was produced by the World Health Organization, with minor changes. It is debatable if this definition is acceptable for newborn situations. According to anecdotal reports, the second wave of SARS-CoV-2 has afflicted newborns in India with greater severity and a broader range of symptoms. Seizures and encephalopathy are common neurological symptoms, as are shock, coronary artery dilatation, arrhythmias, disseminated intravascular coagulation, renal difficulties, and mortality. We are reporting a case series of a neonate with a multisystem inflammatory disease that is temporally linked to prenatal exposure to SARS-CoV-2, who got admit in our NICU, Dr. DY PATIL MEDICAL COLLEGE Kolhapur, Maharashtra. All are preterm, with low birth weight. Out of which three were MAS and one is presented with encephalitis-like symptoms.

Case report

Case 1: Antenatal history was uneventful. Preterm LSCS- in the view of fetal distress with a gestational age of 36.2 weeks, male baby, cried immediately after birth with a birth weight of 1.7kg, with a history of MSL (meconium stained liquor). Was on exclusive breastfeeding for 3 days. Baby develops complaints of dark red color vomiting, respiratory distress, and lethargy on the third day of life. On examination was lethargic, HR: 167 bpm, RR: 73 /min, SPO2 85%, Acrocyanosis with a good peripheral pulse. Intubated and connected to a mechanical ventilator. Chest x-ray showed the picture of MAS (meconium aspiration syndrome). So surfactant was given and IV antibiotic started. MIS-N was suspected because of atypical presentation. Work up for MIS-N was done immediately. Spuriously Covid antibody IgG was positive and there was raised PT: 20(14), APTT: 28(28) INR: 1.6.FFP

transfusion was done immediately and further workup OF MIS-N showed, D - dimer: 7710 LDH: 2353, S.FERRITIN: 973, and CRP: 30 (significant rise). Inj IVIG and Inj LMWH were started immediately. 2D-ECHO was normal. The baby responded to the treatment and was gradually extubated from the mechanical ventilator. Meanwhile baby developed deranged LFT with total bilirubin being 23 and direct bilirubin 7.0.USG abdomen showed impacted sludge in gall bladder. Baby was started on syrup Gardenal, INJ VIT K, VIT A, VIT D, VIT E, VIT K. baby was recovered and discharged.

Case 2: Antenatal history was uneventful. A male baby with gestational age 35 weeks with birth weight 1.5 kg delivered via PTLSCS- i/v/o PIH with doppler changes. On day one of life baby was fine on off O₂ and the chest x-ray was fine. On the third day of life baby developed respiratory distress and had frequent dark red vomiting. So the baby was then mechanically ventilated and MIS-N workup was done was covid antibody IgG positive and have a high level of CRP: 48, D-DIMER: 8200, S. FERRITIN: 983, LDH: 3450. INJ IVIG, INJ LMWH was started then. Along with antibiotics such as inj colistin, inj amikacin, inj levofloxacin, inj fluconazole. 2D-ECHO was normal. The baby responded to the treatment gradually and was extubated from the mechanical ventilator. The baby was gradually brought to full feed and discharged with good weight gain.

Case 3: Antenatal history was uneventful. Preterm LSCS- in the view of fetal distress with the gestational age of 35 weeks, female baby, cried immediately after birth with a birth weight of 1.6kg, with a history of MSL (meconium stained liquor). Was on RT full feed and normal for 3 days. Baby develops complaints of dark red color vomiting, respiratory distress on the third day of life. On examination was lethargic, HR: 147, RR: 82, SPO₂ 75%, cyanosis with a good peripheral pulse. Intubated and connected to a mechanical ventilator. Chest x-ray showed the picture of MAS (meconium aspiration syndrome). So surfactant was given an IV antibiotic started. MIS-N Workup was done immediately in the view of the previous experience. Spuriously Covid antibody IgG was positive and, D- dimer: 6780 LDH: 4340, S.FERRITIN: 873, and CRP: 35 (significant rise). Inj IVIG and Inj LMWH were started immediately. There was raised PT: 21(14), APTT: 28(28) INR: 1.8.FFP transfusion done immediately. 2D-ECHO was normal. The baby responded to the treatment and was gradually extubated from the mechanical ventilator. Meanwhile baby developed deranged LFT with total

bilirubin being 18 and direct bilirubin 9.6, USG abdomen showed impacted sludge in gall bladder. Baby was started on syrup Gardenal, INJ VIT K, VIT A, VIT D, VIT E, VIT K. baby was recovered and discharged.

Case 4: Antenatal history was uneventful. A male baby with gestational age 35.4 weeks with birth weight 1.8 kg delivered via PTLSCS- i/v/o PIH with fetal distress. On the third day of life baby was fine on off O₂ and the chest x-ray was fine. On day 3 of life baby developed neonatal seizures and had frequent dark red vomiting. So the baby was put on o₂ prongs. Inj Midazolam given stat. RBS was 134 at the time of the seizure. Inj Phenobarbitone was given due to repeated episodes of seizure. Then it gets settled. Serum sodium, potassium, calcium, and ABG are within the normal limit. MIS-N workup was done, covid antibody IgG positive and have high level of CRP: 42, D-DIMER: 7402, S. FERRITIN: 1042, LDH: 2950. INJ IVIG, INJ LMWH was started then.2D-ECHO was normal. The baby responded to the treatment gradually. The infant had no further convulsions, and a neurological examination revealed normal tone as well as good suck and Moro reflexes; the baby was also well-breastfed. D-dimer and CRP normalized before discharge.

Discussion

In the second wave of this pandemic, pediatric SARS-CoV-2 infection is on the rise, particularly in the Indian subcontinent. After the first reports from the UK in late April 2020, paediatric MIS-C has been recorded all over the world. The World Health Organization, the Centers for Disease Control, and the Royal College of Paediatrics and Child Health have all proposed diagnostic criteria. MIS-C is more common in older children than classic Kawasaki disease; whether the diagnostic criteria can be applied to neonates is debatable. In newborns, especially those born prematurely, fever may be a less accurate diagnostic criterion. Our patient was experiencing neurological symptoms such as seizures and gastrointestinal symptoms including hematemesis with the normal 2D-ECHO report for all. Inflammatory indicators such as CRP, D-dimer, and lactate dehydrogenase were also elevated in MIS-C, as expected. These elevated markers, however, can overlap in unwell or septic newborns. However, our patient had IgG SARS-CoV-2 antibodies. All are preterm with low birth weight. All mothers have uneventful antenatal history, i.e neither positive for SARS-CoV-2 infection nor history of contact with any such cases. Out of 4 two have meconium aspiration syndrome.

Table 1: Shows baby details Maternal COVID-19 status Clinical presentation Covid antibodies Lab result and treatment

Case no:	Baby details	Maternal COVID-19 status	Clinical presentation	Covid antibodies	Lab result	Treatment
1	Male/36.2wks/1.7kg, Admitted On the third day of life	NIL	Hematemesis, MAS, RDS	Ig G (+) Ig M(-)	Elevated CRP,LDH,D-dimer, S. ferritin	IVIG LMWH
2	Male/35wks/1.5kg Admitted on the third day of life	NIL	Hematemesis, RDS	Ig G (+) Ig M(-)	Elevated CRP,LDH,D-dimer, S. ferritin	IVIG LMWH
3	Female/35wks/1.6kg Admitted on the third day of life	NIL	Hematemesis, MAS, RDS	Ig G (+) Ig M(-)	Elevated CRP,LDH,D-dimer,S.ferritin	IVIG LMWH
4	Male/35.4wks/1.8kg Admitted on the third day of life	NIL	Hematemesis, Seizure	Ig G (+) Ig M(-)	Elevated CRP,LDH,D-dimer, S. ferritin	IVIG LMWH

The management of neonates with possible MIS-C is evolving. No clinical trials have yet included neonates.

Expert opinion based on case reports/series is the most common basis for clinical guidelines. It's debatable whether

they're appropriate for little newborns and premature babies. While the subject is still debatable, we believe there is mounting evidence, including our own example, that neonates can acquire MIS-N as a result of covid with a normal antepartum history.

When the newborn presents with hematemesis on day 3 or 4 after the normal postnatal period of 2-3 days, a high index of clinical suspicion is recommended. Clinicians may confront clinical issues regarding suspected newborn MIS due to poor evidence on the applicability of current diagnostic criteria. IV immunoglobulin, steroids, and heparin should only be administered when absolutely necessary.

Conclusion

Multisystem inflammatory syndrome in a neonate, which is temporally linked to prenatal exposure to SARS-CoV-2, can occur in babies who have no history of SARS-CoV-2 infection. It may or may not be present in a newborn with a fever history. In neonates, there are cases of MIS-N which are not fitting in the criteria of MIS-C defined by WHO. Even though antenatal period events are uneventful, all mothers might be exposed to SARS-CoV-2 without any symptoms. This results in the placental transmission of COVID IgG to the fetus, which later presents as MIS-N in neonates. In my study, all are preterm with fetal distress. So SARS-CoV-2 might course preterm labour with fetal distress. Early institutions of IVIG and LMWH can improve the condition of the baby.

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