

Multi System Inflammatory Syndrome In Neonates (MIS-N): A Case Report

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Abstract:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy may increase the risk of stillbirth, neonatal death, preterm birth, low birth weight, fetal distress, and neonatal asphyxia. Vertical transmission of SARS-CoV-2 is under investigation. A few reports suggest the possibility of SARS-CoV-2 transmission from mothers to their neonates. The SARS-CoV-2 virus was reported as one of the rare causes of fetal inflammatory response syndrome (FIRS) and is associated with multisystem inflammatory syndrome in children (MIS-C).

Keywords: COVID-19, anti SARS-CoV-2 antibodies, multisystem inflammatory syndrome in children (MIS-C)

Introduction:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy may increase risk of stillbirth, neonatal death, preterm birth, low birth weight, fetal distress, and neonatal asphyxia.¹ The possibility of perinatal vertical transmission of SARS-CoV-2 seems very rare. A large prospective national cohort study in the UK included 66 neonates with confirmed SARS-CoV-2 infections; 17 infants were delivered to mothers known to have perinatal SARS-CoV-2 infection, and only two of them were vertically infected. The low placental expression of canonical receptors, with negligible co-transcription of angiotensin converting enzyme (ACE2) and transmembrane protease serine 2 (TMPRSS2) in placenta necessary for the virus entry, may explain this low risk for vertical transmission. The SARS-CoV-2 virus was reported as one of rare causes of fetal inflammatory response syndrome (FIRS) and is associated with multisystem inflammatory syndrome in children (MIS-C).² Here we present one case report of full term new-born infants with multisystem involvement and possible

vertical transmission, in which one had high specific immunoglobulin for SARS-CoV-2.³

Case Report:

A 38-week gestational age male infant weighing 2.7kgs delivered via normal vaginal delivery to 28year old primigravida lady. At the time of admission nasopharyngeal swab for SARS-CoV2 was obtained from mother because of mild respiratory symptoms baby was separated from mother in compliance with hospital policy and due to her mild respiratory symptoms.

Baby was transferred to NICU after 24 hours of life as mother's swab result came out to be positive for SARS-Cov2. After 24hours of life baby developed respiratory distress and was lethargic and had refusal to feed with poor cry, tone and activity.

Baby's COVID-19 RTPCR and Rapid antigen test was done which were negative. Baby's septic screen and Covid Antibody test was sent on 3rd day of life which turned out to be positive. Workup revealed leukocytopenia and lymphocytopenia. C-reactive protein was 54mg/dl and Covid antibody was reactive. D-dimer level was on higher side and

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inflammatory markers Serum ferritin and LDH level was on higher side.

The diagnosis of multi system inflammatory syndrome in neonate (MIS-N) was made. Two doses of IVIG (1g/kg/day) once a day was given and Injection Methylprednisolone (30mg/kg/day) once a day for 5days was given along with empirical antibiotics(ampicillin) was given.

Baby gradually improved after giving IVIG and Methylprednisolone and started accepting oral feeds and was successfully discharged after 15days of NICU stay.

Discussion:

In this report we have accounted for one case of COVID-19 disease during pregnancy, contributing to respiratory distress and multisystem organ involvement. This adds to the growing evidence pointing to the potentially devastating maternal and neonatal outcomes.⁴ The most frequently encountered presentation of the disease during the neonatal period is asymptomatic or mild infection and the seemingly uncomplicated course of most cases.⁵ The literature, however, indicates that a few cases need intensive care and fewer cases required invasive ventilation with extracorporeal membrane oxygenation (ECMO). Current evidence is not clear whether pregnancy-related immune modulation alters the path of the disease by suppressing the exaggerated inflammatory responses observed in this disease and correlated with a bad prognosis.⁶

An intrauterine infection is suggested when a mother tests positive for SARS-CoV-2 within the period of 14 days before birth to 2 days after birth, with the detection of the virus in the neonatal respiratory tract in the first 24 h of life, with either the persistence of swab positivity after 24 h of postnatal life or positive SARS-CoV-2 IgM in the first 7 days of life ⁷. In one report, the vertical transmission was presumed in a newborn by high specific SARS-CoV-2 immunoglobulins level obtained at 2 h of age, but all 5 RT-PCR tests on nasopharyngeal swabs were negative. Zeng et al included six mothers with reported COVID-19 disease, SARS-CoV-2 was not found in the serum or throat swab by RT-PCR in any

of their newborns, with elevated IgG concentrations in five babies, but IgM was detected in two infants.⁸ The possibility of vertical transmission in these cases is uncertain. Of note, in the second case, the mother was infected with SARS-CoV-2 in a period of 14 days before birth to more than 2 days after birth, with a positive nasopharyngeal swab for SARS-CoV-2 in the first 24 h of life of the infant, with persistently positive swabs for 15 days of postnatal life, favoring the conclusion of intrauterine transmission of SARS-CoV-2, despite the negative IgM in the first few days. In these two infants, we assume that the risk of infection during cesarean section or in the postnatal period was extremely low, due to the strict isolation steps applied immediately after delivery, which favors the suspicion of SARS-CoV-2 in utero transmission. Previous reports have not indicated maternal-fetal transmission of SARS-CoV-2, including negative checks of amniotic fluid, umbilical cord blood, vaginal swabs, and breast milk.⁹

The histomorphological features described in placentas from SARS-CoV-2-positive women are still limited to case reports or case series with no pathognomonic findings as reported by Sharps et al.¹⁰ Wong et al also recently reviewed 17 studies demonstrating evidence of SARS-CoV-2 in third and second-trimester placenta cells/tissues.¹¹ The most common finding was changes related to maternal vascular malperfusion (37.8%), including villous infarction, increased perivillous/intervillous fibrin, and decidual vasculopathy. The second most common finding was inflammation (34.7%), including features of maternal inflammatory response (subchorionitis/chorionitis and chorioamnionitis) or fetal inflammatory response (chorionic or fetal vasculitis). Fetal vascular malperfusion (FVM) accounted for 9.2% of all findings, including most frequently chorangioma (33.3%) and villous stromal-vascular karyorrhexis (33.3%), followed by delayed villous maturation, avascular villi, and fetal vascular thrombi. In their review, 2% of all placentas did not show any pathological findings. Our findings are not inconsistent with the published data.

Although none of the cases showed features of maternal malperfusion, both showed foci of chorangiosis consistent with fetal vascular malperfusion. One case showed a few intervillous hematomas, and the other showed delayed villous maturation, also a feature of FVM. Both cases also had umbilical cord abnormalities (a reduced coiling index in the first case and a short cord in the second). These findings are also consistent with a few published reports.¹² Chronic histiocytic intervillitis is one of the reported findings in placentas from SARS-CoV-2-positive women. Two cases of chronic histiocytic intervillitis have been described in each of the three published case series. However, this finding was not observed in any of our two cases.

Unfortunately, immunolocalization of the viral mRNA by in situ hybridization (ISH) and immunohistochemistry (IHC) for SARS-CoV-2 are unavailable in our institution. Eight studies included in the review by Wong *et al*¹¹ did not perform ISH, IHC, or reverse transcription-polymerase chain reaction (RT-PCR). Among the studies that performed any of the above-mentioned ancillary techniques, two showed negative RT-PCR on the examined placentas, and two showed negative ISH and IHC results.

Due to mothers' declining further testing, we performed histopathological examination of the placenta but were unable to investigate the presence of the virus in the amniotic fluid, placental tissue, or cord blood samples. Performing these studies would further clarify the pathogenesis of this illness and augment our conclusions of vertical transmission of SARS-CoV-2 virus. This report suggests the presence of multi-system inflammatory syndrome in the neonates (MIS-N) along with MIS-C, which is an established entity of COVID-19 disease among children. The second case we present supports the possibility of vertical transmission of SARS-CoV-2 with secondary multi-system involvement and inflammation. In this case SARS-CoV-2 PCR was persistently positive with liver and cardiac involvement. Having no fever throughout the course of illness suggests that neonates respond to infection with SARS-CoV-2 differently compared with children. It might be important to reevaluate the

current criteria of MIS- N to be generalizable to neonates or to develop new criteria for diagnosis of multi-system inflammatory syndrome in neonates.

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