Cavitary Lung Lesions in a Neonate: Potential Manifestation of COVID-19 related Multisystem Inflammatory Syndrome

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Abstract

Vertical transmission of the COVID-19 virus from mother to fetus seems to be uncommon, but, the immunological response of the neonates exposed to maternal infection in-utero, needs further research. The hyperinflammatory state of Multisystem inflammatory syndrome in children (MIS-C) predisposes to thromboembolic complications, including pulmonary thromboembolism (PTE). We report a neonate who had multiple cavitary lesions in lung, which we suspect could be a manifestation of MIS-N following maternal COVID-19 infection during pregnancy.

Article Category: Letters to the Editor

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Cavitary Lung Lesions in a Neonate: Potential Manifestation of COVID-19 related Multisystem Inflammatory Syndrome

To the Editor,

Vertical transmission of the COVID-19 virus from mother to fetus seems to be uncommon, but, the immunological response of the neonates exposed to maternal infection in-utero, needs further research. The hyperinflammatory state of Multisystem inflammatory syndrome in children (MIS-C) predisposes to thromboembolic complications, including pulmonary thromboembolism (PTE). We report a neonate who had multiple cavitary lesions in lung, which we suspect could be a manifestation of MIS-N following maternal COVID-19 infection during pregnancy.

Keywords: COVID-19, Neonate, thromboembolism, Pulmonary cavities, Multisystem Inflammatory syndrome

INTRODUCTION:

Among the children infected by SARS-CoV2 virus, most are asymptomatic and only few, especially infants and those with co-morbid conditions, have severe disease. However, MIS-C, is a hyperinflammatory state that predisposes to a prothrombotic coagulopathy known as thrombo-inflammation making patients prone to thromboembolic complications including Pulmonary thromboembolism (PTE)\(^1\). Winant et al\(^2\) observed segmental pulmonary emboli in patients of MIS-C on thoracic imaging and recommended to have high suspicion of embolism in these patients. There are now emerging reports of Neonatal MIS-C (MIS-N), mainly presenting with cardiac manifestations, ground glass opacities in the lungs and elevated inflammatory markers\(^3\)–\(^6\). PTE is not common among the neonatal population and could be a consequence of indwelling central lines, fluid instabilities, sepsis, liver dysfunction, congenital heart disease, occult malignancy, and systemic inflammation that leads to an imbalance between procoagulant and anticoagulant systems in critical neonates\(^7\). Here we report a rare case of a neonate born to mother with COVID 19 infection during pregnancy, who presented with respiratory distress, raised inflammatory markers and cavitary lesions in the lung, which we suspect could have resulted from thromboembolic complication of MIS-N.

CASE REPORT:

An 8-day old male born at 37weeks by Caesarean section to Primigravida mother was referred to our unit with fever, lethargy, and respiratory distress. Mother was diagnosed with SARS-CoV2 infection at 29 weeks of gestation which was mild and had received symptomatic treatment. The total leukocyte count was 31200/cu.mm with 54% neutrophils, positive CRP, raised procalcitonin, and bilateral reticulonodular opacities involving middle and upper zones of lungs on chest radiograph (Table 1, Fig 1a). The neonate was initiated on broad spectrum antibiotics and nasal prong oxygen. Real-time reverse transcription polymerase chain reaction test (RT-PCR) for SARS-CoV2 was negative. Two Blood Cultures were sterile; Cerebrospinal fluid and urine cultures were normal. The infant continued to have fever spikes along with respiratory distress and oxygen requirement. Given the maternal history of COVID infection, nonspecific radiographic findings, with all cultures being sterile, additional investigations were carried out for presence of inflammatory markers, COVID antibodies, D-Dimer levels, 2D Echocardiogram and High resolution Chest Tomography (HRCT) (Table 1, Fig 1b,c). HRCT showed multiple nodules of varying sizes, conglomerate at places noted in both lungs. Majority of the nodules showed evidence of cavitation. Upon doing an interval scan, some nodules which were solid on the earlier scan showed evidence of cavitation. Imaging findings were suggestive of septic embolization of the lungs. Ultrasonography of the abdomen and contrast enhanced CT of whole body was done. Multiorgan affection with similar cavitary lesions or any malignant focus was ruled out. In view of the lab reports suggestive of inflammatory syndrome (leucocytosis, elevated CRP and Procalcitonin, and
reactive COVID-19 antibodies) with non-resolving symptoms, a decision was taken to administer Intravenous Immunoglobulin (IVIG) at 1g/kg/day for 3 days following which the child became asymptomatic and was off oxygen support. In view of the cavitary lesions, investigation for active Tuberculosis was carried out in the neonate and the parents which were also negative. To rule out the possibility of malignancy other tumour markers like β-Human Chorionic Gonadotropin (HCG) and Alpha Feto Protein were done, which were within normal limits. Post IVIG, fever spikes subsided, distress gradually settled and neonate was discharged on breast feeds. On follow up, child is developmentally normal with adequate weight gain.

DISCUSSION:
Vertical transmission of the virus may be rare, however, placentas from infected mothers have shown thrombotic and vascular changes, which suggests that SARS-CoV2 is a highly procoagulant infection and even in absence of fetal viral infection, it can trigger an inflammatory response, leading to multiorgan damage. There are multiple case reports of neonates presenting majorly with cardiac manifestations of shock, arrhythmias, thrombosis, Persistent pulmonary hypertension, as well as respiratory failure, neurological abnormalities and hematological manifestations. All these neonates had history of exposure to maternal COVID-19 infection during pregnancy, positive SARS-CoV2 antibodies and elevated inflammatory and prothrombotic laboratory markers. Coagulation abnormalities and thromboembolic phenomenon are listed as one of potential complications of MIS-C. D-dimer levels have been stated to be the best test for evaluating hemostatic variations associated with COVID-19. Such thromboembolic phenomena are also reported among infants. In a retrospective cohort study by Whitworth et al, out of all children aged 0-21 years admitted with SARS-CoV2 infection or MIS-C, 20 patients were identified with thromboembolism with an incidence of 6.5% in MIS-C patients, out of which 3 patients had pulmonary embolism. Engert et al, reported a moderate preterm infant with petechial bleeds, intracranial haemorrhage, elevated D-dimer levels and thrombocytopenia. The authors hypothesised this to be secondary to maternal hyperinflammatory response following SARS-CoV2 infection during 2nd trimester of pregnancy. In the case series of 20 neonates, Pawar et al described one neonate with a cardiac thrombus. Mamishi et al studied the CT findings in 24 children with SARS-CoV2 infection. Atypical findings were seen in 58% of the patients which included nodular and cavitary lesions. The HRCT in our case showed nodular lesions with central cavitation. In spite of an extensive investigative work up, we could not find a causal relationship of the CT scan findings to any of the conditions that could have caused it like bacterial or fungal sepsis, tuberculosis, congenital lung anomalies or malignancy. The presence of in-utero exposure to COVID 19 virus, raised inflammatory markers and elevated D-dimer levels lead us to conclude that our case could have had PTE as a consequence of MIS-N which resulted in the rare lung lesions. However, due to lack of adequate evidence regarding its use in neonates with MIS-N, we did not give antithrombotic medications. The neonate responded to IVIG and had complete recovery of his clinical symptoms.

CONCLUSION:
MIS-N is an ever-evolving disease entity with widening scope of symptomatology. Thromboembolic complications secondary to inflammatory response after SARS-CoV2 exposure should be considered in infants and children. Diagnostic criteria and management strategies for MIS-N with thromboembolism should be developed, distinct from those currently available for children.

REFERENCES:


**Figure 1 a.**

Chest radiograph showing bilateral reticulonodular opacities in the middle and upper zones of the lungs

**Figure 1 b,c.**

HRCT Coronal and Axial view showing bilateral, multiple, nodular and cavitory lesions in the lungs

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