

Case Report

COVID-19 infected neonate presenting with cytokine storm and sepsis

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ABSTRACT

COVID-19, a clinical syndrome caused by the coronavirus (SARS-CoV-2) became a pandemic following an outbreak of viral pneumonitis, first identified in Wuhan, China. The disease manifestations vary ranging from mild upper respiratory tract infection to severe pneumonitis, acute respiratory distress syndrome (ARDS) and even death. Although most of the neonatal cases are asymptomatic, rarely, they can present with cytokine storm mimicking with similar features of sepsis. This is a case report of SARS-CoV19 positive neonate presenting with sepsis and cytokine storm, 5-day old baby born to SARS-COVID 19 positive mother presented with fever and investigations showed elevated total counts with neutrophilic predominance, thrombocytopenia suggestive of sepsis and increased inflammatory markers suggestive of cytokine storm. Blood culture was sent and baby was started on intravenous antibiotics. In view of cytokine storm intravenous dexamethasone 0.5 mg/kg/day was given intravenously for 5 days. Neonate recovered from illness after 1 week as evidenced clinically and by the fall in inflammatory markers before discharge. This report opens the possibility of having both sepsis and cytokine storm in a SARS-CoV19 positive neonate.

Keywords: COVID-19, SARS-CoV19, Neonatal sepsis, Cytokine storm

INTRODUCTION

The novel coronavirus, SARS-CoV-2, has caused a global outbreak of coronavirus disease 2019 (COVID-19), which began in Wuhan, Hubei Province, China, in December 2019, and has rapidly spread across countries. The clinical spectrum of the disease is varied ranging from mild flu-like illness to florid respiratory failure including acute respiratory distress syndrome in adults while children can present with influenza and gastroenteritis like illness. Cytokine storm can occur following the infection leading to tissue damage, multigrain involvement and even death. In COVID-19 however, it appears that the naive neonatal immune system may have afforded protection against the 'cytokine storm' experienced by adults and so the incidence in the neonatal population remains low however concern has been raised that a cytokine storm and hyperinflammation may increase the risk for poor neurodevelopmental outcomes in the neonate. This is a

case report of a 5-day-old male neonate with SARS-CoV19 infection and sepsis with cytokine storm.

CASE REPORT

Five day old term baby with birth weight of 3.75kg, delivered via Caesarean section to a COVID positive mother in an external care centre. Rooming in and exclusive breast feeding was practiced with proper precautions. Baby later developed fever and irritability. In view of protocol for sending nasopharyngeal and oral swab for SARS-CoV19 of any infant and child having primary contact, same was sent along with sepsis workup.

Reports showed leukocytosis with neutrophilic predominance and thrombocytopenia with elevated c reactive protein and procalcitonin suggestive of sepsis. Baby was started on intravenous antibiotics piperacillin 100 mg/kg/dose twice daily and injection amikacin 15 mg/kg/day for sepsis as it was more common for this age

and treatable. Baby turned out to be SARS-COV 2 positive on day 6 of life and was referred to our designated covid center for further management.

At admission baby was afebrile, vitals were stable and saturation was maintaining on all four limbs. Vitals and temperature were monitored sixth hourly and daily weight checking was done. Baby had two episodes of fever after one day of admission of the range 100 to 101°F. No bleeding manifestations for the neonate in spite of low platelet count. Chest x-ray was taken and was within normal limits. Rooming in was practiced since the neonate was clinically stable and was exclusively breastfed by mother with adequate precautions. Repeat investigations were sent for the neonate on 2nd day of admission which showed features

suggestive of infection leukocytosis, thrombocytopenia, elevated C reactive protein and procalcitonin which pointed towards sepsis and the neonate was on intravenous antibiotics for the same. Inflammatory markers D dimer, serum ferritin, LDH, interleukin 6 were elevated for the child correlating with cytokine storm. Intravenous dexamethasone 0.6 mg/kg/day was added on day 3 of admission in view of cytokine storm. Intravenous dexamethasone was given for 5 days along with antibiotics for sepsis. Baby was asymptomatic throughout. No signs of respiratory distress or desaturation was present. Repeat investigations were sent which showed improving platelet counts, C-reactive protein and procalcitonin in normal range with decreasing levels of inflammatory markers. Clinically baby was active and taking feeds well.

Table 1: Investigations

Variables	Day 5	Day 6	Day 8	Day 10	Day 12
Total count	17,200	39,200	20,300	13,100	15,000
N/L	67/14	82/14	64/27	62/32	55/42
Platelets	218,000	17,000	14,000	64,000	360,000
Hb (g/dL)	17	15	13.7	14	14.2
CRP (mg/L)	1	116	87	31	5.78
Procalcitonin (ng/mL)	-	90	-	58	0.66
S. Ferritin (ng/mL)	-	107	720	689	820
D-dimer (mcg/mL)	-	5	-	2	
LDH (U/L)	-	524	613	600	461
IL-6 (pg/mL)	-	21.8	-	13.55	6



Figure 1: chest xray

Repeat swab for SARS-CoV19 was done for the neonate and turned out to be negative. Baby was discharged home

on day 14 of life with discharge weight of 3.7 kg after proper counselling about the breast feeding and safety precautions and advised for further follow-up to next weeks.

DISCUSSION

SARS-CoV2 infection is on the rise in pediatric population and infection in neonates have also been reported. Although the COVID-19 can affect all age groups, the disease is usually milder in children than in adults, usually accompanied by non-specific symptoms, especially in neonates. This case report is about a covid positive neonate with sepsis and cytokine storm which is a rare occurrence.

Children infected with SARS-CoV 2 usually have contact with a positive case. In neonates' reports have shown the possibility of vertical transmission. The mean incubation period is 5 days with a range of two to fourteen days.^{1,2} The clinical presentation of COVID-19 in children and neonate can range from asymptomatic infection to severe respiratory distress. Common clinical symptoms include fever, fatigue and dry cough. Some patients can have upper respiratory manifestations like nasal obstruction, nasal discharge and sore throat, while others have gastrointestinal symptoms mainly abdominal discomfort, vomiting, abdominal pain, and diarrhea.³

COVID-19 infection is accompanied by an aggressive inflammatory response resulting in the release of a large amount of pro-inflammatory cytokines like IL-6, IL-1, TNF- α , and interferon known as “cytokine storm”.⁴ This increase in interferon resulting in influx of various immune cells resulting from destabilization of endothelial cell to cell interactions, damage of vascular barrier, capillary damage, diffuse alveolar damage, multiorgan failure, and ultimately death. Cytokine storm is responsible for acute lung injury or its more severe form ARDS.⁵ The cytokine storm correlated directly with lung injury, multi-organ failure, and unfavorable prognosis of severe COVID-19. The early recognition of cytokine storm and the prompt treatment can lead to better outcome.⁴

Neonatal sepsis is a serious health issue and is often associated with a high mortality rate. Early diagnosis and implementation of appropriate antibiotic therapy has a crucial role in improving the survival rate of infants with sepsis. Though the “gold standard” for a diagnosis of the systemic infection is the isolation of pathogens from peripheral blood, but the sensitivity of this method is low and thus, a diagnosis of sepsis cannot be excluded even when these results are negative.⁶

Diagnostic markers like C reactive protein, procalcitonin, IL6, IL8, CD11b, and CD64 are early sensitive markers of neonatal sepsis.⁷ In COVID-19 infection C-reactive protein and erythrocyte sedimentation rate are usually increased while procalcitonin levels are normal and the elevation of procalcitonin usually indicates a secondary bacterial infection. Lactate dehydrogenase, ferritin, D-dimer, and creatine kinase elevation is usually associated with severe COVID-19 infection.⁴

Therapeutic options for COVID-19 include steroids, intravenous immunoglobulin, selective cytokine blockade (e.g., anakinra or tocilizumab), Remdesivir, hydroxychloroquine and Janus kinase inhibition.⁸ Tocilizumab and other anti-interleukin-6 (anti-IL6) monoclonal antibodies have been proposed as potential treatment options for patients with COVID-19-related cytokine storm (COVID19-CS) but not much studies are available to show their use in neonates. The randomized evaluation of COVID-19 Therapy (recovery) trial, randomized, open-label trial in hospitalized patients with COVID-19, showed that the mortality rate was reduced in patients who received dexamethasone than among those who received the standard of care.⁹ Several studies have demonstrated the benefit of using low-dose steroids early in the course of infection, including more rapid resolution of hypoxia, less need for mechanical ventilation, fewer ICU transfers, and shorter duration of hospital stay.¹⁰

For this COVID positive neonate with sepsis and cytokine storm low dose steroids under antibiotic coverage was the logical approach.

CONCLUSION

In neonates various presentations of COVID19 infection have to be kept in mind along with the possibility of coinfection leading to sepsis. Timely diagnosis of the infection and intervention is necessary to prevent the various complications. In our case timely administration of steroids for tackling cytokine storm under adequate antibiotic coverage played the crucial role in recovery.

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REFERENCES

1. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, Zhou W. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr.* 2020;174(7):722-5.
2. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during pregnancy and possible vertical transmission. *Am J Perinatol.* 2020;37(08):861-5.
3. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: what neonatologist needs to know. *J Med Virol.* 2020;92(6):564-7.
4. Ragab D, Salah Eldin H, Taeimah M, Khattar R, Salem R. The COVID-19 Cytokine Storm; What We Know So Far. *Front Immunol.* 2020;11:1446.
5. Shimizu M. Clinical features of cytokine storm syndrome. In: Cron R, Behrens E editors. *Cytokine Storm Syndrome*. Cham: Springer. 2019;31-42.
6. Khaertynov S, Boichuk SV, Khaiboullina SF, Anokhin VA, Andreeva AA, Lombardi VC et al. Comparative Assessment of Cytokine Pattern in Early and Late Onset of Neonatal Sepsis. *J Immunol res.* 2017;8601063:8.
7. Ng PC. Diagnostic markers of infection in neonates, *Archives of Disease in Childhood-Fetal and Neonatal Edition.* 2004;89:F229-35.
8. Martinez MA. Compounds with therapeutic potential against novel respiratory 2019 coronavirus. *Antimicrob. Agents Chemother.* 2020;64(5):e00399-20.
9. Recovery Collaborative Group, Horby P, Lim WS. Dexamethasone in hospitalized patients with COVID-19-preliminary report. *N Engl J Med.* 2020;384(8):693-704.

10. Wang Y, Jiang W, He Q. A retrospective cohort study of methylprednisolone therapy in severe patients with COVID-19 pneumonia. *Signal Transduct Target Ther.* 2020;5(1):57.

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