

Management of an Early Onset Sepsis with COVID19 in a Premature Neonate - A Case Report

Mahbod Kaveh

Tehran University of Medical Sciences

seyyed Mohsen sadatinejad (✉ sadatinejad71@gmail.com)

Tehran University of Medical Sciences School of Medicine <https://orcid.org/0000-0002-0456-1644>

Case report

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Abstract

Background: neonates appear to be less affected by COVID-19 than adults. The overall challenge has been for all medical specialties, including neonatal intensive care. Unfortunately, current knowledge about severe acute respiratory distress syndrome of coronavirus 2 (SARS-CoV-2) infection is limited.

Case presentation: In this report, we present an ill premature neonate who were born from mother with negative nasopharyngeal swab test for SARS-COV-2. On the 5th day of life, baby developed respiratory distress. Nasopharyngeal swab test for SARS-COV-2 was positive. Intubation and intratracheal surfactant was implemented. Patient was treated with Intravenous immunoglobulin and corticosteroid over a period of 14 days.

Conclusion: The basis of treatment in neonatal covid19 is supportive care. Some studies have treated infants with various drugs such as Hydroxychloroquine, Favipiravir, and Remdesivir. In our case, we used corticosteroids and IVIg to treat a 5-day-old baby. We got good results after 2 weeks of treatment with dexamethasone 0.3 mg / kg per day and 2 g / kg IVIg (in three divided doses). It seems that these treatments, along with adjuvant ventilation and the use of endotracheal surfactants, can improve the patient's general condition.

Background

According to scientific reports (at the time of writing), neonates appear to be less affected by COVID-19 than adults (1). The overall challenge has been for all medical specialties, including neonatal intensive care. Unfortunately, current knowledge about severe acute respiratory distress syndrome of coronavirus 2 (SARS-CoV-2) infection is limited. Based on studies and case series, most of newborn with this infection have an asymptomatic or mild illness, but a small percentage of patients require neonatal intensive care unit (NICU). Due to the lack of a global guideline at the beginning of the epidemic, many of these infected infants were admitted to the NICU, but as the experience of health workers gradually increased, several local guidelines were introduced. But in some cases, we have to take additional therapies to improve the babies. In the next section, we introduce an infant with COVID-19 infection in Iran. The baby's parents completed a written consent form regarding the patient's report.

Case Presentation

A preterm (gestational age = 34 weeks + 3days) infant boy was born via caesarian section on October 13, 2020, in Tehran Iran. His Apgar scores were 9 and 10 in 1 and 5 minute after birth, respectively. Moreover, the weight after birth was 1610 grams. His 45-years-old mother had 3 previous abortions (one in 8 weeks of gestational age, another one aborted medically due to Down syndrome in 18 weeks of gestational age and the last in 16 weeks of gestational age due to PPROM at 2015) and this pregnancy (gravid 4) was in the result of donated egg and IVF. She had no signs and symptoms since 14 days before delivery (also 14 days after delivery) and had negative nasopharyngeal swab test for SARS-COV-2 (by RT-PCR assay).

At first, the baby was well but gradually became ill during the first day of his life. He got mild respiratory distress and sometimes needed oxygen hood, therefore the patient was transferred to NICU of Bahrami hospital. Laboratory tests and imaging (Fig. 1A) was performed and antibiotic therapy was started (Ampicillin + Cefotaxime).. The baby's respiratory distress gradually improved from the second day of birth and did not need oxygen, and low-volume feeding began.

With increasing daily feeding volume, the baby developed respiratory distress and mottling on the fifth day of his life again. Subsequently, he was intubated due to progressive respiratory condition. After intubation and supportive cares, suddenly patient had status seizures that was not controlled with one loading dose of Levetiracetam and two loading doses of Phenobarbital infusion. Finally one Phenytoin loading dose infusion suppressed seizure clinically. Again Lab tests was performed and antibiotics were leveled up (Vancomycin + Meropenem). Patient had hypokalemia, hypocalcaemia, respiratory acidosis, lymphopenia, elevated LDH, thrombocytopenia and elevated INR (Table1). FFP and platelet was transfused and patient treated with more potassium and calcium supplementations. Chest X-ray showed a diffuse opacities in both lungs (Fig. 1B). He was injected by surfactant (4 cc Crossruff ®) twice through endotracheal tube. Therefore baby improved somewhat due to early intervention and ventilation support.

Table 1
laboratory test on 1st and 5th day of life

Lab tests	1st day	5th day
WBC count/mm ³	9.9×10 ³	5.8×10 ³
Lymphocyte count/mm ³	2.17×10 ³	1.04×10 ³
Hemoglobin gr/dL	16	13.2
platelet count/ mm ³	157×10 ³	40×10 ³
CRP, mg/dl	4	3
Potassium, mEq/L	3.6	2.6
Calcium, mg/dl	8.1	6.3
LDH,IU/L	888	727
AST(U/L)	-	49
ALT (U/L)	-	16
PT, sec	-	16.9
INR	-	1.5
PTT, sec	-	45
Arterial Blood gas		
PH	7.27	7.16
PCO ₂ , mmHg	39	56
HCO ₃ , mEq/L	17.7	19.7
BE, mEq/L	-3	-7

Considering the Covid19 pandemic, nasopharyngeal swab was sampled for SARS-COV-2 that the result was positive thus we isolated him in a separate room. We also implemented strict protective protocols for his nurses. On the next day, sudden severe respiratory distress occurred and chest tube was inserted in regard of pneumothorax. Chest ultrasonography reported mild pleural effusion.

The patient was treated with daily oral Sildenafil due to increased pulmonary artery hypertension (according to echocardiography). Lumbar puncture showed normal values and negative CSF culture so bacterial meningitis was ruled out. Both blood and urine culture tests results was negative. During the following weeks, according to neurological consultation, Phenytoin and Phenobarbital was discontinued but maintenance treatment with Levetiracetam was continued. His brain ultrasonography was normal.

Infectious disease specialist suggested treatment with corticosteroid and IVIG for Covid19 disease, so we treated him with Dexamethasone 0.3mg/kg/day interavenously (twice a day) for following 14 days and IVIG for 3 days(A total of 6 grams). After 4 days of Sildenafil treatment (age: 10 days old), echocardiography reported normal pulmonary artery pressure. Repeated Chest X-ray had better aeration and some opacities was diminished (Fig. 1C).

During the following days, ventilator settings were reduced and we weaned the patient; then, he underwent NIPPV therapy and after 3 day we removed the chest tube (age: 19 days old). We repeated nasopharyngeal swab test for SARS-COV-2 that the result was negative. Serologic lab test result was negative (IgM an IgG against SARS-COV-2). Gradually we tapered Dexamethasone over 5 days. Then little by little, the patient began to be fed with breast milk. Finally patient discharged from hospital at age 30 days old. At age 28 days old, patient had ROP, stage I in Zone III. In follow up, ROP examination had normal report. Also ABR test was normal. at the present, he has a normal neurologic state, normal EEG and normal brain ultrasonography after 6 months and antiepileptic therapy(Levetiracetam) is tapering.

Discussion And Conclusions

There is no consensus on the vertical transmission of Covid19. Some studies have founded mother-to-child transmission of covid19 impossible. Furthermore, some studies claim that vertical transmission is possible(2). In our case, mother had no signs and symptoms of infection and his nasopharyngeal swab test was negative. Although there is some report of possible vertical transmission of coivd19 infection from mother that they had history of disease in 6 weeks before delivery (3). Also with epidemic condition of covid19, we could not exclude the transmission of covid19 from asymptomatic carrier mother to fetus.

There was several studies that reported diagnosis and management of covid19 early sepsis in neonates. Zeng et al in China reported that covid19 presented clinically in 9 percent of neonate as early-onset sepsis(4).Zhu et al. suggested that SARS-COV-2 in neonate can cause respiratory distress, thrombocytopenia or abnormalities in liver function tests or maybe death on neonates (2) in our study, newborn had respiratory distress, lymphopenia, elevated LDH, hypocalcaemia, hypokalemia, thrombocytopenia and elevated INR at 5th day of life. CRP level did not rise. Saeedi et al showed in infants, unlike adults, elevated inflammatory markers are less common, CRP does not increase in neonates, and leukopenia and lymphopenia are less common(5).Serology test (IgM and IgG against SARS-COV-2) was negative. It has been reported that a significant proportion of neonates with positive RT-PCR results had negative antibody tests, maybe due to host factors that effect on the immune response to SARS-CoV-2 (6)

In our case, radiographic findings were nonspecific, also due to instability of the patient, we were not able to get chest CT scan (computed tomography). Some studies showed that radiographic findings in neonates could be normal and may be show thickened lung texture, mild pulmonary infection, ground glass opacity, and patchy shadow under pleura, and in the chest CT scan, we may see subpleural lesions with localized inflammatory infiltration.(4, 5)

During this pandemic, there are few reports of neonatal early-onset infection of SARS-COV-2. Premature neonates maybe at risk of more severe signs and symptoms. Up to now, no valid guideline for the treatment of Covid19 disease in neonates has yet been published. Therefore, the management of Covid19 disease in neonates is usually different in each hospital(7) and in each country, medical groups have been developed guidelines for the neonatal COVID-19 disease (guideline models in Italy(8), United Kingdom(9), United State(10), Islamic Republic of Iran(11) addressed at reference). Undoubtedly, these are urgent steps against the pandemic, but due to constant updates and some controversial data, health systems have difficulty in determining the best guidelines. In addition, it is clear that our knowledge about early onset infection of SARS-COV-2 is incomplete in many ways.

In this paper, we report our experience about use of corticosteroid and IVIg in covid19 pneumonia in one neonate. There is no specific drug for COVID-19. The principle of care is supportive (including oxygen therapy, electrolyte maintenance, acid-base balance, nutritional support). Most of studies for newborns with severe acute respiratory distress syndrome implemented surfactant, nitric oxide, mechanical ventilation. According to some studies, recommended ventilation in neonates with COVID-19 is high-frequency oscillating ventilation(5). In our study, at first we used intratracheal surfactant and Assist Control (A/C) mode ventilation then Synchronized intermittent mandatory ventilation (SIMV) mode ventilation until extubation.

some studies had different experience. Sagheb reported good outcome of using Hydroxychloroquine in treatment of covid19 pneumonia in two cases(12). Kamali used Oseltamivir in a 15 day old neonate and baby discharged with good condition(13) however, there is insufficient data to suggest any benefit of these medication.(14)

Coronado et al used Hydroxychloroquine and azithromycin for a 3-week-old patient(14). Moolasart treated a 47-day-old male newborn with Favipiravir, Hydroxychloroquine, and Lopinavir/Ritonavir. He claimed that a Favipiravir-based regimen may be the drug of choice for coronavirus disease 2019 pneumonia in the newborn(15). Hopwood used Remdesivir and corticosteroid and plasma in a 4 day old neonate that had good outcome(16) in our case, we used corticosteroid and IVIG for treatment of 5 day old neonate. IVIG has been used in some pediatric with Covid19 in special conditions(17). We achieved good results after 2 week treatment of Dexametasone 0.3 mg/kg/day and 2 gr/kg IVIG (in three divided doses). It seems that this treatments, along with adjuvant ventilation and the use of intratracheal surfactants, was able to improve the patient's lung and pleural involvement.

Abbreviations

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; COVID-19: Coronavirus disease 2019; NIPPV: Non Invasive positive pressure Ventilation; CRP: C-reactive protein; CSF: Cerebrospinal fluid; LDH: Lactate dehydrogenase; NICU: Neonatal intensive care unit; RTPCR: Reverse transcription polymerase chain reaction; SARS-COV-2: Severe acute respiratory syndrome Coronavirus-2; WBC: White blood cell; CPK: creatine phosphokinase; BE: Base excess ; PT: Prothrombin time ; PTT: Partial thromboplastin time;

PCO₂ : partial pressure of carbon dioxide ; HCO₃ : Bicarbonate; PPROM: preterm premature rupture of the membranes; IVF: in vitro fertilization; IVIG: Intravenous immunoglobulin; IgM: Immunoglobulin M; IgG: Immunoglobulin G; ROP : Retinopathy of Prematurity; ABR: auditory brainstem response ; EEG: electroencephalogram

Declarations

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Authors' contributions:

Dr Kaveh is the chief manager of Bahrami hospital NICU and he managed this newborn medically. Dr sadatinejad prepared the primary draft of the manuscript and the laboratory tests and prepared pictures and tables. Again Dr Kaveh reviewed and edited the text. Both of authors read and approved the submitted manuscript and have critical roles in caring and treatment of the patients.

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All data including patients' medical records, images and laboratory data are kept in our hospital for the minimum of 10 years based on the local regulations.

Ethics approval and consent to participate :

Not applicable

Consent for publication:

Parents of the affected neonates provided us with a written consent to report on their neonate which the copies are available by request.

Competing interests :

All the authors declare no competing interest in this manuscript.

References

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama*. 2020;323(13):1239-42.
 2. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Translational pediatrics*. 2020;9(1):51.
 3. Hascoët J-M, Jellimann J-M, Hartard C, Wittwer A, Jeulin H, Franck P, et al. Case Series of COVID-19 Asymptomatic Newborns With Possible Intrapartum Transmission of SARS-CoV-2. *Frontiers in pediatrics*. 2020;8.
 4. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA pediatrics*. 2020;174(7):722-5.
 5. Saeedi M, Sangsari R, Mirnia K. COVID-19 in Neonates: A Review. *Iranian Journal of Pediatrics*. 2021;31(1).
 6. Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clinical Infectious Diseases*. 2020;71(15):778-85.
 7. De Luca D. Managing neonates with respiratory failure due to SARS-CoV-2. *The Lancet Child & Adolescent Health*. 2020;4(4):e8.
 8. Management of the newborn with suspected or confirmed SARS-CoV-2 infection. Italy: Magazine of the Italian Society of Neonatology SAfhwnn.
 9. <https://www.rcog.org.uk/globalassets/documents/guidelines/2021-02-19-coronavirus-covid-19-infection-in-pregnancy-v13.pdf> . Accessed 19 February 2021 RCoOaGCC-iipIfhpVAf.
 10. 2021 AAoPCuoC-Afhsoep-n-c-c-iAM.
 11. [https://irimc.org/Portals/0/Images/News/%20%20%20%20%20%20%20-%20%20%20%20%20%2099.pdf](https://irimc.org/Portals/0/Images/News/%20%20%20%20%20%20-%20%20%20%20%20%2099.pdf) . Accessed 27 May 2021 MoHotIRoIGdatoC-inacteAf.
 12. Sagheb S, Lamsehchi A, Jafary M, Atef-Yekta R, Sadeghi K. Two seriously ill neonates born to mothers with COVID-19 pneumonia-a case report. *Italian Journal of Pediatrics*. 2020;46(1):1-6.
 13. Kamali Aghdam M, Jafari N, Eftekhari K. Novel coronavirus in a 15-day-old neonate with clinical signs of sepsis, a case report. *Infectious Diseases*. 2020;52(6):427-9.
 14. Coronado Munoz A, Nawaratne U, McMann D, Ellsworth M, Meliones J, Boukas K. Late-onset neonatal sepsis in a patient with Covid-19. *New England Journal of Medicine*. 2020;382(19):e49.
 15. Moolasart V, Wongsawat J, Phokhom P, Thienthong V. Favipiravir-based regimen for coronavirus disease 2019 pneumonia for a 47-day-old male newborn. *SAGE open medical case reports*. 2020;8:2050313X20964046.
 16. Hopwood AJ, Jordan-Villegas A, Gutierrez LD, Cowart MC, Vega-Montalvo W, Cheung WL, et al. Severe Acute Respiratory Syndrome Coronavirus-2 Pneumonia in a Newborn Treated With Remdesivir

and Coronavirus Disease 2019 Convalescent Plasma. Journal of the Pediatric Infectious Diseases Society. 2020.

17. Yu Y, Chen P. Coronavirus disease 2019 (COVID-19) in neonates and children from China: a review. *Frontiers in pediatrics*. 2020;8:287.

Figures

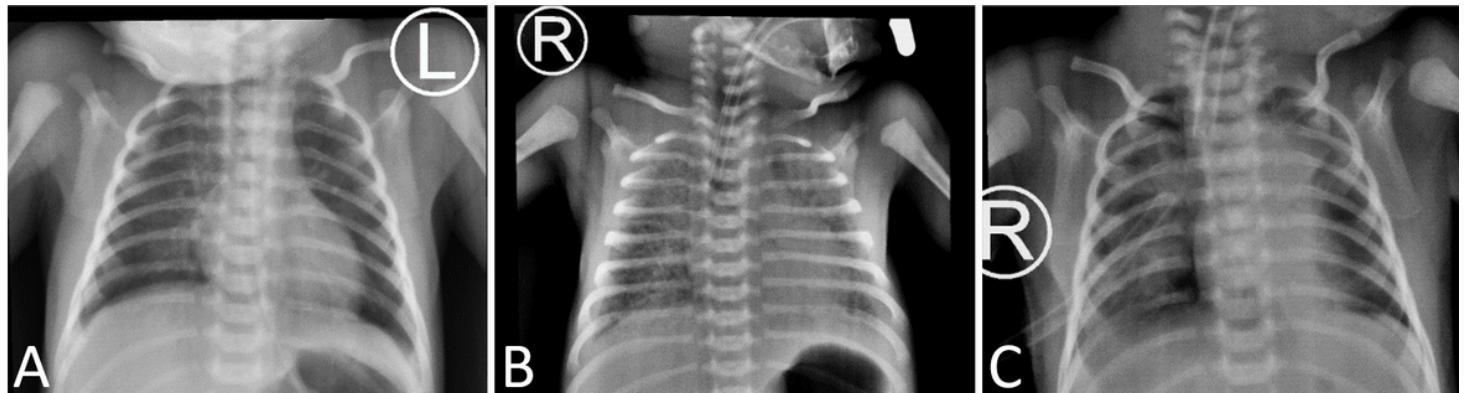


Figure 1

A: chest x-ray after NICU admission . B: chest x-ray after intubation . C : chest x-ray after 10 days