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Management of neonatal sepsis with COVID-19 infection in a premature newborn - A case report

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ARTICLE INFO

Keywords: Neonate Sepsis Pneumonia COVID-19 SARS-CoV-2 Case report

ABSTRACT

Introduction: Neonates appear to be less affected by COVID-19 than adults; yet COVID-19 has been a challenge for all medical specialties, including neonatal intensive care unit (NICU) specialists. Unfortunately, current knowledge about the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is limited. This case report explains how COVID-19 neonatal sepsis was treated with immunomodulatory agents.

Case presentation: In this case, we present a premature male newborn who was ill. He was born to a mother with a negative nasopharyngeal swab test for SARS-CoV-2. On the fifth day of life, the baby developed respiratory distress, and a nasopharyngeal swab test for SARS-CoV-2 tested positive. The baby was intubated, and intratracheal surfactant was administered. The infant was treated with intravenous immunoglobulin (IVIg) and corticosteroids for 14 days.

Patient’s demographics: Age: under 1 month, Sex: Male, Ethnicity: Iranian.

Conclusion: The basics of treatment for neonatal COVID-19 is supportive care. Some studies have treated infants with various drugs such as Hydroxychloroquine, Favipiravir, and Remdesivir; however, in our case, a 5-day-old baby boy was treated with corticosteroids and IVIg. We achieved good outcomes after 2 weeks of treatment with dexamethasone 0.3 mg/kg per day and IVIg 2 g/kg/day (for 3 days). It appears that these treatments, along with adjuvant ventilation and the administration of endotracheal surfactant, can improve a patient’s general condition.

1. Introduction

Available scientific reports, up to now, suggest that neonates appear to be less affected by Coronavirus Disease (COVID-19) than adults; yet, COVID-19 has been a challenge for all medical specialties, including the neonatal intensive care unit (NICU) specialists (Wu and McGoogan, 2020). Unfortunately, current knowledge about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is limited. Based on studies and case studies, most newborns with this infection were asymptomatic or demonstrated mild illnesses, but a small percentage of patients require admission to the neonatal intensive care unit (NICU). Due to the lack of global treatment guidelines at the beginning of the pandemic, many infected infants were admitted to the NICU. As the experience of health workers gradually increased, several local guidelines were introduced.

In some cases, supportive care and antibiotics did not work effectively; therefore, additional therapies were implemented to improve the outcomes of the babies. The next section introduces an infant boy in Iran with COVID-19. The baby’s parents signed a written informed consent form regarding this case report.

2. Case presentation

A preterm 34 weeks + 3 days infant boy was born via a cesarean section on October 13, 2020, to Iranian parents in Tehran, Iran. He was born with a birth weight of 1610 g with Apgar scores of 9 and 10 in the 1st and 5th minute after birth, respectively. His 45-year-old mother had three previous abortions: the first was aborted spontaneously at 8 weeks of gestation, the second was aborted medically at 18 weeks of gestation due to Down’s syndrome, and the third was aborted at 16 weeks of gestation due to PPROM. This pregnancy (gravid 4) resulted from IVF with a donated egg. The mother had no signs or symptoms of the COVID-19 infection fourteen (Moolasart et al., 2020) days prior to delivery nor 14 days post-delivery and tested negative via a nasopharyngeal swab for SARS-CoV-2 (by RT-PCR assay).

At first, the baby did well but gradually became ill during the first
day of life. He developed mild respiratory distress and needed supplemental oxygen via hood at times. On chest auscultation, rales were noted; therefore, the patient was transferred to the NICU of Bahrami hospital. Laboratory tests and imaging (Fig. 1A) were performed, and antibiotic therapy was started (Ampicillin + Cefotaxime). The baby's respiratory distress gradually improved on the second day of life, and he did not need supplemental oxygen. Low-volume feeding was then started.

On the fifth day of his life, while increasing daily feeding volumes, the baby developed respiratory distress, crackles via chest auscultation, mottling, and a decreased pulse pressure. He was subsequently intubated due to worsening respiratory distress and received supportive care. Suddenly, the infant began having status seizures (tonic-clonic movement + upward gaze), which could not be controlled with one loading dose of Levetiracetam and two loading doses of phenobarbital. One Phenytoin loading dose and infusion finally suppressed the seizure activity. Lab tests were again obtained, and more potent antibiotics (Vancomycin + Meropenem) were administered. The infant boy had hypokalemia, hypocalcemia, respiratory acidosis, lymphopenia, elevated LDH, thrombocytopenia, and elevated INR levels (Table 1). FFP and platelets were transfused, and the infant was treated with potassium and calcium supplements. A chest X-ray showed diffuse opacities in both lungs (Fig. 1B), and surfactant (4 mL Crossruff ®) was administered twice via endotracheal tube. The general status of the baby improved thanks to this early intervention and ventilatory support.

Since the baby boy tested positive for SARS-CoV-2, the patient was isolated in a separate room with strict protective protocols. The following day, the infant suddenly developed severe respiratory distress with a pneumothorax requiring a chest tube insertion. Chest ultrasonography was performed, showing a mild pleural effusion.

The patient was treated with daily oral Sildenafil due to increased pulmonary artery hypertension (diagnosed via echocardiography). A lumbar puncture showed normal values with a negative CSF culture; therefore, bacterial meningitis was ruled out. Both blood and urine culture tests were negative. During the next few weeks, after obtaining a normal brain ultrasound, the consulting neurologist discontinued phenytoin and phenobarbital, and maintenance treatment with Levetiracetam was continued.

Infectious disease specialists suggested treatment with corticosteroid and IVIG for Covid-19 disease, so the baby was treated with Dexamethasone 0.3mg/kg/day intravenously (twice a day) for the next 14 days and IVlg 1 g/kg/day for 3 days (for a total of 6 g). After 4 days of Sildenafil treatment (at 10 days old), echocardiography showed normal pulmonary artery pressure. A repeat Chest X-ray showed improved aeration, and some opacities were diminished (Fig. 1C).

During the following days, ventilator settings were reduced, and the baby was weaned from the ventilator. Next, NIPPV therapy was started, and the chest tube was removed after 3 days (at 19 days old). A nasopharyngeal swab test for SARS-COV-2 was repeated, which was negative. A serologic lab test result was negative (IgM and IgG against SARS-COV-2). Gradually, Dexamethasone was tapered over 5 days, and the patient began to feed with breast milk and was finally discharged from the hospital at the age of 30 days. At the age of 28 days, an eye exam showed that the baby boy had ROP stage I in Zone III; however, the ROP examination was normal at the follow-up visit, as was the ABR test. At 6 months of age, his neurologic state was normal, as well as EEG and brain ultrasound, and the antiepileptic therapy with Levetiracetam was tapered.

### Table 1

| Lab tests                      | 1st day | 5th day |
|-------------------------------|---------|---------|
| WBC count/mm³                 | 9.9 × 10⁹ | 5.8 × 10⁹ |
| Lymphocyte count/mm³          | 2.17 × 10⁹ | 1.04 × 10⁹ |
| Hemoglobin gr/dL              | 16      | 13.2    |
| platelet count/mm³            | 157 × 10⁹ | 40 × 10⁹  |
| CRP, mg/dL                    | 3.6     | 2.6     |
| Potassium, mEq/L              | 8.1     | 6.3     |
| Calcium, mg/dl                | 888     | 727     |
| LDH, IU/L                     | –       | 49      |
| AST(U/L)                      | –       | 16      |
| ALT (U/L)                     | –       | 16      |
| PT, sec                       | –       | 16.9    |
| INR                           | –       | 1.5     |
| PTT, sec                      | –       | 45      |
| Arterial Blood gas            | –       | –       |
| PH                            | 7.27    | 7.16    |
| Pco₂, mmHg                    | 39      | 56      |
| HCO₃-, mEq/l                  | 17.7    | 19.7    |
| BE, mEq/l                     | –3      | –7      |

3. Conclusions and discussion

There is still no consensus on the vertical transmission of COVID-19. Some studies have found that mother-to-child transmission of COVID-19 is impossible, whereas others claim that vertical transmission is possible (Zhu et al., 2020). In our case, the mother had no signs and symptoms of infection, and her nasopharyngeal swab test was negative. Although, some reports suggest the possible vertical transmission of COVID-19 from mothers with a history of COVID-19 in the 6 weeks before delivery (Hascöet et al., 2020). Also, considering the COVID-19 epidemic condition, disease transmission from the asymptomatic carrier mother to the fetus may not be excluded.

Several studies reported diagnosis and management of COVID-19 sepsis in neonates. Zeng et al. reported that COVID-19 presented clinically in 9% of neonates as early-onset sepsis in China (Zeng et al., 2020). Zhu et al. suggested that SARS-COV-2 in neonates can cause respiratory distress, thrombocytopenia, liver function test abnormalities, or even neonatal death (Zhu et al., 2020). In our study, newborns had respiratory distress, lymphopenia, elevated LDH, hypocalcemia, hypokalemia,
thrombocytopenia, and elevated INR on the fifth day of life. CRP level did not rise. Saeedi et al. showed that elevated inflammatory markers are less common in infants, unlike adults. They also reported that CRP does not increase in neonates, and leukopenia and lymphopenia are less common (Saeedi et al., 2021). Serology tests (IgM and IgG against SARS-COV-2) were negative. It has been reported that a significant proportion of neonates with positive RT-PCR results had negative antibody tests, possibly due to host factors that affect the immune response to SARS-CoV-2 (Guo et al., 2020).

In our case, radiographic findings were nonspecific. Moreover, we could not get a chest CT scan (computed tomography) due to the patient’s instability. Some studies showed that radiographic findings in neonates could be normal and may show lung consolidation, mild pulmonary infection, ground glass opacity, and patchy shadow under pleura. The chest CT scan may show subpleural lesions with localized inflammatory infiltration (Zeng et al., 2020; Saeedi et al., 2021).

A few reports of neonatal infection of SARS-COV-2 were published during the COVID-19 pandemic. Premature neonates may be at risk of more severe signs and symptoms. Up to now, no valid guideline has been published for the treatment of COVID-19 in neonates. Therefore, the management of COVID-19 in neonates usually varies among hospitals (De Luca, 2020). In each country, medical groups have developed guidelines for neonatal COVID-19, including Italy (Management of the newborn with COVID-19), the United Kingdom (https://www.rcog.org.uk/globalassets/documents/guidelines/2021-02-19-coronavirus-us-covid-19-infection-in-pregnancy-v13.pdf, 2021), and the Islamic Republic of Iran (Sagheb et al., 2020).

These are urgent steps against the pandemic, but health systems have difficulty determining the best guidelines due to constant updates and controversial data. In addition, our knowledge about infection with SARS-CoV-2 is undoubtedly incomplete in many ways.

This paper reports our experience using corticosteroids and IVlg in COVID-19 pneumonia in a neonate. No specific medication is approved for COVID-19; thereby, its management is principally supportive (including oxygen supplementation, electrolyte maintenance, acid-base balance, and nutritional support). Most studies for newborns with severe acute respiratory syndrome used surfactant, nitric oxide, and mechanical ventilation. According to some studies, high-frequency oscillating ventilation is recommended in neonates with COVID-19 (Saeedi et al., 2021). In our study, we first used an intratracheal surfactant and assisted control (A/C) mode ventilation, then synchronized intermittent mandatory ventilation (SIMV) mode ventilation until extubation.

Some studies reported different experiences. Sagheb reported a good outcome of using Hydroxychloroquine in treating COVID-19 pneumonia in two cases (Kamali Aghdam et al., 2020). Kamali administered Oseltamivir to a 15-day-old neonate, and the baby was discharged in good condition (Coronado Munoz et al., 2020). However, there is insufficient data to suggest the superiority of any of these medications (Moolasat et al., 2020). Coronado et al. used Hydroxychloroquine and azithromycin for a 3-week-old patient (Moolasat et al., 2020). Moolasat treated a 47-day-old male newborn with Favipiravir, Hydroxychloroquine, and Lopinavir/Ritonavir. He claimed that a Favipiravir-based regimen might be the drug of choice for COVID-19 pneumonia in newborns (Hopwood et al., 2020). Hopwood used Remdesivir, corticosteroid, and plasma exchange in a 4-day-old neonate, who recovered with a proper outcome (Hopwood et al., 2020). In our case, we used corticosteroids and IVlg to treat a 5-day-old neonate. IVlg has been used in some children with COVID-19 in special conditions (Yu and Chen, 2020). In our case, the proper outcome was achieved after 2 weeks of treatment with Dexamethasonne 0.3 mg/kg/day and 2 gm/kg/day IVlg (for three days). This treatment, along with adjunct ventilation and intratracheal surfactants, appeared to improve the patient’s lungs and pleural involvement.

### Authors’ contributions

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

### Funding

There was no funding resource.

### Availability of data and materials

Data Security: All data, including patients’ medical records, images, and laboratory data, are stored in our hospital for a minimum of 10 years based on the local regulations.

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Written informed consent was obtained from the patient’s legal guardian to publish this case report and any accompanying images. A copy of the written informed consent is available for review by the Editor-in-Chief of this journal.

### Declaration of competing interest

All the authors declare no competing interest in this manuscript.

### Acknowledgments

We would like to announce our sincere thanks to all nursing staff who have a critical role in taking care of these patients.

### Abbreviations

- ALT: Alanine aminotransferase
- AST: Aspartate aminotransferase
- ABR: Auditory brainstem response
- BE: Base excess
- COVID-19: Coronavirus disease 2019
- CPK: Creatine phosphokinase
- CRP: C-reactive protein
- CSF: Cerebrospinal fluid
- EEG: Electroencephalogram
- HCO3: Bicarbonate
- IVF: In vitro fertilization
- IVlg: Intravenous immunoglobulin
- IgM: Immunoglobulin M
- IgG: Immunoglobulin G
- LDH: Lactate dehydrogenase
- NICU: Neonatal intensive care unit
- NIPV: Non Invasive positive pressure ventilation
- PCO2: Partial pressure of carbon dioxide
- PT: Prothrombin time
- PTT: Partial thromboplastin time
- PPROM: Preterm premature rupture of the membranes
- ROP: Retinopathy of Prematurity
- RTPCR: Reverse transcription polymerase chain reaction
- SARS-COV-2: Severe acute respiratory syndrome Coronavirus-2
- WBC: White blood cells

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