Iranian Heart Journal; 2022; 23 (3)

Case Report

Two Neonates With Cyanotic Heart Disease and COVID-19

Alireza Ahmadi[1], MD; Mehdi Ghaderian[1], MD; Mohammad Reza Sabri[1], MD; Ladan Salamati[1], MD; Azadeh Esnaashari[1*], MD;

ABSTRACT

We herein describe 2 neonates with cyanotic-type congenital heart disease and COVID-19. The first case was a boy at 37 weeks of gestational age (GA) who had cyanosis (SpO_2 <90%) on the second day of the birth. He was transferred to the neonatal intensive care unit (NICU) for COVID-19 patients for infection treatment following a positive COVID-19 PCR test. Finally, he had a cardiopulmonary arrest, and cardiopulmonary resuscitation failed. The second case was a boy at 38 weeks of GA. His fetal echocardiography showed a hypoplastic right ventricle with decreased contractility, an atretic tricuspid valve, a hypoplastic pulmonary valve, and a small echogenic focus in the left ventricle. He was then diagnosed with COVID-19 and treated with Kaletra. Follow-up echocardiography showed a functioning shunt, a relieved pericardial effusion, and a normal ejection fraction. He was discharged a week later in good general condition. ***(Iranian Heart Journal 2022; 23(3): 139-143)***

KEYWORDS: Neonates, COVID-19, Cyanotic heart disease

[1] Pediatric Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, IR Iran.

*** Corresponding Author:** Azadeh Esnaashari, MD; Pediatric Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, IR Iran.
Email: a_esnaashari102@yahoo.com **Tel:** +989131038857

Received: February 10, 2021 **Accepted:** June 17, 2021

Novel coronavirus (COVID-19) is a highly contagious disease first identified in December 2019 in Wuhan, China.[1] So rapid was the initial spread of this disease that the World Health Organization (WHO) declared the infection a global pandemic.[2] Only a few reports of neonates suffering from congenital heart disease with COVID-19 exist.[3,4] Here, we describe 2 neonates suffering from cyanotic-type congenital heart disease with COVID-19 infection.

CASE I

On April 19, 2020, in a hospital near Isfahan, a boy at 37 weeks of gestational age was born by Cesarean section with a birth weight of 2450 g, a 1-minute APGAR score of 9, and a 5-minute APGAR score of 10. He had no history of resuscitation, and he was given to his mother for rooming-in. His mother was 30 years old, and he was the second child. The mother had no underlying diseases, and her screen pregnancy test for Down syndrome was positive. Accordingly, she had amniocentesis, and the karyotype result was normal. On the second day of the birth, the baby had cyanosis (SpO_2<90%). He was, therefore, admitted to the neonatal intensive care unit (NICU), where he received supportive and therapeutic care, including proper fluid therapy, oxygen therapy, and antibiotic therapy with ampicillin (50 mg/kg/dose q8h) and gentamicin (2.5 mg/kg/dose q12h). Consultation with a

pediatric cardiologist was requested. Echocardiography findings were pulmonary atresia, an atrial septal defect, a patent ductus arteriosus, and an ejection fraction of 60%. Consequently, prostaglandin E1 (PGE1) (0.01 u/kg/min) was started for him. The laboratory findings are summarized in Table 1. All the results were within the normal range for neonates.

Table 1: Primary laboratory findings

Variables	Amount
WBC	7300/µL
Hb	18.6 g/dL
PLT	222000 /µL
BUN	4
Cr	0.38
Na	141
K	4.3
Alb	3.5
Ca	10.6
ABG	
PH	7.37
PCO_2	44
HCO_3	24.6
Blood culture	Negative

A chest X-ray showed oligemia with a normal cardiothoracic ratio. On day 6 (April 26), the neonate was transferred to Chamran Hospital in Isfahan (Iran) for cardiac evaluation and intervention. On admission, he was intubated because of apnea, and mechanical ventilation was started for him. The results of the laboratory tests are listed in Table 2.

Table 2: Laboratory findings in Chamran Hospital

Variables	Amount
WBC	9400/µL
Hb	13 g/dL
PLT	297000 /µL
CRP	3+
Urea	12
Cr	0.38
BS	120
Na	142
K	4
Ca	8.5
Mg	2
ABG	
PH	7.33
PCO_2	52

The antibiotics were changed to cefotaxime and vancomycin, and PGE1 was continued. Because of his anemia, packed red blood cells (RBCs) were transfused for him. The next day, the laboratory results showed leukopenia and coagulopathy, and he was treated with fresh frozen plasma. Angiography was postponed until improvements in the sepsis. On day 4 of his admission, the neonate developed thrombocytopenia, followed by edema and ascites. The antibiotics were changed to meropenem and vancomycin, and a pharyngeal swab specimen was taken to evaluate for COVID-19 infection by the reverse transcription-polymerase chain reaction (RT-PCR) assay. The result of the assay was positive. In the BACTEC blood culture, the Gram-negative *Bacillus*, *Acinetobacter*, was grown. His parents' PCR test results were negative. Afterward, he was transferred to the NICU for COVID-19 patients to receive treatment for the infection. His condition precluded high-resolution computed tomography. On May 5, the boy suffered a cardiopulmonary arrest, and, unfortunately, cardiopulmonary resuscitation was unsuccessful.

CASE II

A boy at 38 weeks of gestational age was born on April 4, 2020, in a private hospital in Isfahan via emergent Cesarean section due to a decreased fetal heart rate. His birth weight was 2800 g; additionally, he had a 1-minute APGAR score of 9 and a 5-minute APGAR score of 10. He was the second child of his 29-year-old mother. The neonate was admitted to the NICU due to cyanosis and decreased SpO_2. In the 22nd week of her pregnancy, the mother underwent fetal echocardiography. The findings were a hypoplastic right ventricle with decreased contractility, an atretic tricuspid valve, a hypoplastic pulmonary valve, and a small echogenic focus in the left ventricle.

After the boy's admission to the NICU, consultation with a pediatric cardiologist was requested. Echocardiography findings were tricuspid atresia, a restrictive small ventricular septal defect, a hypoplastic right ventricle with normal related great arteries, mild pulmonary stenosis with small confluent pulmonary artery branches, a small atrial septal defect, and a patent ductus arteriosus. Supportive and therapeutic care, including proper fluid therapy and antibiotic therapy with ampicillin (50 mg/kg/dose q8h) and gentamicin (2.5 mg/kg/dose q12h), was started for him. His SpO_2 level ranged from 75% to 85%, and he did not need oxygen therapy or PGE1. The parents discharged the baby with personal satisfaction. Five days later, they took their baby (16 days old) to a pediatric cardiologist due to cyanosis. The boy was referred for emergent patent ductus arteriosus stenting or a Blalock–Taussig (BT) shunt operation to Chamran Heart Hospital. On physical examination, the patient, who was lethargic, had cyanosis, normal pulses, no heaves or thrills, single S1 and S2, a grade II/VI systolic murmur at the left sternal border, and an SpO_2 level ranging from 55% to 60%. Electrocardiography demonstrated a sinus rhythm with left axis deviation and posterior force.

A chest X-ray showed a normal cardiothoracic ratio and decreased pulmonary vascular markings. Hence, PGE1 (0.01 u/kg/min) was started. Additionally, antibiotic therapy (cefotaxime [50 mg/kg/dose q8h] and vancomycin [10 mg/kg/dose q6h]) was added. Afterward, he developed apnea, for which he was intubated and placed on mechanical ventilation. The laboratory findings on the first day of admission are listed in Table 3.

Table 3: Primary laboratory data

Variables	Amount
WBC	12500/µL
Hb	16.2g/dL
PLT	381000 /µL
BUN	19
Cr	0.4
Na	140
K	3.8
Bilirubin (T)	15
Bilirubin (D)	0.9
PT	15
INR	1.2
PTT	36
Ca	10
BS	110
ABG	
PH	7.32
PCO_2	61
CRP	Negative
Blood culture	Negative

Brain sonography was normal. On April 20, angiography showed that the patent ductus arteriosus was tortoise and unsuitable for stenting. Therefore, the neonate was referred to surgeons for a BT shunt operation. On April 21, a right BT shunt operation was performed on the patient. Subsequently, a continuous drip of heparin and inotropic drugs was infused, and aspirin (5 mg/kg/d) and Plavix (1 mg/kg/d) were replaced. In the PICU, after 10 days, he could not be weaned from the ventilator. Feeding was started with an OG tube. On May 2, he was extubated; nevertheless, his blood pressure was dependent on dopamine, and sometimes his SpO_2 would decline. On May 3, echocardiography revealed left ventricular systolic dysfunction (ejection fraction =53%) with a functioning BT shunt and mild pericardial effusion. Consequently, digoxin was started for the patient, and dopamine was tapered and discontinued. For antibiotic discontinuation, complete blood count, C-reactive protein (CRP), and BACTEC blood culture were investigated.

The laboratory results on May 4 were a white blood cell count of 8200 (L=54.5 and N=39.6), a hemoglobin level of 16.1, a platelet count of 260 000, an erythrocyte sedimentation rate of 2 mm/h, and CRP 3+. Accordingly, a pharyngeal swab specimen

was taken to evaluate for COVID-19 infection by RT-PCR, and the result was positive. His blood culture was negative. The patient had no cough, fever, or respiratory distress; he only received nasal oxygen (3–5 Lit/m). Then, the neonate was transferred to a pediatric COVID-19 center for more evaluation and treatment. High-resolution computed tomography was normal. He was treated with Kaletra. The PCR test was done for his parents, and the result was negative. Follow-up echocardiography showed a functioning shunt, a relieved pericardial effusion, and a normal ejection fraction. He was discharged a week later in good general condition.

DISCUSSION

The clinical course of COVID-19 could be milder in children than in adults.[5] Clinical data on COVID-19 in newborns are still very limited. On the other hand, in patients with congenital heart disease and, especially, the cyanotic type, the signs and symptoms of the disease might be confused with COVID-19.[6] Hence, when a newborn presents with decreased oxygen saturation and nonspecific signs and symptoms of sepsis, COVID-19 should be considered in the differential diagnosis. Concerning both of our patients, the result of the PCR test for their mothers was negative. In a study in Spain reporting the first case of neonatal infection due to COVID-19, the initial test for the patient was negative, while the parent's results were positive. However, after 36 hours, the second sample of the patient was positive.[7] Our presented cases our different in that their case seems to have been an instance of horizontal transmission. In a study performed in the Iranian city of Zanjan on a 15-day-old neonate with clinical signs of sepsis, the PCR test results were positive for the patient and his parents.[8] Some articles have considered pregnant women a high-risk group, but the latest data do not confirm this notion.[9,10] There is currently no information of fetal-maternal or vertical transmission.

CONCLUSIONS

The signs and symptoms of COVID-19 in neonates are variable. Therefore, in neonates with congenital heart disease and nonspecific symptoms of infection, screening for COVID-19 should be performed.

Ethical Statement: This study was approved by the Ethics Committee of Isfahan University of Medical Sciences (ethics code: IR.MUI.MED.REC.1399.386). Written informed consent was obtained from the parents of the 2 cases presented herein.

Conflict of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Organization WH. Coronavirus disease 2019 (COVID-19): situation report, 72. 2020.
2. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta bio-medica: Atenei Parmensis. 2020; 91(1):157-60.
3. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. Journal of medical virology. 2020; 92(6):564-7.
4. Mimouni F, Lakshminrusimha S, Pearlman SA, Raju T, Gallagher PG, Mendlovic J. Perinatal aspects on the covid-19 pandemic: a practical resource for perinatal–neonatal specialists. Journal of Perinatology. 2020:1-7.
5. 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.
6. Tan W, Aboulhosn J. The cardiovascular burden of coronavirus disease 2019

(COVID-19) with a focus on congenital heart disease. International Journal of Cardiology. 2020.

7. Díaz CA, Maestro ML, Pumarega MTM, Antón BF, Alonso CP, editors. First case of neonatal infection due to COVID-19 in Spain. Anales de Pediatria; 2020: Elsevier.

8. 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.

9. Dashraath P, Jeslyn WJL, Karen LMX, Min LL, Sarah L, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. American Journal of Obstetrics and Gynecology. 2020.

10. Qiao J. What are the risks of COVID-19 infection in pregnant women? The Lancet. 2020; 395(10226):760-2.