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Neonatal Sepsis as a Risk Factor Associated with Severe COVID-19: A Case Report with Clinical and Imaging Features

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Abstract

Background: It has been believed that infants are at a lower risk for the severe symptoms and complications that arise from COVID-19. This report represents details on a newborn with sepsis that has been diagnosed with COVID-19 and, unfortunately, did not survive.

Case presentation: The case was a 1-day-old female newborn, admitted to the surgical intensive care unit in Namazee Hospital, Shiraz, Iran, for a bladder exstrophy operation. She gradually started to deteriorate on the fourth day after the surgery, diagnosed with sepsis based on the results of her blood culture. Progressively, her vital signs and blood tests fell within normal ranges after being treated with broad-spectrum antibiotics. Without any fever, the neonate became severely irritable on the 16th day after her birth and hospitalization. Considering lymphopenia, high CRP, and abnormal chest x-ray, pharyngeal swab sampled for COVID 19. The newborn died from multi-organ failure on the 18th day of life. Reverse transcription-polymerase chain reaction (RT-PCR) confirmed the COVID 19 infection in the dead newborn. The parents' pharyngeal sample, however, was negative for COVID 19.

Conclusion: Growing awareness of sepsis as a risk factor for the severity of the COVID-19 infection in the neonatal period can be a form of knowledge for physicians to begin early treatment and reduce odds of mortality in this group of patients.

Key Words: Coronavirus, COVID-19, Neonate, Sepsis.

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1- INTRODUCTION

After the World Health Organization (WHO) described COVID-19 as a worldwide public health emergency in January of 2020, the first pediatric age group cases were reported from China in March 2020 (1, 2). According to the current literature, clinical features of COVID-19 in children can range from asymptomatic to severe respiratory distress. It is considered that COVID-19 in pediatrics is milder with a favorable outcome as compared to adults (3, 4). The COVID-19 is very contagious; the main route of this viral transmission is through respiratory droplets and close physical contact (5). Recently, the possibility of intrauterine transmission from mother to child during pregnancy and in the period of delivery is a concern for obstetrics and neonatologists (6).

Neonatal sepsis is divided into early-onset occurrences which are between the ages of 0 to 3 days old, or late-onset from 4 days of life or later. The cause of early-onset sepsis is an acquisition of maternal microorganisms via hematogenous, transplacental spread from an infected mother or when passing through the colonized birth canal at delivery. Late-onset sepsis is acquired from the environment; the most common organisms that have been implicated are coagulase-negative staphylococcus, staphylococcus aureus, and Escherichia coli (7, 8).

Little is known about the deficient outcomes of COVID-19 in neonates with the underlying disease. This report presents details on a newborn with late-onset sepsis that passed away from the COVID-19 infection.

2- CASE PRESENTATION

The newborn's parents were Caucasian, healthy, and non-consanguineous from Shiraz, Iran. The mother was 36 years old with a history of gestational diabetes who had been controlling her blood sugar during the pregnancy with the help of the obstetrics. She had no history of hypothyroidism, heart disease, and hypertension. She had two healthy children with no previous history of miscarriage or sibling deaths.

At 17:00 on April 4, 2020, the newborn was born at 35 weeks of gestation with a favorable Apgar score following the cesarean section procedure that took place due to the fetal intrauterine distress in Namazee hospital, Shiraz, Iran. Initial physical examination showed her birth weight of 2720 g (90th percentile), a length of 45 cm (50th to 75th percentile), and a head circumference of 32 cm (50th to 75th percentile). Her axillary temperature was 36.8˚C, with a pulse rate of 126/min, respiratory rate of 34/min, and blood pressure of 63/34 mmHg. The oxygen saturation was 95% while the patient was breathing ambient air. The neonate had a congenital disability; the urinary bladder had exstrophy and was protruded through the abdominal wall. She had no other abnormality in the pelvic bones, pelvic floor, and genitalia. Vitamin K was injected to prevent coagulopathy in the newborn.

She was transferred to the surgical intensive care unit for a bladder exstrophy operation. The newborn was given formula around 30 ml every 3 hours, and she was closely monitored. On the second day of life, she had leukocytosis with a WBC count of 21200, and the result of urinalysis revealed protein=3+, blood=3+, RBC= many, and WBC= 28-30 per high-powered field. She was treated for a suspected urinary tract infection with intravenous ampicillin and amikacin. Surgical management was performed to repair the bladder exstrophy, reconstruction of the bladder neck, and reconstruction of the abdominal wall during the third day of her life (April 7).

On April 11, the fourth day after surgery, the patient deteriorated with respiratory

acidosis with a PH of 7.3, Pa CO2 of 50 mm Hg, bicarbonate of 30 mmol/L, and pO2 of 86 mmHg. Simultaneously, the laboratory examination presented leukopenia, anemia with high CRP. She had a fever, and samples of the eye, urine, nose, throat, operation site, and blood were taken within 24 hours following deterioration. Due to respiratory distress, she was intubated and put under mechanical ventilation. After the blood culture results, amikacin was changed to vancomycin to stop the growth of staph coagulase-negative.

Respiratory support continued for 14 days of her life (18 April) when PaCO2 had decreased to 38 mm Hg, and PH became 7.42, with the O2 saturation being above 90%. Her vital signs were stable, and blood tests were within the normal ranges. It was, then, started to gradually wean off the mechanical ventilation.

On April 20, the neonate became severely irritable without any fever. A chest X-ray showed generalized patchy opacities in both lung fields with no abnormalities in the heart. The cultures of blood and other related sites were obtained again. The ultrasounds of the brain were normal. The next day on April 21, blood investigations revealed neutropenia, lymphopenia, anemia with elevated CRP levels as well as electrolyte imbalance. Due to the continuation of her irritability, cerebral fluid (CSF) samples were obtained at 17 days of age with no evidence of meningitis. Transthoracic echocardiography exhibited mild left ventricular hypertrophy with a small patent ductus arteriosus (PDA) and severe pulmonary hypertension.

Considering lymphopenia, high CRP, and abnormal chest x-ray, pharyngeal swab sampled for COVID 19.The newborn received 1gr/kg intravenous immunoglobulin daily for two days due to suspected COVID 19. **Table 1** presents the patient's laboratory investigations during the course of the hospital stay. The clinical symptoms, blood tests and imaging findings deteriorated; the newborn expired as a result of multi-organ failure on April 22. The results of blood cultures were negative, while reverse transcription-polymerase chain reaction (RT-PCR) confirmed the COVID 19 infection in the deceased newborn. Repeated neonatal chest x-rays showed patchy opacities in both lung fields with no abnormalities in heart (**Fig. 1**). After finding evidence of COVID 19 infection, the parents were tested, and the pharyngeal sample was negative COVID 19. CT scanning of the lungs was performed for preliminary screening of the mother, which showed no abnormal findings.

3- DISCUSSION

There is a limited amount of data surrounding the COVID-19 viral infection in newborns. Therefore, the exact incidence, clinical symptoms, and severity of it are still unclear. We describe a neonate with late-onset sepsis who died with COVID-19 infection while her mother had no infection with COVID-19.

Based on reviewing the available data in the public databases, the risk of severe symptoms and mortality following COVID-19 is more prevalent in patients with underlying diseases such as diabetes mellitus, cardiovascular diseases, and immunodeficiency (9-11). The present newborn developed sepsis during the hospital course; however, it appears that sepsis can impact the severity of a COVID-19 infection similar to the results of previous studies (12, 13). The role of sepsis in an inflammatory response includes the release of inflammatory cytokines such as IL-1, TNF, and IL-17 in the excessive amount, which is known as the cytokine storm, immense release of the complement and innate immune system stimulation (14). It is suggested that the patient suffering from COVID-19 with underlying sepsis burdens fails to resolve

the persistent and ongoing inflammation, immune cell dysfunction, and cytokine storm, all of which degrades the ability to clear viral infections and leads to the damage of various tissues.

Table-1: Newborn's laboratory investigations during the course of the hospital stay

Laboratory Data	Normal Value (units)	Day 2	Day 4	Day 7	Day 14	Day 17	Day 18
WBC	4000-10000 cells/mm3	212000	14200	3100	8500	1600	800
Hb	12-18 gm/dL	17.3	13	10.2	11	10	7.6
Platelet	150-450×10^3/mm^3	254000	300000	355000	450000	110000	178000
CRP	<6 mg/dL	1	NM	7	2	3	80
BUN	8-20 mg/dL	8	10	12	20	42	43
Cr	0.6-1.2 mg%	0.1	0.1	0.2	0.5	3	2
Na	136-145 (mEq/L)	146	144	139	130	115	132
K	3.5-5.5(mEq/L)	6	4.7	3.8	6	7.1	7.5
Calcium	8.6-10.3 (mg/dL)	9	NM	NM	NM	9.9	9
SGOT	<37 (1U/L)	32	NM	NM	54	58	NM
SGPT	<41 (1U/L)	36	NM	NM	39	42	NM
Mg	1.6-2.5 (mg %)	NM	NM	NM	NM	1.6	NM
Phosphorus	4.8-7.9 (mg %)	NM	NM	NM	NM	4.5	NM
Procalcitonin	< 0.15 ng/mL	NM	NM	NM	NM	0.10	NM
Total bilirubin	0.1-1.2 (mg/dL)	2.9	8.6	7.6	NM	2.9	NM
Blood culture	NM	NM	NM	Staph coagulase negative	Negative	Negative	NM
Urine culture	NM	NM	NM	Negative	Negative	Negative	NM
Wound culture	NM	NM	NM	Negative	Negative	Negative	NM
CSF culture	NM	NM	NM	Negative	NM	Negative	NM

WBC, white blood cells; Hb, hemoglobin; CRP, C reactive protein; BUN, blood urea nitrogen; Cr, creatinine; Na, sodium; K, potassium, CSF, cerebrospinal fluid; NM, not measured

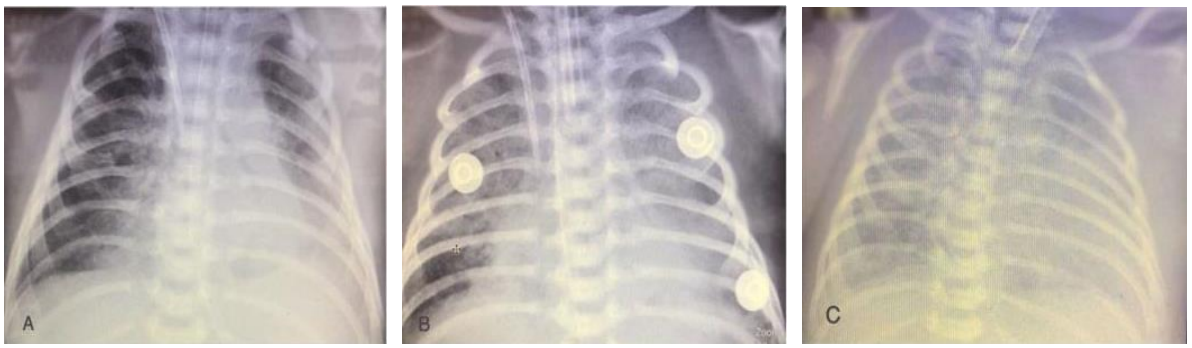

Fig. 1: Serial chest X-ray of the newborn obtained from April 20 to April 22, 2020.On April 20, a radiograph showed generalized scattered patchy opacities in both lung fields (Panel A). On April 21, diffuse patchy opacities in both lungs with atelectasis in the left upper lobe and some parts of left lower lobe, suggestive for active pulmonary infiltration and diffuse alveolar damage (Panel B). Day on death, the last radiograph showed whitish lung without normal lung in favor of diffuse alveolar damage in acute respiratory distress syndrome (Panel C).

The first cases of neonatal COVID-19 infection were confirmed in China, March 2020 (2). Clinical symptoms of newborns suffering COVID-19 infection were reported as fever, poor feeding, lethargy, mild respiratory symptoms, dry cough, nasal stuffiness, respiratory distress, abnormal liver function, thrombocytopenia, thermal instability and cutaneous mottling (3, 15, 16). Medical records of our newborn indicate that there was no fever detected in the hospital course. In agreement with the case, an analysis made in China regarding 1,099 patients with COVID-19 revealed that multiple patients did, in fact, not present a fever (17). With that being said, severe irritability needs to be mentioned as a symptom of COVID-19 in each suspected newborn, similar to our patient.

A report from Iran has indicated leukopenia and lymphopenia in 30% and elevated CRP in 100% of pediatric patients with COVID-19 (13). This is consistent with the findings in our newborn with leukopenia, lymphopenia, and high CRP. There are a lot of studies for human-to-human transmission of COVID-19 via respiratory droplets, close contact, aerosols, and possibly fecal-oral transmission. COVID-19 is also reported by vertical transmission from mother to fetus during delivery because neonates were noted to be infected within the first few hours after birth (18, 19). According to our data, fever was not present in the newborn's mother during delivery and postpartum; negative results of PCR for COVID-19 in the mother were obtained, and a normal chest x-ray in the first days of life in the newborn. Thus the possibility of transmission of COVID-19 from mother to the newborn ruled out. It is possible that the newborn was infected after birth due to close physical contact with health care personnel in the neonatal ICU or the operating room. Asymptomatic patients between medical staff can cause the spread of viruses via respiratory transmission; we have limited samples of PCR for COVID-19 among hospital staff. There is a high probability of contamination with COVID-19 via hospital equipment such as urinary catheter and endotracheal intubation as well. There is a report that intravenous immunoglobulin has been used as a potential therapy to treat patients with COVID-19 (20), but it was without efficacy in this newborn.

4- CONCLUSION

Neonatologists and physicians should be concerned about COVID-19 in neonates with underlying diseases such as sepsis.

5- INFORMED CONSENT

The consent for publication is obtained from the newborn's parents.

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