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Case Report

CASE REPORT

Case Report of Severe COVID-19 Pneumonia in a Term Newborn

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ABSTRACT

Coronavirus disease (COVID-19) has been shown to affect all age groups. The data in the literature usually admit a milder form of disease in infants and newborns than adults. COVID-19 is rarely seen in newborns and an urgent diagnosis should be made in any suspicious situation. A 6-day-old female newborn was admitted to our hospital with fever and dyspnea without cough. A rapid reverse-transcription polymerase chain reaction COVID-19 showed a positive result. Chest computed tomography revealed bilateral and widespread pulmonary involvement. After support therapy, the newborn was successfully discharged. We should carefully consider the new type of coronavirus as an agent for pneumonia in newborns with fever and dyspnea together with non-symptomatic family history. Our case was one of the interesting reported cases of severe pneumonia presenting in the perinatal period.

KEYWORDS: coronavirus, pneumonia, newborn

INTRODUCTION

A new type of coronavirus disease (COVID-19) was first reported at the end of 2019 [1]. The first cases in Turkey were reported in March 2020 [2]. The World Health Organization declared COVID-19 as a pandemic infection in March 2020. This new type of coronavirus may cause a mild type of upper respiratory airway disease or pneumonia [3]. According to the current literature, children represent 1–5% of all diagnosed COVID-19 patients. Severe disease may occur in pediatric patients who are less than 1 year old or have underlying diseases [3]. The most common symptoms in children are fever, fatigue and cough. Some patients may have nasal congestion, runny nose, sore throat and gastrointestinal symptoms [4, 5].

Half of the newborn cases had direct contact with COVID-19 infected mothers. The median age during diagnosis was 5 days of age [5, 6]. Some of these

newborns infected with COVID-19 were shown to have fever and dyspnea and received respiratory and medical treatment for a few days [4–6]. According to the literature, one of the four babies was non-symptomatic, whereas the rest had mild symptoms of typical acute respiratory infection and/or gastro-intestinal system complaints. Most of the newborn patients with COVID-19 infection are supported with room air and discharged after 10 days of hospitalization with a good prognosis [4, 5]. According to case reports from China and Turkey, the reported neonates presented with fever and dyspnea and received mechanical ventilation for a few days. Their reported median age at diagnosis was 5 days. They also reported 3 neonatal deaths because of prematurity but not related to COVID complications [3–6].

Because of these reports, we should carefully and rapidly diagnose newborn cases for the prognosis of the disease [4–8]. This is an interesting Turkish case of a COVID-19 positive neonate who required non-invasive respiratory support because of severe pneumonia but was successfully managed.

CASE PRESENTATION

A 3500 g baby girl was delivered via spontaneous vertex delivery at term in a state hospital to a 30 years old para 3 mother. The baby was discharged without any problem on postnatal Day 2. The baby was brought to our facility on the sixth day of life with fever and feeding difficulty prior to presentation. There was no history of cough, body rash, vomiting or diarrhea. There was no family history suggestive of lung disease, smoking nor consanguinity. Physical examination revealed a bodyweight of 3200 g, tachypnea (respiratory rate of 72/min) and tachycardia (heart rate of 172/min). Her oxygen saturation was 89% in room air. Bilateral rales were determined in respiratory system examination. Cardiovascular examination revealed no pathology. No cough, rash, vomiting or diarrhea was detected. The baby was transferred to our neonatal intensive care unit and pre-diagnosed as having respiratory distress, pneumonia and sepsis. The baby was isolated. Oxygen therapy was initiated. Blood gas parameters were pH= 7.49, pCO_2= 30.8 mmHg, pO_2= 48 mmHg, HCO_3 = 23.1 mEq/l, BE= 0.9 mmol/l, O_2 Sat= 91% and lactate: 2.8 mmol/l. Complete blood count, [white blood cells (WBC)= 10.500/μL (lymphocytes ratio = 14.5% and neutrophil ratio: 74%), hemoglobin= 18.9 g/l, hematocrit= 54.5% and platelet count= 392×10^9/l] and biochemical parameters (liver and renal function tests) were all in normal ranges in accordance with the age of the baby. C-reactive protein was 5 mg/l (reference range: 0–5 mg/l). Interleukin 6 was also found to be 796 pg/ml (reference range: 0–3.4 pg/ml). Chest X-ray revealed bilateral interstitial and radial infiltration, which was more prominent in the right lung, reaching from the bilateral paracardiac area and spreading toward the periphery of the lungs (Fig. 1A). Blood, urine and cerebrospinal fluid samples were taken in order to eliminate possible sepsis, urinary tract infection and meningitis. Samples were also taken with nasal/pharyngeal swab in order to differentiate viral and atypical causes of pneumonia and sepsis. Antibiotic therapy was initiated with ampicillin and cefotaxime. Non-invasive intermittent positive pressure respiratory ventilation [rate: 30/min, positive end-expiratory pressure (PEEP): 6 mmHg, fraction of inspired oxygen (FiO_2): 30%] was initiated because of worsening respiratory distress and permanent respiratory acidosis at the second day of hospitalization. We rechecked the respiratory system and X-ray showed bilateral increased infiltrated area in the parenchyma of the lungs at the second day of hospitalization (Fig. 1B). Esophageal, stomach and duodenum radiography were performed with contrast material in order to differentiate a diagnosis of gastroesophageal reflux disease that may cause pneumonia but this revealed no pathology. Echocardiography was performed in order to detect possible congenital heart disease mimicking respiratory distress and no pathology was found. Because of the persistent fever, we rechecked the family history and tried to identify if any related viral agent was related to this condition. To investigate COVID-19 infection we tested our patient and her parents with reverse-transcription-polymerase chain reaction (RT-PCR), which was found to be positive both in our patient and her parents on the second day of hospitalization. Chest computed tomography (CT) identified sub-pleural ground-glass opacities, consolidation with surrounding halo signs, fine mesh shadow, tiny nodules, linear atelectasis,

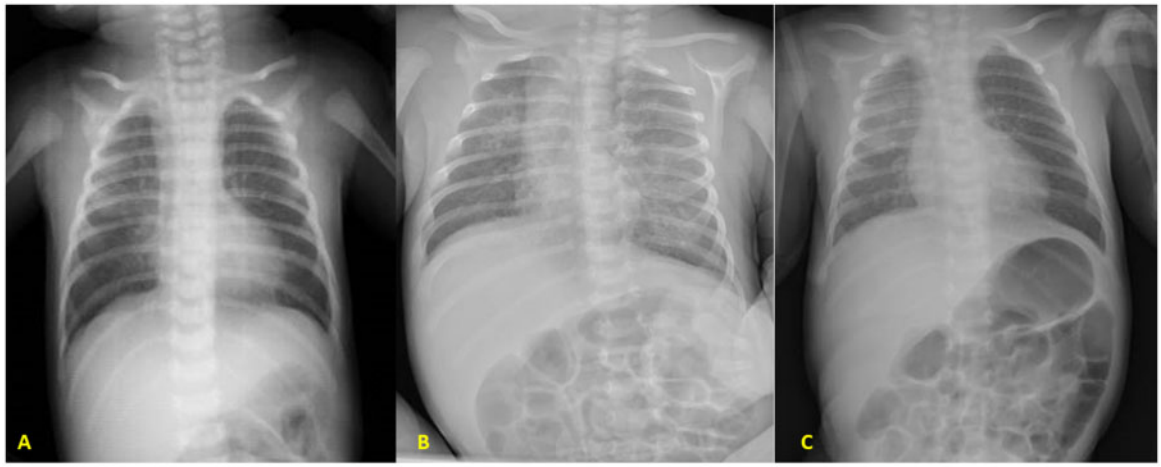

Fig. 1. Chest X ray images of the patient. (**A**) At the time of hospitalization, (**B**) on the second day of hospitalization and (**C**) on the eighth day of hospitalization (end of treatment).

fibrous band and homogenous infiltration, which was bilateral but more prominent in all segments (upper, middle, lower) of the right lung. No pleural effusion was detected (Fig. 2). Further tests performed for other viral and atypical agents of pneumonia (*adenovirus, bordetella pertussis/parapertussis, chlamydia pneumonia, mycoplasma pneumonia, metapneumovirus, rhinovirus, influenza virus A/B, parainfluenza, respiratory syncytial virus* and *cytomegalovirus*) were negative. Blood, urine and cerebrospinal fluid cultures were negative. Our baby was breastfed and her mother's milk was found to be negative for COVID-19. Medical history, physical examination, laboratory results and radiological findings showed a COVID-19 positive baby with pneumonia. We started to treat the baby according to the guidelines recommended by Ministry of Health of Turkey for novel coronavirus on the second day hospitalization. Hydroxychloroquine and azithromycin therapy was given for 5 days [9]. After this treatment, control chest X-ray showed a dramatic decrease in infiltration of the left lung but no change in the right lung (Fig. 1C). COVID-19 PCR tests were positive on the second and fifth days of hospitalization. Tests became negative on the 10th day of hospitalization. Fever diminished at the second day of hydroxychloroquine (3 mg/kg PO TID) and azithromycin (5 mg/kg/day) therapy. We continued non-invasive intermittent positive pressure ventilation for 7 days and non-invasive continuous positive airway pressure for 5 days. At the 13th day of hospitalization, free oxygen was initiated. The baby was isolated up to her discharge. We also quarantined the family for 14 days. We discharged the baby on postnatal Day 33 and followed up in the outpatient clinic. Information on the consideration and management of the disease is shown in Fig. 3. Informed consent was obtained from the patient's parents to publish the case information and accompanying images and laboratory studies.

DISCUSSION

Previously reported papers of COVID-19-infected newborns were especially about non-symptomatic or mildly symptomatic babies who never received strict respiratory support. We aimed to present this report because this case was one of the most interesting cases reported in newborns, this case having early symptoms that began in the perinatal period of life and progressed to severe pneumonia.

The clinical course of COVID-19 in children is milder than in adults [1]. The most common clinical symptoms are fever, fatigue and cough [4]. In the literature, infection has been reported in very few neonatal cases, including an 18 h old non-symptomatic infant, a 5 days old infant with fever and a 17 days

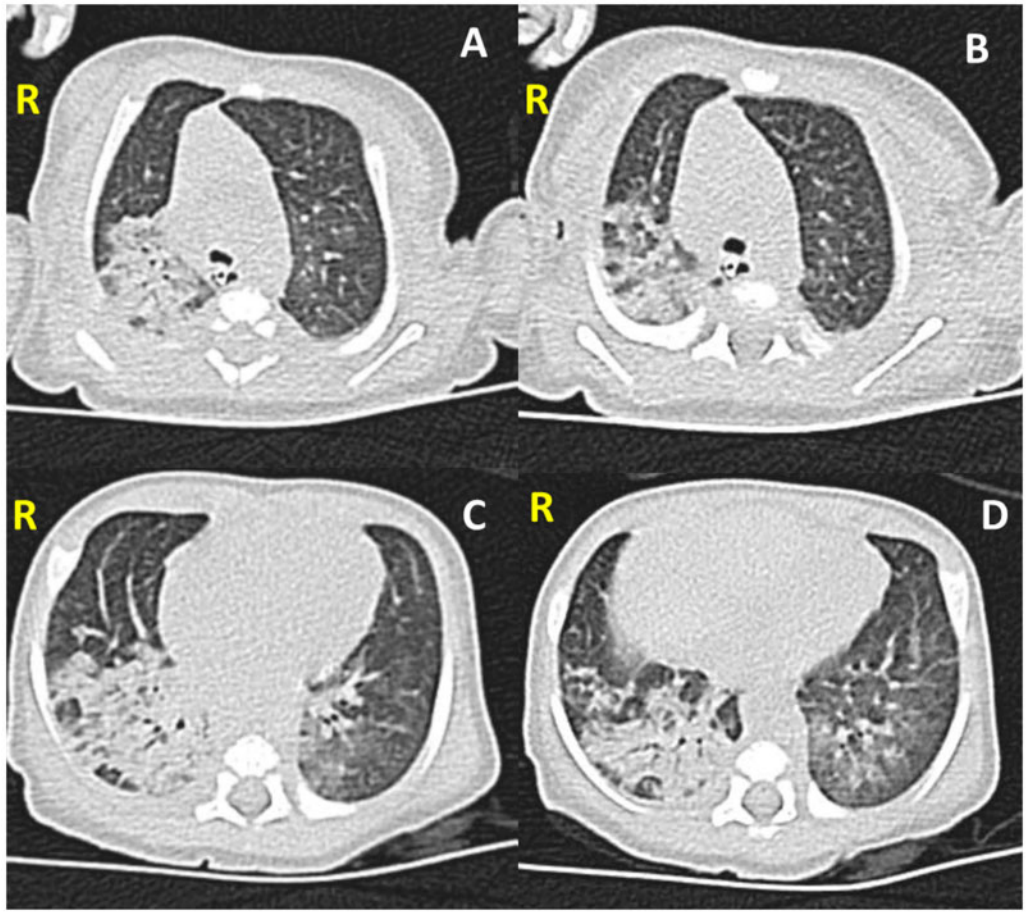

Fig. 2. Chest CT findings on the second day after the hospitalization. (**A**) Upper segment, (**B** and **C**) middle segment and (**D**) lower segment. Bilateral ground-glass opacities, consolidation with surrounding halo sign, fine mesh shadow and tiny nodules fibrosis lesions and linear atelectasis.

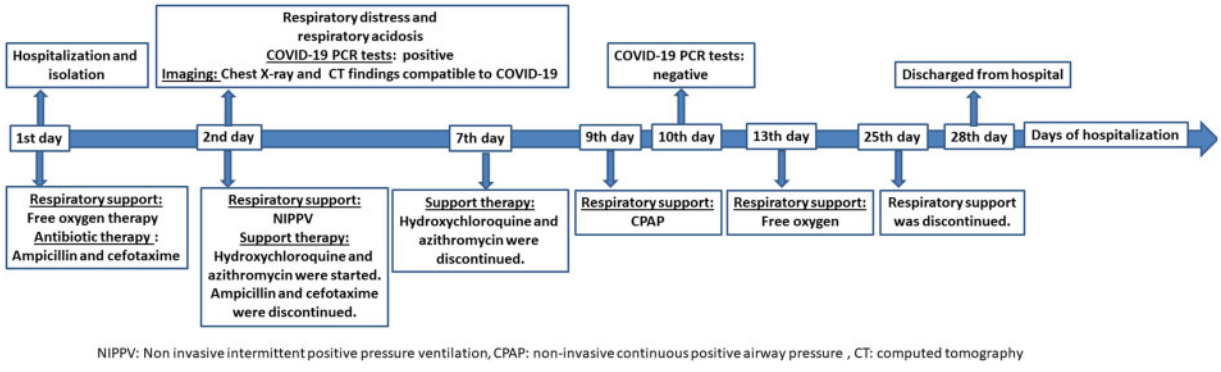

Fig. 3. Clinical consideration and management of the patient.

old infant with cough and vomiting [4, 10, 11]. Moreover, they reported an abnormal pleural line, increase and fusion of B-line, pulmonary edema of differing severity, pulmonary interstitial syndrome and a small area of consolidation in the pulmonary ultrasound at the time of presentation. They showed that there was significant parenchymal infiltration in two cases, small strip or patchy high-density shadow in two cases, and ground glass change in one case in the chest CTs at admission [12].

The first newborn case from Spain, whose birth weight was 2500 g, and whose mother was reported to be COVID-19 positive, was admitted to the hospital with respiratory symptoms on the ninth day of life, and mild findings were detected on chest X-ray. During the follow-up, her clinical situation improved after 24 h of admission [13]. Our patient was term and presented with severe pneumonia. Our patient was evaluated as the most interesting case in terms of receiving non-invasive respiratory support for a long time. Most cases reported with newborn infants were non-symptomatic or with mild symptoms.

The reason why children and newborns are less symptomatic or non-symptomatic compared to adults and less susceptible to COVID-19 than adults remains uncertain [14]. However, there are some hypotheses that try to clarify this situation. Otto *et al.* [15] showed that children who were vaccinated (diphtheria, pertussis, tetanus, *Haemophilus influenzae* type B and poliomyelitis) in the third month of life had fewer symptomatic infections than children with delayed or partial immunity. The theory of vaccination may not come first on our list since our patient was 6/7 (not in the third month of life) and may not be expected to have had all these vaccines at birth. Another hypothesis includes angiotensin-converting enzyme 2 (ACE2), a highly expressed membrane-bound amino peptidase, which plays a vital role in lung alveolar epithelial cells, enterocytes of the small intestine and the immune system. The tissue distribution of ACE2 may differ between adults and children and the maturity and function of ACE2 in children may be lower than adults as well [16, 17]. It was found that ACE2 expression in rat lung was dramatically decreased with age. This finding may not be consistent with the relatively low susceptibility of children to COVID-19. On the other hand, studies show that ACE2 is involved in protective mechanisms of the lung. It may protect against severe lung injury induced by respiratory virus infection in an experimental mouse model and in pediatric patients [3]. Moreover, since the immune system development of children is ongoing, they may not be able to initiate an adult-like cytokine storm [18].

COVID-19 tends to be more severe if it occurs together with adult-specific comorbidities (such as cardiovascular disorders and diabetes). Moreover, children might be less prone to develop the chaotic inflammatory host response that contributes to the clinical picture of COVID-19 and the disease seems to have a milder clinical course in children than in adults. However, the proportion of asymptomatic infections seems to be lower in children than in adults [6]. In addition, some hypotheses have been made, including mal-adapting immune response in the elderly compared with children, developmental changes in immunity, with a predominant innate response to infectious stimulus in young infants, effects of lung development and ageing, differences in the physiology and anatomy of the respiratory tract and the crucial role of comorbidities in outcomes. Also, children's healthier endothelium may protect them from progression to severe/fatal disease, in contrast to what may happen in adults, in whom problems with the endothelium seem to be related to a worse prognosis [19].

Our case who had severe pneumonia, which has not been reported previously in a newborn, was diagnosed with COVID-19 infection with complaints that started on the sixth day of the perinatal period. Her fever subsided with hydroxychloroquine and azithromycin treatment, and her clinical condition improved with long-term respiratory support treatment. As in our case, apart from all these hypotheses, many other mechanisms could explain the picture that progresses slowly in newborns [3, 14].

There is still no clear information about maternal–fetal transmission and/or breastfeeding [3, 14]. In addition, the COVID-19 virus has never been found so far in umbilical cord blood of neonates or in the amniotic fluid of most of the COVID-19 positive pregnant women [20]. However, the possibility of infection symptoms is reported to be very low if

there is a transition during delivery [3]. The risk of fetal infection due to maternal–fetal transmission of the virus is one of the most debated aspects, implying that infection in neonates could be prevented in the peripartum period [20]. According to the available reports, neonatal COVID-19 appears to have horizontal transmission and seems to be paucisymptomatic or asymptomatic, compared to older age groups [19]. The absence of symptoms in the mother prior to the hospitalization of our case suggests that the baby may have been infected non-symptomatically at birth or from the mother immediately after birth. Our neonate was infected very probably after delivery and not vertically. The possibility of transmission via the community is also considered. Nevertheless, it should be borne in mind that COVID-19 can cause severe pneumonia, as in our case, when infecting newborns. In addition, chest CT findings may be in line with the findings in pediatric and adult patients [21].

Our case of severe COVID-19 pneumonia was a rare presentation of COVID-19 infection in a neonate. Most of the neonatal COVID infections are widely reported to be asymptomatic or mild in presentation. However, the underlying cause of the severe course of COVID-19 pneumonia in our patient was not clear. It has been reported that the clinical course is more severe in preterm babies [19]. Neonatologists should bear in mind the possibility of a term neonate presenting with severe COVID-19 infection.

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