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Case Report / Приказ болесника

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**Pulmonary air leak syndrome in premature infant
born to mother with coronavirus disease**

Плућни синдром цурења ваздуха код претерминског новорођенчета
рођеног од мајке са коронавирусном болешћу 2019

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Pulmonary air leak syndrome in premature infant born to mother with coronavirus disease

Плућни синдром цурења ваздуха код претерминског новорођенчета рођеног од мајке са коронавирусном болешћу 2019

SUMMARY

Introduction The clinical course of premature infants born to mothers with coronavirus disease 2019 (COVID-19) has not been well characterized. The aim of this paper was to report a complicated clinical course with pulmonary air leak syndrome (pneumomediastinum and pneumothorax) in a premature infant born to mother with COVID-19.

Case outline The patient was a male infant born at 35 weeks of gestation. The mother had confirmed coronavirus pneumonia 6 days prior to delivery. At approximately 25 hours of age, chest X-ray showed pneumomediastinum, giving the classic “spinnaker sail” sign. After intubation, chest X-ray showed the typical “angel wing” sign, which represents pneumomediastinum and bilateral pneumothorax (pulmonary air leak syndrome).

Conclusion Based on the presented case, we believe that the mother's COVID-19 infection is an additional risk factor for the occurrence of pulmonary air leaks in the infant. To confirm this hypothesis as well as explain the exact pathophysiology of air leakage in COVID-19, larger, prospective, and well-designed studies are needed.

Keywords: coronavirus disease 2019; premature infants; pulmonary air leak syndrome; pneumomediastinum; pneumothorax

САЖЕТАК

Увод Клинички ток претерминске новорођенчади, рођене од мајке са коронавирусном болешћу 2019 (ковид 19) није довољно испитан. Циљ овог рада је био да прикаже претерминско новорођенче са плућним синдромом цурења ваздуха (пнеумомедијастинум и пнеумоторакс) рођеног од Ковид-19 позитивне мајке.

Преглед болесника Болесник је мушко новорођенче рођено у 35. недељи гестације. Мајка је шест дана пре порођаја имала коронавирусну упалу плућа. Радиграфија грудног коша новорођенчета у 25. сату по рођењу, показала је неувичајени пнеумомедијастинум - знак „троугластог једра“. Након интубације, на радиграфији грудног коша приказује се „знак анђeosких крила“, који представља пнеумомедијастинум и билатерални пнеумоторакс (плућни синдром цурења ваздуха).

Закључак На основу приказаног случаја, сматрамо да је ковид 19 инфекција мајке додатни фактор ризика за појаву плућног синдрома цурења ваздуха код новорођенчета. За потврду ове хипотезе, као и за објашњења тачне патофизиологије цурења ваздуха код ковид 19, потребне су веће, проспективне и добро осмишљене студије.

Кључне речи: коронавирусна болест 2019; претерминско новорођенче; плућни синдром цурења ваздуха; пнеумомедијастинум; пнеумоторакс

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is a highly contagious and potentially life-threatening disease. The COVID-19 pandemic has been declared by the World Health Organization (on March 11th, 2020) as a global public health emergency [1]. The disease is mild in most people, but in some, it may progress to pneumonia, acute respiratory distress syndrome, and multiorgan dysfunction. Disease in infants and children has also been reported to be significantly milder than in adults. Mortality rates range between 0-12% in the pediatric population [2].

The published data on premature infants born to mothers with COVID-19 has been limited. Studies had no evidence to suggest that the development of COVID-19 pneumonia in the third trimester of pregnancy could lead to the occurrence of severe adverse outcomes in

infants [3, 4]. But some studies describe a very complicated clinical course with pulmonary air leak syndrome in preterm infants born to mothers with COVID-19. The management of these infants presents a significant challenge [5, 6].

The aim of this paper was to report very complicated clinical course with pulmonary air leak syndrome in the preterm infant born to mother with COVID-19.

CASE REPORT

A patient was a male infant born at 35 weeks of gestation with a birth weight of 2,600 g. He was born to a 31-year-old (gravida 2, para 2) who had received treatment for hypothyroidism in pregnancy.

Maternal history was significant for cough and fever 6 days prior to delivery. She was admitted to the hospital one day prior to delivery and tested positive for SARS-CoV-2 on reverse transcriptase-polymerase chain reaction (RT-PCR) by nasopharyngeal swab. After chest X-ray she was diagnosed with COVID-19 pneumonia. Laboratory findings showed a high level of C-reactive protein (61mg/L) and a slightly lower white blood cell count ($5.6 \times 10^9/L$). Caesarian section was performed at 35 weeks of gestation after premature rupture of membranes. At the time of delivery, she was on high-flow nasal cannula oxygen therapy and prophylactic anticoagulation with low-molecular-weight heparin due to the risk of thrombosis in pregnancy and COVID-19.

The patient (male premature infant) was vigorous at birth, Apgar scores were 8 and 8 at 1 and 5 minutes, and he required only the fraction of inspired oxygen (FiO_2) of 0.3. The infant was immediately separated from the mother, transferred to the Pediatric hospital, and admitted to an isolation room due to maternal COVID-19. Initial chest X-ray was suggestive of respiratory distress (Figure 1A), and his initial capillary blood gas showed a pH of 7.3, PCO_2 4.6, PO_2 4.8, and base excess of -6.2. The infant was started on caffeine prophylaxis for apnea of prematurity and empiric antibiotics (ampicillin and gentamicin) due to preterm labor. He was tested negative for SARS-CoV-2 on RT-PCR by nasopharyngeal swab.

A few hours after the birth, the infant developed increased work of breathing, so, he was transferred to the neonatal intensive care unit and nasal continuous positive airway pressure respiratory support was commenced.

At approximately 25 hours of age, the infant had desaturations requiring an increase in oxygen supplementation, and chest X-ray showed an unusual radiographic finding of

pneumomediastinum - a central area of radiolucency projected over the mediastinum separating the thymic lobes upwards and outwards, giving the classic "spinnaker sail sign" (also known as a "angel wing sign") (Figure 1B). Because of respiratory deterioration infant was intubated. Chest X-ray after intubation revealed pneumomediastinum and bilateral pneumothorax requiring thoracic drainage (Figures 1C, 1D, and 1E).

Mechanical ventilation with a positive end-expiratory pressure of 6 cm of H₂O, FiO₂ of 0.6, and a mean airway pressure of 22 cm of H₂O was started. Exogenous surfactant instillation resulted with improvement in oxygen requirement.

Antibiotics were replaced to meropenem and amikacin, and were discontinued after 72 hours, upon the report of negative cultures.

Follow-up chest X-ray showed incomplete resolution of air leaks (Figure 1F).

The infant's respiratory function improved, he was extubated on the 8th hospital day, and chest tubes were removed the next day.

The need for supplementary oxygen therapy was decreased, and the infant was placed in a crib, bottle-fed, and discharged from the hospital 7 days after extubation. No air leakages were detected in a chest X-ray performed before hospital discharge.

This case report was approved by the institutional ethics committee, and written consent was obtained from the patient for the publication of this case report and any accompanying images.

DISCUSSION

COVID-19 is a highly contagious and potentially life-threatening disease, especially in pregnancy [7]. The published data on premature infants born to mothers with COVID-19 has been limited [7, 8]. It is reliably known that the mother's COVID-19 infection leads to preterm delivery, but the connection to the occurrence of pulmonary air leak in the newborn has not been fully proven. Pulmonary air leaks in infants are certain to be associated with high morbidity and mortality [7, 9, 10].

This Case Report shows the clinical course of the premature infant born to mother with COVID-19 pneumonia. He had initial mild (moderate) respiratory distress complicated by the development of severe pulmonary air leak syndrome (pneumomediastinum, bilateral pneumothorax) with unusual chest X-ray signs ("spinnaker sail" or "angel wing" sign).

The infant had some risk factors for air leak: male sex, late preterm gestation, and cesarean delivery predispose him to transitory tachypnea, which leads to pulmonary air leak. Considering the severity of our patient's clinical condition, we believe that COVID-19 maternal pneumonia in the third trimester of pregnancy was an additional risk factor for preterm delivery, caesarean section, and pulmonary air leak syndrome in infants.

Our opinion is supported by published studies on term and preterm infants from COVID-19 positive mothers with pulmonary air leak syndrome, as well as the fact that pneumomediastinum is considered the leading cause of maternal death [11]. Recent review studies reveal a high incidence of air leaks in patients with COVID-19, even in the absence of any traditional risk factors [12].

Although the precise pathophysiology of air leaks with COVID-19 is still unknown, some studies suggest that a variety of factors may contribute to its development [12, 13]. According to Harancang et al., COVID-19 starts an inflammatory dysregulation that results in diffuse damage and alveolar rupture [14].

On the other hand, several studies didn't suggest that the development of COVID-19 pneumonia in the third trimester of pregnancy could lead to the occurrence of severe adverse outcomes in infants [2, 3, 15].

A national prospective epidemiological study that included all infants with COVID-19 in Spain (40 cases), showed that clinical manifestations were mild, such as upper respiratory airway infections, febrile syndrome, acute gastroenteritis, apnea, and mild respiratory distress. The most severe manifestations occurred in the two preterm infants with pneumonia and in the infant with bronchiolitis due to rhinovirus co-infection. Respiratory support was required in a few cases, and in those who did need it, oxygen and non-invasive systems were briefly used [6].

Anand and colleagues described 65 infants born to COVID-19 positive mothers. Approximately one-third of the cohort was born preterm (40%). Of the 65 infants, 7 tested positive for COVID-19. Six of the 7 infants were asymptomatic, and one infant received respiratory support (CPAP) for 48 hours [16].

Also, very complicated neonatal illness with pulmonary air leak syndrome was described in preterms born to mother with COVID-19. The management of these infants presents a significant challenge [4, 5].

Piersigilli and colleagues describe a female infant at 26 gestational weeks born to mother who developed COVID-19 positive bilateral pneumonia. Despite the initial clinical stability and the requirement of low FiO₂, 12 hours after the less invasive surfactant administration procedure, she developed a pneumothorax requiring thoracic drainage [5]. In our patient, air leak developed before surfactant administration, which excludes surfactant as an etiological factor.

Reddy and associates presented two preterm infants born to mothers with COVID-19, who also developed acute onset severe air leak syndrome requiring thoracic drainage [4].

In another study by Kamity and colleagues, they assumed that in utero exposure to SARS-CoV-2 leads to fetal pneumonitis, which is the reason for the increased susceptibility to pneumothorax. They advise increased vigilance in infants born to COVID-19 positive mothers even when their SARS-CoV-2 PCR is negative [17].

Zhu and colleagues, in a clinical analysis of 10 infants born to mothers with COVID-19 pneumonia, concluded that perinatal COVID-19 may have adverse effects on infants, causing problems such as premature labor, respiratory distress, and even death. Seven out of nine infants had abnormal chest computer tomography with a picture of neonatal respiratory distress syndrome, infection, and pneumothorax [18].

Wróblewska-Seniuk et al. concluded that higher respiratory distress rates and the need for respiratory support in infants resulted only from COVID-19 infection in the mother. However, according to the authors, the mechanism of pulmonary air leak is not easily explicable [13].

Despite the increasing amount of published data on COVID-19 in pregnancy, there is insufficient good-quality data to draw unbiased conclusions regarding the influence of maternal COVID-19 infection on the occurrence of pulmonary air leak in infants [19].

We believe, based on our case, that COVID-19 infection in the mother is an additional risk factor for the development of pulmonary air leak in the infant. This statement is supported by the high incidence of pneumomediastinum in patients with COVID-19 infection and the fact that pneumomediastinum is the most common cause of death in pregnant women with COVID-19 [11, 12, 14].

To confirm this hypothesis as well as explain the exact pathophysiology of air leakage in COVID-19, larger, prospective, and well-designed studies are needed.

In accordance with the obtained data, the guidelines for neonatal care and treatment, especially respiratory support, should be revised. In any case, we recommend special attention to prevent COVID-19, systematic screening of suspected infections during pregnancy, and extended intensive follow-up for infants, especially preterm infants.

Conflict of interest: None declared.

Paper accepted

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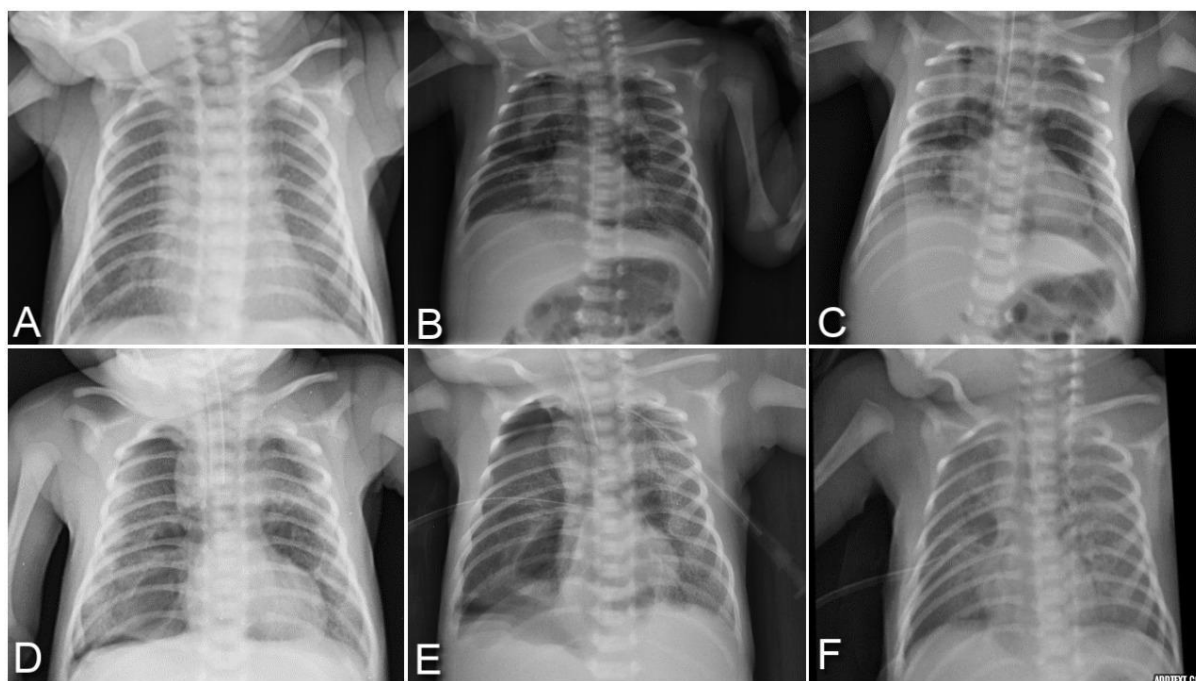


Figure 1. Chest radiographs; on admission, a chest X-ray showed granular lungs with air bronchograms in the central regions (A); after worsening health conditions, chest X-ray showed unusual pneumomediastinum – a central area of radiolucency projected over the mediastinum, giving the classic “spinnaker sail” sign (B before and C after intubation); chest X-ray after seven hours showed the typical “angel wing” sign – bilateral hyperlucency representing air leak into the pleural cavities – pneumothoraces (D), which required bilateral thoracic drainage followed by chest tube placement (E); a repeat chest X-ray was performed at the age of nine days, which showed partial resolution of the pneumomediastinum and gradual improvement of the patient’s symptoms; the patient was extubated (F)