



Rapid recovery achieved by intensive therapy after preterm cesarean section for worsening COVID-19-induced acute respiratory failure: A case report and literature review

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ABSTRACT

A 31-year-old woman (gravida 3, para 2) presented at hospital in the 33rd week of gestation with concerns of general malaise, a productive cough, and impaired taste. She was diagnosed with coronavirus disease 2019 (COVID-19) after a nasal antigen test; a computed tomography (CT) scan of the chest showed pneumonia. The patient developed dyspnea on the third day of hospitalization, and it worsened the following day. Oxygen inhalation and steroid administration were started. Since the dyspnea was worsening, an emergency cesarean delivery was performed to allow intensification of maternal treatment. A postoperative CT scan showed that the pneumonia was getting worse, and the administration of remdesivir was started immediately. The dyspnea improved rapidly, and medication was discontinued on postoperative day 4. The patient was discharged on postoperative day 6. Thus, a patient in the third trimester of pregnancy with COVID-19 whose respiratory condition worsened was successfully treated by early delivery and subsequent intensive treatment.

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1. Introduction

The number of cases of novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has increased rapidly since the first case was reported in China in December 2019. There is still no consensus on the progression of COVID-19 in pregnant women. Some studies have reported that it is more severe in pregnant women than in the general population and increases the occurrence of adverse perinatal outcomes, such as maternal death, intrauterine fetal death, and neonatal death. [1–3] Other studies have reported that the severity of the disease is similar to that in the general population, that most cases are asymptomatic, and that vertical transmission and neonatal infections are rare. [4] [5] This discrepancy may be explained by reports that indicate that COVID-19 is more severe in maternal patients infected in the third trimester of pregnancy than in those infected in the first trimester. [6] We report a case of cesarean delivery for a pregnant woman with acute respiratory distress due to COVID-19 in the preterm of the third trimester, and review the literature.

2. Case Presentation

The patient was a 31-year-old woman, gravida 3 para 2, 156 cm tall, and body weight of 57 kg. She developed general malaise in the 32nd week of gestation (32⁺³). Five days later (33⁺¹), she presented at a hospital emergency department with a productive cough and an altered sensation of taste. On examination, her body temperature was 37.0 °C; heart rate, 100 bpm; respiratory rate, 16 bpm; blood pressure, 93/48 mmHg; and oxygen saturation (SpO₂) at room temperature was 98%. A nasal antigen test for SARS-CoV2 was positive, and a simple chest computed tomography (CT) scan showed multiple mottled infiltrative shadows and reticular lesions in both lung fields, as well as prominent interlobular septal wall thickening (Fig. 1A). The patient was diagnosed with COVID-19 pneumonia and admitted to the infectious disease ward for treatment. Since there were no signs of dyspnea and SpO₂ at room temperature was relatively well maintained, at 95%–97%, the patient was simply monitored, without being given oxygen or medication. The non-stress test (NST) was conducted and showed a reactive pattern.

The patient developed dyspnea on hospital day (HD) 2 (33⁺³ week of gestation), and it worsened the following day (HD3). Nasal cannula oxygen therapy (2 L/min) and intravenous administration of dexamethasone 6.6 mg/day were started. Her vital signs were as follows: body temperature, 37.5 °C; pulse, 117 bpm; respiratory rate, 30 bpm; blood

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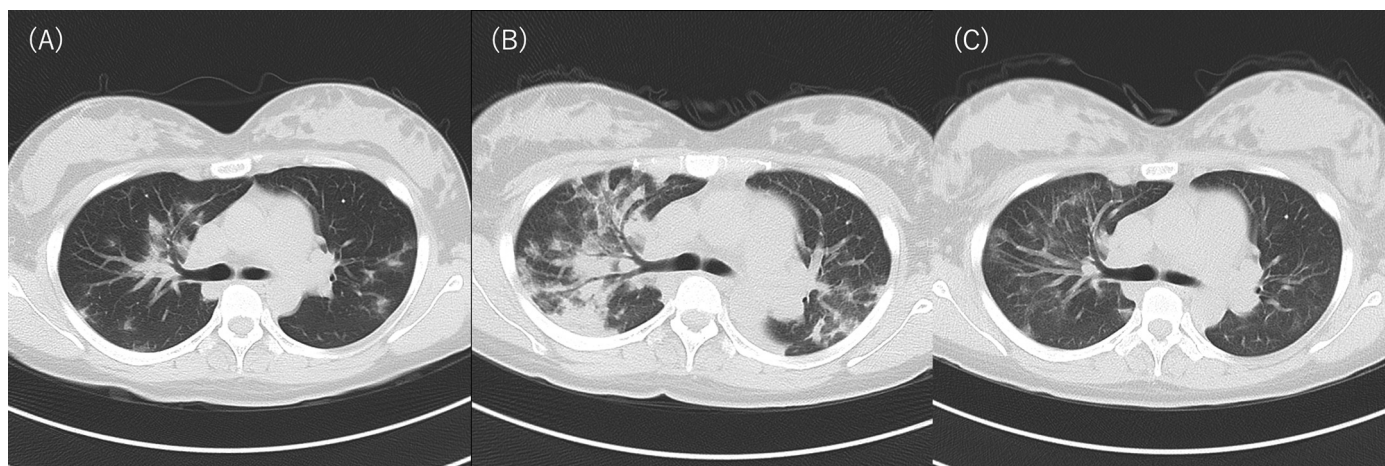


Fig. 1. Chest CT images: (A) on admission; (B) immediately after cesarean section; (C) on postoperative day 4.

pressure, 97/61 mmHg; and SpO₂, 95% (O₂ 2L/min). On HD4 (33⁺⁵ weeks of gestation), the patient's dyspnea worsened, and the oxygen flow rate was increased to 4 L/min; SpO₂ showed a decreasing trend at 92%–94%. Vital signs were obtained again: body temperature, 37.0 °C; pulse, 106 bpm; respiratory rate, 36 bpm; blood pressure, 103/58 mmHg; and SpO₂, 97% (O₂ 4L/min). The NST again showed a reactive pattern.

With the patient's breathing deteriorating, a decision was made to perform a cesarean section immediately so that maternal treatment could be intensified; we expected early delivery to improve the patient's lung capacity. Once this decision was made, two additional doses of dexamethasone (6.6 mg) were administered to the patient every 6 h prior to surgery to prevent respiratory distress syndrome in the neonate. The surgery took 58 min, and the patient lost 450 mL of blood (including amniotic fluid). The amniotic fluid was stained with green meconium. A male neonate was born with a body weight of 2375 g and an Apgar score of 3/7 (1/5 min). He was placed in the neonatal intensive care unit. Results of the umbilical artery blood gas analysis were as follows: pH, 7.291; pCO₂, 57.8 mmHg; pO₂, 16.7 mmHg; HCO₃⁻, 27.8 mmol/L; BE, 1.3 mmol/L; and lactate 1.3 mEq/L.

A chest CT scan of the patient immediately after surgery showed worsening of the infiltrative lesions in both lungs (Fig. 1B). She was started on remdesivir 200 mg/day soon after the surgery and 100 mg/day from the next day on. To prevent thrombosis, heparin calcium 5000 IU was administered subcutaneously every 12 h starting 2 h after surgery.

On postoperative day 1 (HD5), the dyspnea resolved and the oxygen flow rate was gradually decreased. On postoperative day 3 (HD7), oxygen administration was no longer necessary, and it was stopped. On postoperative day 4 (HD8), a chest CT scan showed improvement of the infiltrative lesions in both lungs (Fig. 1C) and blood tests showed no coagulation abnormalities. Subsequently, dexamethasone, remdesivir, and heparin calcium administration were discontinued.

The patient was discharged on postoperative day 6 (HD10). The neonate underwent nasal antigen testing for SARS-CoV-2 on the day of birth and again the following day. Both results were negative. Histopathological analysis of the placenta and umbilical cord showed no inflammatory cell infiltration or other obvious abnormal findings.

3. Discussion

We report the successful treatment of a pregnant woman who contracted COVID-19 in the third trimester. The treatment strategy used two approaches: 1) early elective cesarean delivery to enable an immediate improvement of the patient's respiratory status, as

well as early pharmacological treatment; and 2) subsequent intensive pharmacological treatment to arrest the respiratory decline. During pregnancy, lung compliance is usually reduced due to the high plateau pressures caused by reduced functional residual capacity, compression of the diaphragm by an enlarged uterus, and compression of the chest wall by swollen breasts. These physiological changes would have a negative impact on a deteriorating respiratory status during pregnancy. [7] Since oxygen consumption increases by 20%–30% in the third trimester, the risk of developing severe respiratory lesions due to COVID-19 is considered to be high. [8] A study of the severity of illness in 1219 pregnant women with COVID-19 reported a severity rate of 12%, a maternal mortality rate of 0.3%, and a rate of admission to an intensive care unit of 4.8%. These rates were higher than those previously reported, [9] probably because most patients in the study were diagnosed during the third trimester of pregnancy (the median number of weeks of pregnancy was 37.7 [range, 33.7–39.1]).

It has also been reported that pregnant women with severe COVID-19 have a higher risk of perinatal complications. [9] In cases of acute respiratory distress syndrome (ARDS) during pregnancy, high rates of intrauterine fetal death, spontaneous onset of labor, and fetal distress have been reported, regardless of whether the patients had COVID-19. [10] Additionally, a high rate of abnormal fetal heart rate waveforms has been reported in pregnant women with COVID-19; this may be due to factors such as maternal hypoxia, cytokine storm, maternal fever, uterine irritability, and reduced oxygen transport through the placenta caused by the maternal anticoagulant state. [11] Therefore, if the mother does not respond to treatment, it is necessary to consider expediting delivery before the disease becomes severe. There are case reports of patients with COVID-19 who became severely ill during pregnancy and yet showed improvement after undergoing cesarean section. [2,12,13] For example, Oram et al. mentioned that expediting delivery contributed to the improvement of oxygenation and respiratory compliance in pregnant women with deteriorating respiratory status. [13] Thus, it can be inferred that early delivery by cesarean section is an important treatment option for pregnant women with COVID-19. Catanzarite et al. stated that considering the impact of ARDS on fetal well-being, the best option is to perform preterm delivery if the maternal patient is more than 28 weeks pregnant. [10] In this case, the patient developed COVID-19 in the 33rd week of pregnancy. The patient's respiratory condition improved after early delivery. Shrinking of the uterus and the subsequent increase in lung compliance due to the expansion of lung volume is thought to have contributed to the improvement in her respiratory status.

Starting medication at an early stage, before the disease became severe, helped prevent maternal complications. Oram et al. stated that the

advantage of preterm delivery was that it eliminated not only maternal concerns, but also concerns about the effect of maternal ARDS treatment on the fetus. [13] In this case, the early cesarean delivery allowed us to intensify maternal treatment.

The efficacy of remdesivir, favipiravir, and chloroquine as therapeutic agents for COVID-19 has been reported since the early days of the epidemic. [14–16] Remdesivir was used to treat this patient. The U.S. National Institutes of Health (NIH) recommends that remdesivir be used for mild to moderate COVID-19 and for severe cases soon after onset. [17] In fact, some studies have shown that early administration of remdesivir improves patient outcomes. [18] Based on these reports, we believe that treatment was successful for this patient as the early cesarean delivery was performed when COVID-19 was at a moderate level of severity, enabling administration of remdesivir immediately after surgery and before the disease became severe.

The NIH guidelines recommend that steroids be administered to moderately or severely affected COVID-19 patients. [17] Steroids were administered to the patient from an early stage. The use of steroids in pregnant women to improve the short-term prognosis of the neonate is of concern in cases where preterm delivery is required to intensify maternal treatment and improve maternal outcomes. [19] However, since the common dose of steroids for preterm births (12 mg every 24 h for 2 days) is well tolerated and within the recommended dosage range of corticosteroids for COVID-19 patients (low to moderate dose [0.5–1.0 mg/kg/day] for less than 7 days), [20] the effect on maternal care is considered to be minimal. Currently, however, there is no consensus on the administration of steroids in COVID-19 for the short-term prognosis of neonates at the time of delivery. Hence, the dosage and timing of steroid administration should be discussed with physicians and neonatologists.

Presently, there is a scarcity of data on pregnant women with severe COVID-19, and therefore, there is no established method of management. However, pregnant women with COVID-19 may be at high risk of developing severe respiratory lesions, especially if the disease is contracted in the third trimester of pregnancy. If COVID-19 worsens during pregnancy, expediting delivery may improve maternal outcomes or enable maternal treatment to be escalated. These options should be carefully considered before developing a treatment strategy. An accumulation of related data would help determine best practice in similar scenarios.

Contributors

Ayumu Ito was responsible for the acquisition, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content, and treatment of the patient.

Eijiro Hayata was responsible for revising the draft article critically for important intellectual content, and treatment of the patient.

Masahiko Nakata was responsible for revising the draft article critically for important intellectual content, and supervision.

Tomoyuki Shigeta was responsible for revising the draft article critically for important intellectual content, and treatment of the patient.

Yasuhiko Nakamura was responsible for revising the draft article critically for important intellectual content, and treatment of the patient.

Kazuma Kishi was responsible for revising the draft article critically for important intellectual content, and supervision.

Hitoshi Yoda was responsible for revising the draft article critically for important intellectual content, and supervision.

Mineto Morita was responsible for supervision, and final approval of the version to be submitted.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

Consent was obtained from the patient after she regained capacity.

Provenance and Peer Review

This case report was peer reviewed.

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