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Severe COVID-19 during pregnancy treated with pulse corticosteroid therapy and mid-trimester termination: A case report

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ABSTRACT

Background: At the early stage of the pandemic, severe COVID-19 was thought to be rare among pregnant women. However, cumulating data showed that gestational state is a risk factor for severe pneumonia, particularly due to the hyperinflammatory state. Recent reports suggested the efficacy of pulse corticosteroids in stopping the cytokine storm in people infected with SARS-CoV-2, but limited data exists regarding its use in pregnant women. Moreover, pregnancy termination is a treatment option in this population, but it has been reported mainly in the third trimester and rarely in the second trimester.

Case Presentation: A 37-year-old woman infected with SARS-CoV-2 at 23 weeks of gestation presented with fatigue and dyspnea but soon deteriorated to severely acute respiratory failure and cytokine storm requiring mechanical ventilation combined with hemodialysis just one day after hospitalization. Low-dose corticosteroids and antibiotics were initiated, followed by antiviral therapy, anticoagulant and high-dose corticosteroid therapy. On hospital day 3, a decision to terminate her pregnancy was made; termination led to significant improvement in her clinical condition and a gradual decrease in demand for oxygen supplementation as well as the corticosteroid dose. She was discharged two weeks after admission.

Conclusions: Due to the specific immune response, pregnant women with COVID-19 may differ from others in their clinical presentation, especially the probability of classic acute respiratory distress syndrome (ARDS). This report provides evidence related to the efficacy of pulse corticosteroids on this group and the influence of the mid-trimester termination on recovery.

1. Introduction

At the early stage of the coronavirus disease 2019 (COVID-19) pandemic, most studies reported that very few pregnant women developed severe forms of the disease; however, recent data indicates that they may face severe morbidity and mortality [1]. A hospital analysis in the UK showed that pregnant women with COVID-19 at 20 weeks of gestation and beyond are five times more likely to be admitted to intensive care units than those before 20 weeks of gestation [2].

COVID-19 can involve a hyperinflammatory response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Some articles underline pulse corticosteroid therapy as an effective immune modulator in critically ill COVID-19 patients [3,4]. However, limited data exists regarding the effectiveness of this therapy for pregnant women, as well as regarding the indications for a medical abortion in mid-trimester as a treatment option.

Abbreviations: COVID-19, Coronavirus disease 2019; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; RT-PCR, Reverse transcription-polymerase chain reaction; CBC, Complete blood count; SpO2, Saturation of peripheral oxygen; Vt, Tidal volume; PEEP, Positive end expiratory pressure; FiO2, Fraction of inspired oxygen; CRP, C-reactive protein; CRRT, Continuous renal replacement therapy; ABG, Arterial blood gas; ARDS, Acute respiratory distress syndrome; HFNC, High-flow nasal cannula; ECMO, Extracorporeal membrane oxygenation.

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2. Case Presentation

A 37-year-old woman (G2P1) with no previous medical history was admitted to intensive care in 2021 at 23 weeks of gestation. She complained of a one-day history of fatigue and dyspnea, followed by a positive result on a real-time reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2. On admission, she was alert and well oriented. Her vital signs were normal; she was apyretic but mild dyspnea was noted, with the respiratory rate at 20 breaths per minute. Physical examination revealed diffuse crackles over both lungs and a saturation of peripheral oxygen (SpO2) at 89% in room air. The diagnosis of COVID-19 pneumonia was made at this time.

The patient received oxygen delivery through a nasal cannula at 3 l per minute, which then doubled to 6 l per minute. She was treated with dexamethasone 4 mg/1 ml × 2 ampoules and amoxicillin/ clavulanic acid because of clinical suspicion of bacterial superinfection pneumonia. In addition, remdesivir 200 mg was initiated after informed consent was given by the patient; no abnormality was noted on her liver and renal function test. The complete blood count (CBC) showed mild normochromic normocytic anemia and thrombocytopenia with platelet count 140 G/L while the biochemistry profile included a bedside capillary glucose level of 148 mg/dl and hypokalemia, which was treated with potassium chloride 10%.

The obstetrics consultant concluded that no obstetric intervention was needed at the time. However, the patient's clinical condition deteriorated quickly. Her respiratory rate increased to 25 breaths per minute accompanied with accessory muscle involvement, leading to her SpO2 levels fluctuating between 80% and 90%. Consequently, her oxygen supplementation was upgraded to an oxygen mask with a reservoir bag at 12 l per minute. Due to her rapid clinical decompensation, there was a clinical suspicion of hyperinflammatory response, although her ferritin level was later at 237.4 ng/ml, just a bit higher than the normal range. An increasing corticosteroid dose was initiated with methylprednisolone 125 mg × 3 vials.

On the morning of hospital day 2, the patient was still in severe respiratory failure with combined respiratory and metabolic acidosis (Table 1). Her bad response to the oxygen supplementation led to endotracheal intubation, with the initial ventilator settings of tidal volume (Vt) 350, positive end expiratory pressure (PEEP) 10, fraction of inspired oxygen (FiO2) 100%. She continued to be treated with remdesivir and methylprednisolone 125 mg × 4 vials. Enoxaparin was added and antibiotics were upgraded to piperacillin/tazobactam. Her SpO2 was still so low that an alveolar recruitment maneuver with high PEEP at 16 cm H_2O was needed to increase it to 88% - 90%. The diagnosis of acute respiratory failure due to severe COVID-19 pneumonia was made at this time. Her ferritin level changed insignificantly but a high C-reactive protein (CRP) level was recorded, 108.13 mg/dl. Later, due to continued decline of her clinical status, the patient was indicated for continuous renal replacement therapy (CRRT) to resolve the cytokine storm. Her capillary blood glucose fluctuated between 152 and 162 mg/dl.

The CRRT ended the next day (hospital day 3) and her condition was reassessed. Her vital signs were insignificant except for a respiratory rate of 24 breaths per minute and a SpO2 at 90%. The ABG readings revealed respiratory acidosis (Table 1) and the CRP level decreased to 71.34 mg/l. Her hypokalemia had been corrected but her platelet count was still low. Physical examination revealed peripheral edema and low urine output. She continued to receive remdesivir, while the pulse corticosteroid dose was doubled to 125 mg methylprednisolone x 8 vials. Her circulatory overload persisted, with evidence of a dilated inferior vena cava on ultrasound, which was then treated with furosemide. On the same day, an obstetrics consultant came to a decision to terminate the pregnancy to improve the mother's clinical condition. As the patient was still in an induced coma for the mechanical ventilation, informed consent was taken from her legal guardians, including both her parents and her husband. An ultrasound scan showed no fetal abnormality. The medical abortion was done by vaginal misoprostol 200 μg. The fetus was a male weighing 400 g, with no respiratory activity or heartbeat.

The next day, pulse corticosteroids and remdesivir were continued. Her SpO2 was 93% and her acid-base disorder had improved (Table 1). Her urine output increased to 4600 ml. Diffuse alveolar infiltrates at the bottom of both lungs evident on chest X-ray (Fig. 1), along with a good response to high PEEP ventilation, had led to a diagnosis of acute respiratory distress syndrome (ARDS). On this day, the patient received one more session of hemodialysis.

The next morning, her SpO2 increased to 97% with Vt 350 ml, PEEP 16 and FiO2 55%. Due to her significant clinical improvement, the pulse corticosteroid dose was reduced to 125 mg methylprednisolone x 4 vials, which was then gradually reduced to standard dose (dexamethasone 4 mg/1 ml × 2 ampoules). Remdesivir was discontinued. In the next three days, the PEEP and FiO2 setting gradually decreased to 8 and 40%, respectively, while she continued to be treated with enoxaparin. Furosemide therapy was also maintained until her circulatory overload had resolved.

On hospital day 8, the patient was extubated and the corticosteroid dose was gradually reduced (see Table 2). Her SpO2 was maintained at 97–98% on highflow nasal cannula (HFNC) and her level of consciousness returned to normal. Oxygen delivery via nasal cannula was gradually decreased.

On hospital day 11, her real-time RT-PCR result for SARS-CoV-2 was negative. Her hemoglobin, platelet concentration and blood glucose rose to normal values, while her CRP level decreased to 17.45 mg/dl. Two days later (hospital day 13), the oxygen therapy was stopped and the patient was still able to get a SpO2 of 94–96% in room air. Her chest X-ray showed remarkable radiological improvement (Fig. 2).

A repeat negative test result led to her discharge on hospital day 16. At follow-up 17 days after discharge, she had fully recovered and the evidence of past pneumonia had nearly resolved (Fig. 3).

Table 1
Arterial blood gas (ABG) readings between hospital day 2 and hospital day 4.

Arterial blood gas	Hospital day 2	Hospital day 3	Hospital day 4
pH	7.252	7.19	7.4
pCO2 (mmHg)	45.9	67.1	46.1
PO2 (mmHg)	80	40	67
HCO3- (mmHg)	20.2	25.7	31.6

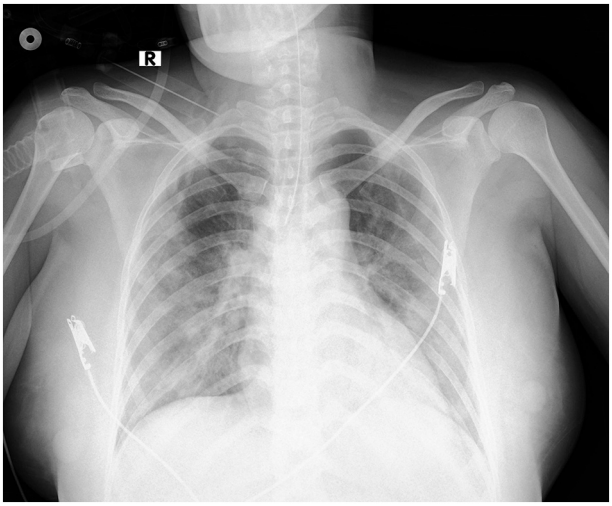

Fig. 1. Chest X-ray taken on hospital day 4.

Table 2
Summary of corticosteroid use during hospitalization.

Date	Corticosteroid use
Hospital day 1	Dexamethasone 4 mg/1 ml × 2 ampoules Methylprednisolone 125 mg × 3 vials
Hospital day 2	Methylprednisolone 125 mg × 8 vials
Hospital day 3	Methylprednisolone 125 mg × 8 vials
Hospital day 4	Methylprednisolone 125 mg × 8 vials
Hospital day 5	Methylprednisolone 125 mg × 4 vials
Hospital day 6	Methylprednisolone 125 mg × 4 vials
Hospital day 7	Methylprednisolone 40 mg × 2 vials
Hospital day 8	Dexamethasone 4 mg/1 ml × 2 ampoules
Hospital day 9	Dexamethasone 4 mg/1 ml × 2 ampoules
Hospital day 10	Corticosteroids use ended

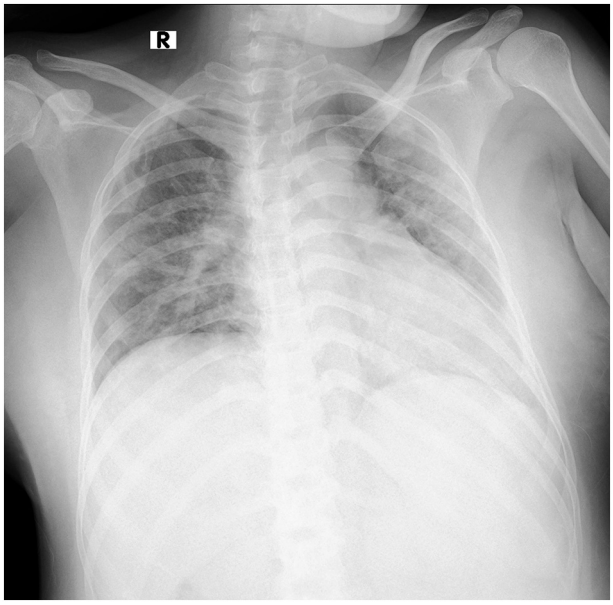

Fig. 2. Chest X-ray taken on hospital day 13.

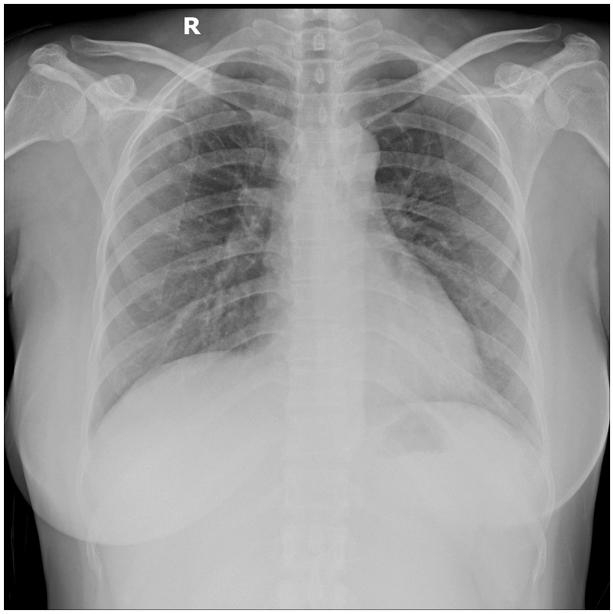

Fig. 3. Chest X-ray taken at follow-up 17 days after discharge.

3. Discussion

Pregnant women are considered a high-risk group, due to their specific immunological changes during gestation [5]. Pregnant women can experience severe COVID-19, with admission to an ICU, a need for extracorporeal membrane oxygenation (ECMO) and invasive ventilation. They are also more likely to deliver preterm and their neonates are also more likely to be admitted to a neonatal ICU [6].

The RECOVERY trial and RCOG deduced that pregnant women should receive oral prednisolone or intravenous hydrocortisone, especially in moderate to severe COVID-19 [7]. However, according to Saad et al., prednisolone is preferred because it has proven efficacy in acute lung injury and its placental transfer is limited [8]. Moreover, it is better metabolized by the placenta, which helps alleviate corticosteroids' adverse effects on the fetus [9]. That is why prednisolone is a viable option, as in our case. Pulse therapy in this patient was initiated soon, based on her rapidly worsening clinical status and increased CRP level, not her ferritin. Women are at increased risk of iron-deficiency anemia during pregnancy [10]; moreover, serum ferritin is at a maximum at 12–16 weeks of gestation; it then falls due to hemodilution and mobilization of iron stores [11]. This means that the ferritin level in a pregnant woman should be cautiously interpreted. To aid the interpretation of ferritin concentration, concurrent measurement of an acute phase response protein, which is commonly CRP, is recommended by the WHO [12]. In this patient, this application of pulse corticosteroids helped reduce the CRP level and improve the mother's clinical condition, especially after the medical abortion.

In this case, the relatively high PEEP setting is worth discussing. It is well known that COVID-19 pneumonia can be of a "non-ARDS" type, characterized by a dissociation between the severity of the hypoxemia and the maintenance of relatively good respiratory mechanics [13]. This type of pneumonia lacks the prerequisite for higher PEEP to work (lung recruitability): the PEEP level should be limited to 8–10 cmH2O since higher levels can cause decreased pulmonary compliance and right heart function. However, in our patient, a higher PEEP was needed to get an acceptable SpO2 value. Her gestational status could be a cause of decreased respiratory mechanics, expressed by her significant improvement after pregnancy termination. Our patient's acute respiratory failure was actually the classic ARDS and she responded well with high PEEP ventilation. ARDS occurs as a complication of COVID-19 in 32.8% cases [14].

Medical abortion in this case was a turning-point. Mid-trimester termination is a real challenge, even in non-COVID and non-intubated patients. To our knowledge, there are very few case reports about this indication in pregnant women infected with SARS-CoV-2, especially in the second trimester, as in this case. One such case was reported by Abu-Yaqoub et al. in 2021 [15]. The decision is made according the mother's clinical condition, as well as the risks of preterm delivery, fetal growth restriction or even stillbirth. The improvement after abortion in the present case may be related to uterine decompression and improved lung compliance [14].

Despite the successful management of our case, it still has some limitations. Because of a lack of resources, we were unable to monitor closely all the complications of pulse corticosteroid therapy (besides blood glucose), or the viral load after treatment with remdesivir. Nevertheless, our case adds information on COVID-19 presentation in the second trimester of pregnancy and management with pulse corticosteroid therapy combined with pregnancy termination.

Contributors

Thinh N. Bui was responsible for the conceptualization of the report, was directly involved in patient care, and reviewed and revised the final version of the manuscript.

Nhat M. Huynh contributed to data acquisition, was directly involved in patient care, and reviewed and revised the final version of

the manuscript.

Nguyen-Huy Do-Tran was responsible for the conceptualization of the report, generated the first draft, and reviewed and revised the final version of the manuscript.

Hoang-Anh Ngo was responsible for the conceptualization of the report, contributed to data acquisition, and generated the first draft.

Hung Tran was directly involved in patient care, and reviewed and revised the manuscript.

Nhan T. Nguyen was directly involved in patient care, and reviewed and revised the final version of the manuscript.

Tung T. Pham was directly involved in patient care, and reviewed and revised the final version of the manuscript.

Kha D. Le was directly involved in patient care, and reviewed and revised the final version of the manuscript.

Thu-Anh Nguyen was responsible for the conceptualization of the report, generated the first draft, and reviewed and revised the final version of the manuscript.

All authors read and approved the final version of the manuscript.

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Patient consent

Obtained.

Provenance and peer review

This article was not commissioned and was peer reviewed.

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Conflict of interest statement

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

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