



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal Pre-proof

Critical respiratory failure in pregnancy complicated with COVID-19: A case report

Yukiko Chinen, Yoshino Kinjyo, Keiko Mekar, Tadatsugu Kinjo, Yuuri Higure, Takeshi Kinjo, Kazuya Miyagi, Hisako Yamada, Hitoshi Masamoto, Hideki Goya, Tomohide Yoshida, Sakiko Maeshiro, Masashi Nakamatsu, Jiro Fujita, Yoichi Aoki



PII: S2214-9112(21)00027-8

DOI: <https://doi.org/10.1016/j.crwh.2021.e00309>

Reference: CRWH 309

To appear in: *Case Reports in Women's Health*

Received date: 3 March 2021

Revised date: 17 March 2021

Accepted date: 19 March 2021

Please cite this article as: Y. Chinen, Y. Kinjyo, K. Mekar, et al., Critical respiratory failure in pregnancy complicated with COVID-19: A case report, *Case Reports in Women's Health* (2018), <https://doi.org/10.1016/j.crwh.2021.e00309>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2018 Published by Elsevier.

Critical respiratory failure in pregnancy complicated with COVID-19: A case report

Yukiko Chinen¹, Yoshino Kinjo¹, Keiko Mekar¹, Tadatsugu Kinjo¹, Yuuri Higure², Takeshi Kinjo², Kazuya Miyagi², Hisako Yamada¹, Hitoshi Masamoto¹, Hideki Goya³, Tomohide Yoshida³, Sakiko Maeshiro⁴, Masashi Nakamatsu^{2,4}, Jiro Fujita^{2,4}, Yoichi Aoki^{1,*} yoichi@med.u-ryukyu.ac.jp

¹Department of Obstetrics and Gynecology, Graduate School of Medicine, University of the Ryukyus, 207 Uehara Nishihara, Okinawa 903-0215, Japan

²Department of Infectious, Respiratory, and Digestive Medicine, University of the Ryukyus, 207 Uehara Nishihara, Okinawa 903-0215, Japan

³Department of Pediatrics, Graduate School of Medicine, University of the Ryukyus, 207 Uehara Nishihara, Okinawa 903-0215, Japan

⁴Infection Control Team, University of the Ryukyus Hospital, 207 Uehara Nishihara, Okinawa 903-0215, Japan.

***Corresponding author:** Department of Obstetrics and Gynecology, Graduate School of Medicine, University of the Ryukyus. 207 Uehara Nishihara, Okinawa 903-0215, Japan.

Abstract

The case is presented of a 29-year-old primiparous woman who was COVID-19-positive at 34 weeks of gestation and who developed severe acute respiratory distress syndrome. After a four-day history of fever and mild dyspnea, she was referred to hospital. Ciclesonide, dexamethasone, heparin sodium, and sulbactam/ampicillin were initiated, followed by remdesivir and tocilizumab. On the

fourth day after admission (at 34 weeks 5 days of gestation), respiratory failure required ventilator management. An emergency cesarean section was performed and a 2565-g male infant was delivered with an Apgar score of 8/8 and negative COVID-19 status. However, on the following day the patient's respiratory condition deteriorated and mechanical ventilation was initiated. Subsequently, her respiratory condition quickly improved and mechanical ventilation was terminated 4 days after intubation. She was discharged 12 days after cesarean delivery. Our case provides additional evidence that raises concerns regarding the unfavorable maternal consequences of COVID-19 infection during pregnancy.

Keywords

COVID-19, pneumonia, pregnancy, respiratory failure

Introduction

Coronavirus disease 2019 (COVID-19) can cause rapid progression of viral pneumonia, leading to acute respiratory distress syndrome (ARDS) requiring intubation. In the early period of the COVID-19 pandemic, the limited data that were available on COVID-19 infection in pregnancy indicated largely mild disease and good treatment outcomes with infections in the third trimester [1]. However, recent reports have demonstrated that COVID-19 infection during pregnancy is associated with increased risks of hospitalization, admission to an intensive care unit (ICU), and management with mechanical ventilation, but not with death [2]. Nevertheless, maternal deaths due to COVID-19 have been reported in the second or third trimesters [3]. Moreover, pregnant women may be at an increased risk of illness from COVID-19 compared with

nonpregnant women. Preexisting comorbidities, high maternal age, and high body mass index seem to be risk factors for severe COVID-19. Rates of preterm birth are higher in pregnant women with COVID-19 than in pregnant women without the disease [4]. Pregnant women with COVID-19 who experience respiratory failure present multiple management challenges.

Here, the case of a COVID-19-positive, 29-year-old primiparous Japanese woman at 34 weeks of gestation presenting with severe respiratory compromise is presented. She experienced critical respiratory failure. Her clinical course and medical management are described.

Case presentation

A 29-year-old primiparous woman (body mass index 27.5 kg/m²) was referred to university hospital at 34 weeks and 2 days of gestation because of a positive throat swab for severe acute respiratory syndrome coronavirus 2 on quantitative real-time polymerase chain reaction. The patient had a 4-day history of fever and dyspnea. On admission, her body temperature was 39.0°C and saturation O₂ (SpO₂) was 95% (room air). A chest computed tomography (CT) scan revealed bilateral multifocal ground-glass opacities with partial consolidation, corresponding to COVID-19 pneumonia (Figure 1). Laboratory data showed a white blood cell (WBC) count of 8800/μL, lymphocyte 12.4%, C-reactive protein (CRP) 3.54 mg/L, D-dimer 2.3 μg/mL (<1.0 μg/mL), and IL-6 487 pg/ml (<4.0). Maternal laboratory values during the course of treatment are presented in Table 1, and the timeline of her treatment is detailed in Figure 2. Ciclesonide inhalation 400 μg/day, dexamethasone 6.6 g/day, heparin sodium 10,000 U/day, and sulbactam/ampicillin 6 g/day were initiated. On the second day after

admission, the patient continued to have high fever with chill and shivers, and her dyspnea worsened. SpO₂ was 95% with a 1 L/min oxygen flow through nasal cannula. Remdesivir 200 mg/day and tocilizumab 8 mg/kg were administered on the next day. On the fourth day after admission (at 34 weeks and 5 days of gestation), her respiratory condition rapidly worsened, and the SpO₂ was 94%–95% with a 3–4 L/min oxygen mask. Laboratory data showed WBC count of 9000/μl, lymphocyte 11.5%, CRP 10.41 mg/L, and D-dimer 1.5 μg/mL, and chest CT findings showed rapid deterioration (Figure 1). The patient's respiratory failure required ventilator or extracorporeal membrane oxygenation (ECMO) management.

It was believed that delivery might decrease maternal oxygen consumption and improve lung mechanics. In addition, it would be easier to manage the patient's breathing after delivery. An emergency cesarean section was performed in the negative-pressure operating room under spinal anesthesia, and a 2565-g male infant was delivered with an Apgar score of 8/8 and pH 7.295 of the umbilical artery. The newborn was admitted to the negative pressure room of the neonatal ICU. The patient's fever subsided, but her SpO₂ remained at 94%–95%, even with a 10L/min oxygen mask on the day after the cesarean section. The patient's respiratory condition deteriorated, and pneumonia findings on chest CT had worsened, showing rapidly increased consolidation with air bronchogram in both lung fields. The patient was subsequently intubated and put on mechanical ventilation at the ICU. The initial conditions for the mechanical ventilation were as follows: tidal volume 400 mL, respiratory rate 16 breaths/min, positive end-expiratory pressure 15 cm H₂O, and fraction of inspired oxygen (FiO₂) 100%. The ventilator setting and arterial blood gas analysis are shown in Table 2. The patient's respiratory condition quickly improved; she was successfully

taken off mechanical ventilation 4 days after her first day of intubation and was discharged 12 days after cesarean delivery. She did not develop sepsis, renal failure, stroke, thromboembolism or cardiomyopathy during the course of treatment. There was no evidence of maternal or fetal vascular malperfusion or acute or chronic inflammatory pathology in the placenta. The infant's breathing and circulation were stable, and chest X-ray showed no abnormal findings. Nasal swabs for SARS-CoV-2 were negative at 24 and 60 h postpartum.

Discussion

Our case provides additional evidence that raises concerns regarding the possibility of unfavorable maternal consequences of COVID-19 infection during pregnancy [5-7]. Although most mothers infected with COVID-19 have mild disease that does not require treatment, it has been reported that a number of mothers have been admitted to the ICU and some patients have required ECMO [3, 8-10].

On admission, our patient seemed to have mild to moderate disease; however, 3 days later, her disease progressed rapidly, and the respiratory failure was considered to require ventilator or ECMO management. The rationale for early delivery, at 34 weeks of gestation, by cesarean section included the opportunity to safely transport the patient to the operating room and the assumption that delivery could decrease maternal oxygen consumption and improve lung mechanics. In addition, delivery made it easier to manage the patient's breathing. It has been speculated that changes in cardiovascular function and immune response during pregnancy exacerbate COVID-19 infection [11]. Physiological changes during pregnancy reduce the mother's resistance to infection [12]. In addition, anatomical changes (e.g., an increase in the transverse diameter of the

thorax with diaphragmatic elevation) lead to maternal vulnerability to hypoxic conditions [13]. Vasodilatation and changes in pulmonary volume can induce mucosal edema and increased upper-airway secretions. Furthermore, changes in cell-mediated immune capacity during pregnancy increase pregnant women's susceptibility to viral infections [14]. These findings have important implications for both the severity and quick progression of the disease and rapid improvement after delivery.

After cesarean section, the patient's fever quickly remitted; however, her respiratory condition deteriorated, and the pneumonia findings on chest CT worsened. Re-expansion of the lungs and increased blood volume in the reflux circulation after delivery might have contributed to the deterioration of these conditions. Accordingly, the patient was placed on mechanical ventilation in the ICU. However, the patient was no longer pregnant and she experienced successful and rapid improvement 4 days after the start of intubation. She was discharged with her baby 12 days after cesarean delivery. The infant had an uneventful course without transplacental or vertical transmission of COVID-19 [15].

The timing of delivery should be determined by considering the progression of acute respiratory distress syndrome and age of gestation. Because the risk factors for obstetric patients of progression to severe disease, ICU care or maternal death remain unknown [3, 10], it is unclear whether it is better to wait for maternal decompensation. Our patient was already at 34 weeks of gestation, which was adequate for fetal lung maturation. Delivery before maternal decompensation might have been an option. Pregnant women should be considered vulnerable persons for whom exposure to COVID-19 must be prevented by all means.

This case report provides additional evidence that raises concerns about the unfavorable maternal consequences of COVID-19 infection during pregnancy.

Contributors

Yukiko Chinen drafted the manuscript.

Yoshino Kinjyo contributed to the review and editing of the manuscript.

Keiko Mekarū contributed to the review and editing of the manuscript.

Tadatsugu Kinjo contributed to the review and editing of the manuscript.

Yuuri Higure contributed to the review and editing of the manuscript.

Takeshi Kinjo contributed to the review and editing of the manuscript.

Kazuya Miyagi contributed to the review and editing of the manuscript.

Hisako Yamada contributed to the review and editing of the manuscript.

Hitoshi Masamoto contributed to the review and editing of the manuscript.

Hideki Goya contributed to the review and editing of the manuscript.

Tomohide Yoshida contributed to the review and editing of the manuscript.

Sakiko Maeshiro contributed to the review and editing of the manuscript.

Masashi Nakamatsu contributed to the review and editing of the manuscript.

Jiro Fujita contributed to the review and editing of the manuscript.

Yoichi Aoki drafted the manuscript.

All authors contributed equally to the creation of this case report.

Conflict of interest

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

Funding

No funding from an external source supported the publication of this case report.

Patient consent

Consent was obtained from the patient after she regained capacity.

Provenance and peer review

This case report was peer reviewed.

Acknowledgement

The authors would like to thank Enago (www.enago.jp) for the English language review of this article.

References

1. 1. Chen L, Li Q, Zheng D, et al. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China. *N Engl J Med* 2020 Jun 18;382(25):e100. doi:10.1056/NEJMc2009226. Epub 2020 Apr 17. PMID: 32302077; PMCID: PMC7182016.
2. 2. Ellington S, Strid P, Van Tong T, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by

Pregnancy Status — United States, January 22–June 7, 2020 *Weekly* / MMWR
Morb Mortal Wkly Rep 2020 June 26; 69(25):769–775.

3. 3. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19. *Am J Obstet Gynecol* 2020 Jul;223(1):109.e1-109.e16. doi:10.1016/j.ajog.2020.04.030. PMID: 32360108; PMCID: PMC7187838.
4. 4. Allotey J, Stallings E, Bonet M, et al. for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020 Sep 1;370:r3320. doi:10.1136/bmj.m3320.
5. 5. Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. *Viruses* 2020 Feb 10;12(2):194. doi:10.3390/v12020194. PMID: 32050635; PMCID: PMC7077337.
6. 6. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;395(10226):809–15.

7. 7. Breslin N, Baptiste C, Miller R, et al. COVID-19 in pregnancy: early lessons. *Am J Obstet Gynecol MFM* 2020 May;2(2):100111. doi:10.1016/j.ajogmf.2020.100111. PMID: 32518902.
8. 8. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARSCoV-2 infection during pregnancy. *J Infect* 2020;S0163-4453:30109–2.
9. 9. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS- CoV-2 infection during pregnancy. *J Infect* 2020;S0163-4453:30109
10. 10. Andrikopoulou M, Madden N, Weir T, et al. Symptoms and Critical Illness Among Obstetric Patients With Coronavirus Disease 2019 (COVID-19) Infection. *Obstet Gynecol* 2020 Aug;136(2):291-299. doi:10.1097/AOG.0000000000003996. PMID: 32459701.
11. 11. Zaigham M, Anderson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand* 2020 Jul;99(7):823-829. doi:10.1111/aogs.13867. doi:10.1111/aogs.13867.
12. 12. Goodnight WH, Soper DE. Pneumonia in pregnancy. *Crit Care Med* 2005;33:S390-S397.
13. 13. O'Day MP. Cardio-respiratory physiological adaptation of pregnancy. *Semin Perinatol* 1997;21:268-275.

14. 14. Nelson-Piercy C. Respiratory disease. In: Handbook of Obstetric Medicine.

Boca Raton: CRC Press; 2015:371 p.

15. 15. Vivanti AJ, Vauloup-Fellous C, Prevot S, et al. Transplacental transmission of

SARS-CoV-2 infection. *Nat Commun* 2020 Jul 14;11(1):3572.

doi:10.1038/s41467-020-17436-6. PMID: 32665677; PMCID: PMC7360599.

Figure 1: (a) On admission of the patient at 34 weeks and 2 days of gestation, a chest computed tomography scan revealed bilateral multifocal ground-glass opacities with partial consolidation (arrows). (b) Chest computed tomography at 34 weeks and 5 days of gestation showed rapid deterioration.

Figure 2: Timeline of the patient's treatment.

Table 1 Maternal laboratory values during the course of treatment

Variable	Normal reference range	Admission	Day 4 (Emergency C/S)	Day 5 (Day after C/S)	Day 9 (5 days after C/S)
WBC count $\times 10^3/\mu\text{L}$	3.1-8.4	8.8	11.4	12.4	9.5
Neutrophil %	40-69	80.7	85.8	72.0	59.0
Lymphocyte %	26-46	12.4	11.5	7.0	30.0
Hemoglobin mg/dL	11.4-14.6	10.2	9.0	11.0	12.2
Platelet count $\times 10^3/\mu\text{L}$	138-309	190	172	179	398
Ferritin ng/mL	10-80	41.6		81.5	

	(1 day after C/S)	(2 days after C/S)	(3 days after C/S)	(4 days after C/S)
Ventilator Mode	ASV/PSV – ASV/SIMV	-----	-----	-----
FiO ₂	0.7 – 0.5 – 0.45	0.3	0.25	0.25
PEEP cm H ₂ O	15	15 – 10	10	7 – 5
pH	7.334	7.354		7.423
Pco ₂ mmHg	42.8	41.8		41.5
Po ₂ mmHg	77.0	101.0		93.1
HCO ₃ mEq/L	21.9	22.6		26.6
BE mEq/L	-3.0	-2.2		2.5
SAT %	95.2	97.5		

C/S; cesarean section, ASV; Adaptive Support Ventilation, PSV; pressure support ventilation, SIMV; synchronized intermittent mandatory ventilation

Highlights

- A COVID-19-positive woman at 34 weeks of gestation presented with respiratory failure.
- An emergency cesarean section was performed at 34 weeks and 5 days of gestation.
- The patient's respiratory condition deteriorated the following day.
- Mechanical ventilation was initiated and was terminated four days after intubation.
- The case illustrates the unfavorable maternal consequences of COVID-19 infection during pregnancy.