Severe pneumonia in a critically ill pregnant patient with COVID-19 infection: A case report

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Severe pneumonia in a critically ill pregnant patient with COVID-19 infection: A case report

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Abstract: Here, we report a critical case of maternal COVID-19 infection in the third trimester of pregnancy showing severe outcomes for mother and infant.

Keywords. COVID-19, Pregnant woman, Preterm delivery

Tweetable abstract COVID-19 infection in pregnancy may cause severe outcomes for mothers and infants. Early detection and initiation of appropriate management are crucial.

Introduction

The recent epidemic of novel coronavirus (COVID-19) that started from Wuhan, China, has continued to receive worldwide attention since the initial reports in December 2019.[1] To the best of our knowledge, the number of studies documenting the clinical condition of pregnant women with COVID-19 are few.[2,3] Moreover, reports on critically ill pregnant women with severe pneumonia are rare.[4] Pneumonia during pregnancy is associated with increased morbidity and mortality.[5] Previous studies have only described the general epidemiological findings, clinical presentation, and clinical outcomes of patients with COVID-19 pneumonia. However, specific information on critically ill pregnant patients is scanty.[2,3] Herein, we report the first case of a critically ill pregnant woman with COVID-19 pneumonia in her third trimester of pregnancy.

Case report

On Feb 1, 2020, a 31-year-old pregnant woman presented to our emergency department at the Affiliated Xiaolan Hospital, Southern Medical University, Zhongshan City having had fever for 3 hours and a 4-day history of sore throat and occasional dry cough. At the time of hospital visit, she was 35 weeks plus 2 days pregnant. She disclosed that she had returned to Zhongshan on January 24 after a family visit to Xiaogan,

Hubei Province, China. She also informed the doctor that she had self-isolated at home immediately after returning from Xiaogan as advised by the Chinese government.

On January 28, 4 days after she returned to Zhongshan from Hubei Province, she developed a high fever. Her body was generally weak, and she had dry cough and sore throat, without dyspnea, expectoration, chest pain, or diarrhea. Physical examination recorded a body temperature of 39.3°C, blood pressure of 118/66 mmHg, pulse of 128 bpm, respiratory rate of 23 bpm, and oxygen saturation of 97% under room air, and a fetal heart auscultation of 160 bpm. No jaundice, bleeding dot nor skin rash were found, but throat congestion and grade I bilateral tonsil swollen were seen. Lung auscultation revealed moist rales in the lower left lung. Chest radiography was not performed after admission because the patient and her family members were concerned about the effects of radiation on the fetus. Complete blood count (CBC) after admission showed normal white-cell count (6.8×10^9/L, normal range $3.5\tilde{}9.5\times10^9$/L), low lymphocyte count (0.884×10^9/L, normal range $1.1\tilde{}3.2\times10^9$/L), normal hemoglobin (110×10^9/L, normal range 110˜150g/L) and normal platelets (160×10^9/L, normal range $125\tilde{}350\times10^9$/L) . Real-time RT-PCR tests for influenza A and B viruses using nasopharyngeal swab samples were negative.

Although the patient reported that she had not travelled to Wuhan and had not come to contact with infected people during her travel to Hubei, the local and municipal health departments were immediately notified about her visit. Consequently, she was isolated, put on supplemental oxygen (delivered by nasal cannula at 1-2/L per minute) and received physical cooling. Supportive therapies and oseltamivir were administered as empirical therapy. Center for Disease Control and Prevention (CDC) staff from Zhongshan City and Guangdong Province recommended that she undergo a test for COVID-19 infection and in-situ isolation treatment on the basis of current Chinese CDC "persons under investigation" case definitions. Nasopharyngeal and oropharyngeal swab specimens were collected in accordance with Chinese CDC guidance and sent to Zhongshan Second People's Hospital (designated hospital in Zhongshan, China) for further confirmation. A multidisciplinary team (MDT) co-management was initiated by Xiaolan hospital, together with intensive care clinicians to manage her condition.

Four hours after admission, the patient complained of myalgia, nausea and vomiting with a body temperature of 39.4°C, pulse of 170 bpm, respiratory rate of 35 bpm, and her oxygen saturation values dropped to 94% when breathing room air. At this time, she was put on oxygen flow support (delivered by nasal cannula at 4-6/L per minute), antipyretic therapy consisting of 600 mg of ibuprofen and continuous physical cooling. Seven hours after admission, the patient complained of left chest pain and mild breathing difficulty. Her oxygen saturation had decreased (SpO2 87% supplemental oxygen delivered through mask at 6˜8/L per minute). The patient and her family members agreed that she undergo a Chest CT scan under radiation protection. Unenhanced chest CT showed a large opaque patchy shadow in the lower lobe of the left lung. (Figure 1) During this time, laboratory tests showed leucopenia (white blood cell count: 1.8×10^9/L), hypopotassemia, impaired liver function, elevated levels of C-reactive protein and procalcitonin, creatine kinase and D-dimer. Blood gas analysis indicated respiratory failure, respiratory acidosis and metabolic acidosis. (Table 1) Fetal heart rate monitoring showed there was reactive NST (+), the baseline of fetal heart rate was 140 beats per minute, fetal heart rate fluctuated at 130˜170 beats per minute. (see Supplementary material, Figure S1)

Although her high fever had resolved, symptoms such as left chest pain, dizziness and shortness of breath, body temperature of 37.4°C, blood pressure of 100/50 mmHg, pulse of 170 bpm, and respiratory rate of 45 bpm were observed. Her oxygen saturation dropped to 80.8% even though she was put on supplemental high flow oxygen delivered at 10 15/L per minute via conventional mask. Thus, blood cultures were carried out. A diagnosis of COVID-19 pneumonia was made. In addition, severe pneumonia with acute respiratory distress syndrome (ARDS), septic shock, liver and renal dysfunction were detected. Oxygen therapy supplementation was changed to high flow nasal cannula (HFNC) oxygen therapy, with a concentration of oxygen 90%, flow rate of 60 L/min, and the temperature was controlled at 34. The patient received immediate respiratory and circulatory support, intravenous immunoglobulin, maintenance of internal stability, and antiviral treatment plus imipenem cilastatin sodium (by 1.0 g administered intravenously every 8 hours).

Given her changing clinical condition, the multidisciplinary management team decided to terminate her preg-

nancy as soon as possible. Preoperative continuous fetal heart rate monitoring result was reactive NST (+), the fetal heart rate fluctuated between 150 and 170 beats per minute. This heart rate dropped to 140 beats per minute half an hour before cesarean section. Caesarean section was performed under general anesthesia in a designated isolation room, by designated personnel with specialized infection control preparation and protective gear. A preterm male infant was delivered within 13 minutes, with a 1-minute APGAR score of 1. The baby was diagnosed with severe neonatal asphyxia and hypoxic-ischemic encephalopathy and neonatal resuscitation was applied immediately. Even with active resuscitation, the baby's APGAR score remained poor. (see Supplementary material, Table S1 to S2) The patient's family members requested termination of resuscitation, leading to the death of the baby two hours after birth.

For the patient, postoperative continuous supportive treatments comprising ventilatorassisted breathing, sedation, anti-infection (1.0 g imipenem cilastatin sodium administered intravenously every 8 hours combined with 0.5g levofloxacin administered intravenously every day), intravenous immunoglobulin, blood transfusion, and maintenance of internal environment stability was given. The patient's hypoxemia resolved, her blood pressure was 103/58 mmHg, pulse was 132 bpm, and oxygen saturation value was 100%. By this time, patient's nasopharyngeal swabs were positive for COVID-19 on real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) test. A diagnosis of critical COVID-19 pneumonia was confirmed. Once her vital signs stabilized, she was transferred to a designated hospital in Zhongshan, China by Feb 2, 2020. The patient's shock was corrected, heart, liver and kidney function improved. However, her lung condition deteriorated as a result of continuous aggravation, she received ECMO treatment on Feb 6, 2020. Patient's vital signs remained stable. (Figure 2) Results of follow-up treatment for the patient are pending.

Specimen testing for COVID-19

Initial respiratory specimens (nasopharyngeal and oropharyngeal swabs) collected from the patient on admission day tested positive for COVID-19. Results of blood culture on admission day revealed*Streptococcus parasanguinis* infection.

Discussion

This case report highlights evidence of severe outcomes of COVID-19 infection on the mother and infant. We describe lessons pertaining to the early management of pregnant women with COVID-19 infection. Pregnant women are susceptible to COVID-19, and are therefore likely experience severe adverse pregnancy outcomes. Pregnant women have a highly sensitive inflammatory response to viral respiratory infection. Infections during pregnancy rapidly progresses, especially in the middle and late stages of pregnancy, rendering pregnant women more likely to develop complications or even severe cases. This points to high risk of serious damage to the mother and/or infant. Thus, timely and appropriate management is crucial for pregnant women with COVID-19 infection.

For pregnant women suspected of COVID-19 infection, immediate chest CT examination is recommended before nucleic acid testing is performed. This is because chest CT examination can effectively perform early detection and evaluation of lung injury, which are early symptoms of COVID-19 pneumonia.[6] Notably, this should be performed after obtaining the patient's sufficient informed consent and implemented under necessary radiation protection measures for pregnant women.

Managing pregnant women in the context of COVID-19 epidemic remains extremely complex and challenging.[4] Given that viral pneumonia in pregnancy cause complications with potential to rapidly deteriorate, it is recommended that pregnant patients be isolated in a designated unit and co-managed by anti-infection teams, obstetrics, ICU and other related departments. Although treatments of COVID-19 pneumonia are similar for pregnant and non-pregnant patients, the condition of fetus should be carefully and closely monitored, as the clinical signs and symptoms may worsen along disease progression. In case the healthy condition of the pregnant woman becomes critical, her life should always be given priority, and possible termination of pregnancy should be considered. In this report case, the patient showed progressive decline in blood oxygen, and hypoxemia seemed difficult to correct even with progressive increase in oxygen therapy support. Her anoxic state improved after timely cesarean section. However, the sharp decrease in

blood oxygen concentration due to severe maternal respiratory complication resulted in acute fetal hypoxia leading to neonatal death. (see Supplementary material, Table S2)

Laboratory tests performed at admission revealed leukopenia and lymphopenia. However, the number and proportion of lymphocytes decreased sharply as the disease progressed. This implies that lymphocytopenia is a prominent feature of critically ill patients with COVID-19 infection, and may reflect the severity of this disease.[7] Other biochemical markers that were increased include serum levels of procalcitonin, IL-6 and serum amyloid A and thus may also indicate severity of COVID-19 infection. It worth noting that these inflammatory biomarkers are non-specific, thus they should be applied with caution when assessing pregnant patients with COVID-19. Given the lack of large cohorts of pregnant women with COVID-19 infection, we believe that lessons learnt from the present case are useful in guiding future management of such women.

Conclusion

COVID-19 infection in pregnancy may cause severe outcomes for mothers and infants. Early detection and initiation of appropriate management are therefore crucial. An important clinical manifestation of critically ill pregnant women infected with COVID-19 is the progressive decline in blood oxygen and hypoxemia that is difficult to correct even with supportive oxygen therapy. The degree of lymphocytopenia, markedly increased serum procalcitonin, IL-6 and amyloid A are prominent features of critically ill patients.

Disclosure of interests

All authors declare that they have no conflicts of interest.

Contribution to authorship

XW and DW drafted the first version of the manuscript. XW and SH were involved in conception, planning and carrying out of the case report and the present follow-up study and reviewed the manuscript. CB, MH, MS, WL, CC, XZ and JL were involved in planning, carrying out and analyzing the work in the present study. CB and JL were involved in the work in the present follow-up study. XW, DW, SH, CB, MH, MS, WL, CC, XZ and JL edited the manuscript, and read and approved the final version.

Details of ethics approval

This case study, including its publication, was approved by the Ethics Committee of Xiaolan Affiliated Hospital of Southern Medical University, Zhongshan, Guangdong Province, China. The patient's family members gave written consent on behalf of the patient for the permission to the publication of her clinical data (including the images).

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Figure and Table Legends

Figure 1. (A - E.) Unenhanced chest CT showing large opaque and ground glass patchy shadows in the lower lobe of the left lung.

Figure 2. Shown are the chest radiographs on day 2 and 21 after the onset of illness. The trachea was intubated and mechanical ventilation instituted in the period between the acquisition of the two images. (A) Ground glass density, (B) linear grid and patchy shadows were diffused in both lungs, no obvious pleural effusion was observed.

Table 1 . Clinical laboratory results of the patient.

Supporting Information

Figure S1. Fetal heart rate monitoring showing reactive NST (+), with a baseline of fetal heart rate of 140 beats per minute, fetal heart rate fluctuating at 130˜170 beats per minute.

Table S1. Baby's Apgar score.

Table S2. Clinical laboratory results of the newborn.

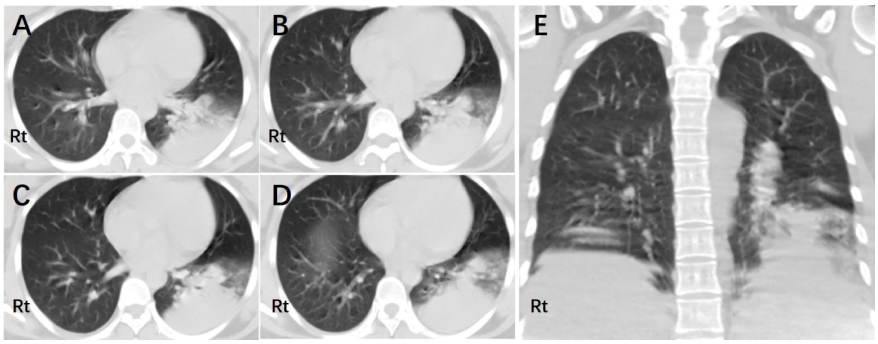

Table 1 . Clinical Laboratory Results Of The Patient.

Measure	Reference Rang	Specimen Collection Time					
		5:32	12:14	16:38	17:54	18:14	20:53
White-cell count (WBC,10^9/L)	3.5–9.5	6.8	1.8 ↓↓	-	2.2 ↓↓	-	1.1 ↓↓
Lymphocytes (LYMPHR,10^9/L)	1.1–3.2	0.884↓	0.223 ↓↓	-	0.242 ↓↓	-	0.069 ↓↓
Lymphocytes ratios (%)	20–50	13 ↓	12.4 ↓↓	-	11 ↓↓	-	6.3 ↓↓
Absolute neutrophil count (NEUT,10^9/L)	1.8–6.3	5.658	1.546 ↓	-	1.907 ↓	-	1.001 ↓
Neutrophil ratios (%)	40–75	83.2	85.9	-	86.7	-	91.0
Hemoglobin (HGB,g/L)	115–150, 110–150•	110	108, 105• ↓	93• ↓	103 ↓	122•	91, 91• ↓
Red-cell count(RBC,10^9/L)	3.8–5.1	3.48	3.34	-	3.27	-	2.80	-
Hematocrit (HCT,L/L)	35–45, 35–53•	32.5	30.8, 31•	27• ↓	30.9	36•	26.1, 27• ↓
Platelet count (PLT,10^9/L)	125–350	160	155	-	177	-	130
Sodium (mmol/L)	136–145, 135–145•	-	135, 137.5•	136•	135	135.3•	141, 141.20•
Potassium (mmol/L)	3.5–5.2, 3.6–4.8•	-	2.6, 2.370• ↓	3.07• ↓	3.2 ↓	2.95• ↓	3.1, 2.88• ↓
Chloride (mmol/L)	96–108, 95–105•	-	102, 114•	110•	104	110•	105, 112•
Calcium(mmol/L)	2.08–2.60, 1.15–1.35•	-	-, 0.68• ↓	0.87• ↓	1.8 ↓	1.01• ↓	0.78• ↓
Glucose (mmol/L)	3.90–6.10, 3.90–6.40•	-	5.15, 5.10•	5.8•	7.00	6.4•	7.05, 6.3•
Acidity (pH)	7.35–7.45•	-	7.403•	7.129• ↓	-	7.173• ↓	7.27• ↓
Corrected partial pressure of carbon dioxide (pCO2,mmHg)	35–45•	-	17.9• ↓	41.5•	-	35.70•	44.1•
Corrected partial pressure of oxygen (pO2,mmHg)	80–100•	-	61.8• ↓	60.3• ↓	-	104•	118.3•
Carbon dioxide content) (CO2,mmol/L)	23–29, 24–32•	-	11.4• ↓	14.7• ↓	11.6 ↓	14.1• ↓	17.1, 21.1• ↓
Base Excess(BE,mmol/L)	-3–3•	-	-11.7• ↓	-14.8• ↓	-	-14.8• ↓	-7.1• ↓
Anion gap (AG,mmol/L)	8–16•	-	15•	15.6•	-	15.3•	12.3•
Blood lactic acid (mmol/L)	0.5–2.0•	-	4• ↑↑	4.1• ↑↑	-	3.8• ↑↑	6.3• ↑↑
Blood urea nitrogen (BUN,mmol/L)	2.6–8.8	-	2.3	-	2.6	-	2.6
Creatinine (CRE,umol/L)	41–81	-	85 ↑	-	83 ↑	-	70
Alanine aminiotransferase (ALT,U/L)	7–40	-	142 ↑	-	130 ↑	-	123 ↑
Asparatate aminiotransferase (AST,U/L)	13–40	-	235 ↑	-	228 ↑	-	221 ↑
Lactate dehydrogenase (LDH,U/L)	120–250	-	259 ↑	-	351 ↑	-	350 ↑
Total bilirubin (TBIL,umol/L)	0–21.0	-	13.1	-	16.6	-	19.2
Total protein (TP,g/L)	65.0–85.0	-	55.3 ↓	-	56.4 ↓	-	50.9 ↓
Albumin (ALB,g/L)	40–55	-	29.4 ↓	-	33.1 ↓	-	31.1 ↓
Prealbumin (PAB,mg/L)	200–400	-	-	-	-	-	92 ↓
Creatine kinase (CK,U/L)	38–174	-	45	-	132	-	109
Cholinesterase–MB isozyme (CK-MB,U/L)	<24	-	17	-	75 ↑	-	83 ↑
N-terminal pro-brain natriuretic peptide (pg/ml)	<300	-	353.1	-	-	-	-
High sensitivity troponin (pg/ml)	<14	-	4.8	-	-	5.3	-
Prothrombin time (PT,S)	10.4–12.6	-	11.5	-	11.4	-	11.7
Thrombin time (TT,S)	16–21	-	21.1 ↑	-	58.8 ↑↑	-	28.7 ↑
International standardized ratio (INR)	0.85–1.20	-	0.99	-	0.98	-	1.01
Fibrinogen (Fbg,g/L)	2.0–4.0	-	4.42 ↑	-	3.32	-	3.03
D-dimer (ug/L)	<256	-	4743 ↑↑	-	4159 ↑↑	-	2576 ↑↑
C-reactive protein (CRP,mg/L)	<10.0	-	60.8 ↑	-	-	-	-
Procalcitonin (PCT,ng/ml)	<0.050	-	7.29 ↑ ↑	-	-	-	18.19 ↑ ↑
Interleukin-6 (IL-6,pg/ml)	<7.0	-	-	-	-	-	>5000 ↑ ↑
Serum amyloid A (SAA,mg/L)	<10	-	-	-	-	-	143.9 ↑ ↑

• Results are from blood gas analysis.
↑ The value in the patient was above normal.
↓ The value in the patient was below normal.