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Severe COVID-19 in a Postpartum Woman: A Three-Month Challenge with Convalescent Plasma and Corticosteroid

Zahra Soleimani[1,2], Sedigheh Hantoushzadeh[3], Azam Soleimani[4]*

1. Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.
2. Fetal Health Research center, Hope Generation Foundation, Tehran, Iran.
3. Valiasr Maternal Fetal Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran.
4. Cardiac Rehabilitation Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

***Corresponding author:** Azam Soleimani; **Email:** asoleimanii@gmail.com

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Abstract

Introduction: Management of seriously ill patients infected with new corona virus (SARS-CoV-2) is challenging especially in pregnancy and postpartum state.

Case presentation: A 39- year-old primigravid critically ill woman with acute respiratory distress (ARDS) due to confirmed SARS-CoV-2 infection underwent urgent cesarean delivery (a healthy neonate) at 33 weeks and 5/7 of pregnancy. She received treatments including hydroxychloroquine, antivirals and broad-spectrum antibiotics while she was intubated for mechanical ventilation. In spite of all treatments, she developed a critical course after the mild primary clinical improvement. Convalescent plasma transfusion as a rescue treatment was performed and led to an improvement in her general condition and delayed gradual recovery in respiratory function after two months.

Conclusion: The promising role of early treatment with convalescent plasma transfusion in seriously ill pregnant women infected with SARS-CoV-2, needs to be elucidated by further randomized studies.

Key words: Blood Component Transfusion; Convalescent Plasma Transfusion; COVID-19; Pregnancy; SARS-CoV-2

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INTRODUCTION

The new corona virus is known as "Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2)", responsible for COVID-19 disease originated in China and rapidly becomes a pandemic. Pregnant women are suggested to be at special risk with regard to attenuating immune system and are proposed to be at increased risk of adverse outcome (1). Management of seriously ill patients infected with new corona virus (SARS-CoV-2) is challenging especially in pregnancy and postpartum state. Multiple investigational agents have been introduced for critically ill patients with partial clinical response in most cases (2).

Convalescent plasma transfusion (CPT) containing antibodies of recovered patients has been reported to be promisingly responsive in the management of 80 Chinese patients with SARS pneumonia in 2003 (3). Although there are debates and concerns, the Food and Drug Administration (FDA) has approved this treatment for severe or life threatening cases with COVID -19 (4).

We presented a seriously ill COVID-19 infected pregnant patient with acute respiratory distress syndrome (ARDS) with supportive care and CPT.

CASE PRESENTATION

A 39-year-old primigravid otherwise healthy Iranian woman at 33 and 5/7 weeks of pregnancy was admitted to the hospital with complaints of dyspnea, fever and dry cough for 4 days. At presentation, she was ill and febrile (oral temperature: 38.8 °C), hypoxemic (hemoglobin O_2 saturation (SPaO2) of 88% on room air) with respiratory rate of 33/minute, stable blood pressure (130/80 mmHg) and tachycardia (heart rate:100 bpm).

Due to sepsis, fetal tachycardia (fetal heart rate: 170 bpm), breech presentation of the fetus, and concern for deterioration of patient's condition, the patient underwent an urgent cesarean delivery with spinal anesthesia under O2 therapy via face mask and while receiving first dose of antibiotics. A healthy neonate with an Apgar score of 7 in 5 minutes and negative pharyngeal sample for SARS-CoV-2 (taken just after delivery) was born.

Several hours after delivery, she was transferred to

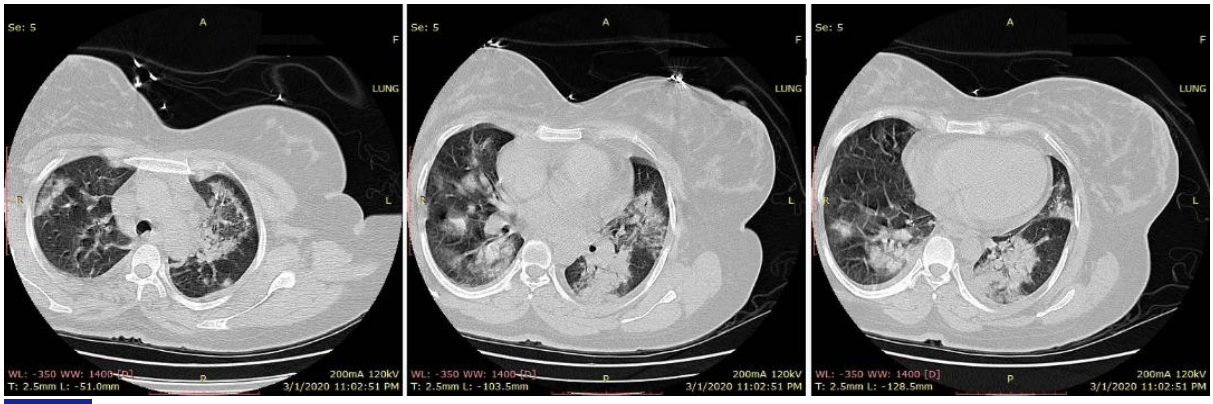

Figure 1: A mid thoracic slice of chest HRCT scan with multiple patchy ground glass infiltrations and small bilateral pleural effusion at admission.

the intensive care unit (ICU) due to persistent hypoxemia (SPaO2 of 60%) and severe respiratory distress, and underwent intubation with mechanical ventilation support (system mode: SIMV, FIO2:100%, rate:22/min, TV:300 ml, SPaO2 of 91%). Standard ICU care and prophylactic dose of enoxaparin were initiated. Due to a high clinical suspicion for COVID-19, lymphopenia and presence of multiple patchy ground glass opacities compatible with viral pneumonia on the lung computed tomography (CT) scan that was taken after intubation (figure 1), four drug regimens with hydroxychloroquine, Lopinavir /ritonavir, oseltamivir, and ribavirin were initiated based on that time guidelines of health ministry.

Wide spectrum antibiotics including azithromycin, levofloxacin, vancomycin and meropenem were administered sequentially due to poor clinical response, severe ARDS, persistent elevated inflammatory markers and significant leukocytosis with possible bacterial super infection, while nasopharyngeal swab for SARS-CoV-2 was reported to be positive (taken at admission). Fever, agitation, PaO_2/FIO_2<200, mild leukocytosis, progressive lymphopenia, rising lactate dehydrogenase (LDH), elevated C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) despite normal procalcitonin, normal liver enzymes and renal function were evident during the first week of admission. On hospital day (HD) 8, patient showed some clinical improvement, became afebrile and fully conscious, with $SPaO_2$ of 93% on FIO_2 sets at 60%. Soon after, she experienced deterioration in the clinical status

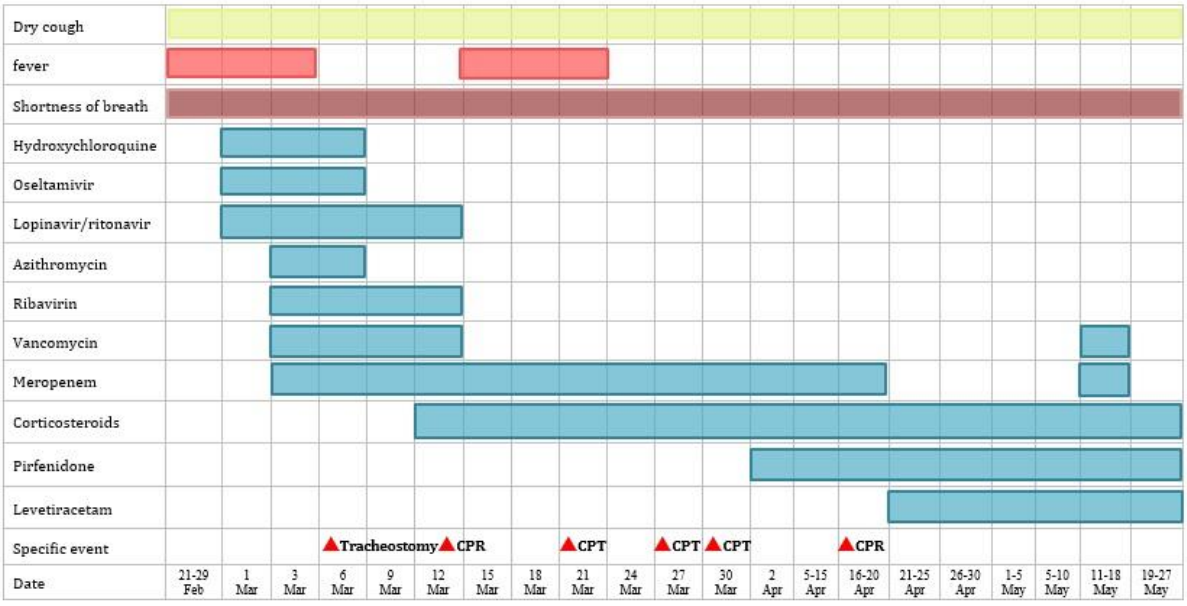

Figure 2: Timeline of disease course according to days from hospital admission. (CPR: cardiopulmonary resuscitation; CPT: convalescent plasma therapy)

Table 1: Clinical and laboratory findings of the patient before and after three sessions of plasma transfusion therapy

Variable	Reference range	HD 1 admission	HD21 Just before First CPT	HD 22 24h post CPT	HD25	HD29 Second CPT	HD30	HD32 Third CPT	HD33	HD35	HD 47	HD 60	HD 79
Fever (°C)	<37.3	38.8	38.5	37.6	37	37.3	37.1	37.2	37	36.5	36.7	37	37.1
Consciousness	-	C	A	A	C	C	C	C	C	C	A	A	C
PAO2/FIO2	-		120	110	167	68	105	90	70	120	75	140	210
Leukocyte count (×10³per µL)	3.9- 11.1	11.2	23.2	10.4	7.5	9.2	13.1	16.7	12.6	7300	11	8.4	7.2
Absolute neutrophil count (per µL)	-	9968	20603	8008	6315	6624	11528	14028	10478	5800	8954	5462	4896
Absolute lymphocyte count (per µL)	-	985	1322	1248	1050	1472	1074	1319	1441	1390	1551	2063	1749
Hemoglobin (g/dl)	11.6- 15.3	11.5	11.5	9.6	9.7	8.9	9.1	9.5	7.7	9.3	8.7	9.3	8.6
Hematocrit (%)	34- 46	33.7	37.7	31.4	31.4	28.5	31.2	30.5	25.3	31.3	27.2	29.1	25.9
Platelet count (×10³per µL)	155- 440	176	286	217	188	213	289	217	189	193	161	431	234
LDH (U/L)	207- 414	560	2215	1653	1118	1123	1411	2140	1849	1100	864	-	-
Procalcitonin (ng/ml)	<0.5	0.1	0.52	0.3	0.09	-	0.3	-		-	-	-	-
CRP (mg/L)	<5	10	11.2	9.3	10	10.3	10.1	10.7	9.8	7	18.2	7.3	19
ESR 1sth hour (mm/hour)	Up to 20	120	118	98	-	-	96	101	92	78	-	-	-
Interleukin-6 (pg/ml)	<0.5	-	8.1	14.9	-	-	36.8	-	-	-	-	-	-
Ferritin(ng/ml)	<5.9	-	633	493	-	-	766	-	-	-	-	-	
IgG (mg/dl)	5-148	-	1160	1057	-	-	818	-	-	-	-	-	

C: Conscious; A: Agitated; HD: hospital day; CPT: convalescent plasma therapy; IgG: immune globin G

with recurring fever, agitation, requiring frequent administration of sedatives, persistent hypoxemia on 90-100% of FIO_2 and some episodes of bradycardia. She finally developed asystole requiring cardiopulmonary resuscitation for 10 min on HD 12 (figure 2). Echocardiography performed three hours after resuscitation, showed preserved right and left ventricular systolic functions.

After that, she developed a critical course with fluctuating body temperature, escalating LDH levels and leukocyte counts, progressive lymphopenia and persistent low PaO_2/FIO_2, despite a full supportive ICU care and two pulses of methyl prednisolone followed by intravenous hydrocortisone in divided doses. Given her clinical deterioration, convalescent plasma transfusion, as a rescue treatment was decided to be infused after written informed consent was obtained from the patient and her family.

A suitable candidate for plasma donation was selected based on approved criteria (approval ID project: IR.TMI.REC.1398.031). Eventually 1500^{cc} of CPT was performed in three sessions on HD21, 29 and 32 (figure 2).

She did not experience any transfusion reaction or adverse events during the three CPT. Together with the clinical improvement, resolving of fever, gradual increase in PaO_2/FIO_2, laboratory results showed a decrease in the leukocytosis, the acceptable lymphocyte count and a constant decrease of in LDH, CPK, ESR and CRP levels after episodes of plasma infusion with no meaningful changes in serum ferritin, total immunoglobulin G (IgG) and interleukin 6 (IL-6) levels (table1). Packed red cells were transfused in four sessions for severe anemia (hemoglobin <7mg/dl) and pirfenidone as an anti-inflammatory and antifibrotic agent was started. Under full ICU care, after a period of fluctuations in PaO_2/FIO_2, she experienced the clinical and cognitive improvement and extubation on HD 70 and finally discharged on HD 88 on supportive oxygen therapy.

Discussion

Considering pregnancy as an immune-compromised state, implementing specific well-defined strategies and a multidisciplinary approach for management of COVID-19 in

obstetrics is highly recommended (5, 6). In a meta-analysis on 192 articles about COVID-19 in pregnancy, ICU admission, invasive ventilation and extracorporeal membrane oxygenation (ECMO) were more common in pregnant as compared with age-matched non-pregnant women with overall 339 death between 41664 women (1). Neutralizing antibody may suppress viremia via facilitating the clearance of the virus and reducing viral invasion to the host specific cells. The peak of viremia occurs in the first week of infection while the host immune response has a delay. It is suggested that better results may be obtained with early plasma transfusion (7). Eligible patients for CPT based on the FDA recommendation are those with confirmed COVID-19 exhibiting serious disease as" dyspnea, respiratory rate ≥ 30/min, SaO2 ≤ 93%, PaO2/FIO2 < 300, and/or infiltrations in more than half of the lung fields" or patients with life-threatening signs including "respiratory failure, septic shock, and/or multiple organ dysfunction" (4). CPT in a seriously ill post-partum woman with ARDS and septic shock due to SARS-CoV$_2$ infection was reported recently by Zhang B et al with favorable clinical outcome. In their study, postpartum patient underwent ECMO and continuous renal replacement therapy (CRRT) on HD 6. Convalescent plasma was transfused on HD 19 with extubation on HD40 and patient discharge on HD 46 (8). CPT has been used as a successful treatment, combined with corticosteroid for a midterm pregnant woman in our center (9). The case of this study, presented at beginning of the SARS-CoV-2 outbreak, without adequate evidence for COVID-19 treatments, became a candidate for CPT after failing most recommended drugs. Although promising results were achieved in her clinical condition based on blunting clinical severity, it seems that lung injury was more profound to respond to this immune therapy. Initiating this treatment earlier in the disease course may result in higher clinical benefits especially when the viral load is high as it was in this patient.

Conclusions

The promising role of early treatment with convalescent plasma transfusion in seriously ill pregnant women infected with SARS-CoV-2, needs to be elucidated by further randomized studies. Longstanding disease course with wax and wane respiratory function may be encountered in the clinical management of COVID-19.

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Authors' contribution

Dr Z. Soleimani was the main responsible physician of the patient and Dr S. Hantoushzadeh and Dr A. Soleimani were consultant physicians. All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

None declared.

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