CASE REPORT

Use of Remdesivir in severe COVID-19 Pregnant Patient

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Abstract

The current coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on our healthcare system. Still, very little is known about the treatment modalities in the context of severe COVID in pregnancy. We describe a case of a 28-year-old patient who presented with severe COVID-19 and was admitted to our intensive care unit (ICU) in her third-trimester pregnancy with a progressive increase in oxygen requirement. Remdesivir may prove beneficial in reducing the inflammatory response and controlling the direct viral damage due to severe COVID-19 pneumonia resulting in favorable maternal and fetal outcomes.

Keywords: COVID-19, High flow nasal cannula, Remdesivir, Third trimester.

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Introduction

As per Centers for Disease Control and Prevention recommendations, pregnant women are included in the "increased risk" category for COVID-19 illness. However, the absolute risk for severe COVID-19 is low. Still, this category of pregnant patients has an increased risk of ICU admission, need for mechanical ventilation and extracorporeal ventilatory support, and death compared with symptomatic nonpregnant women.[1] There are various reported cases in the literature where pregnant patients presented with COVID-19.[2] We report a case of a 28-year-old female pregnant patient who presented with severe COVID-19. She had a progressive increase in oxygen requirement in ICU. After initiating treatment with remdesivir, she had a favorable maternal and fetal outcome.

Case History

A 28-year-old gravida 2 para 1 was admitted to our ICU at 23 weeks and 4 days of gestation with complaints of sudden breathlessness. She was maintaining an oxygen saturation (SpO_2) of 88% at ambient air and her respiratory rate (RR) was 25 breaths/minute. The patient was tested for reverse transcriptase polymerase chain reaction positive at home, 5 days before admission. The patient had shortness of breath, anorexia, and reduced oral intake for the last 6 days. She had no coexisting comorbidities. She had a previous history of uneventful elective lower segmental cesarean section 4 years back with the delivery of an alive baby. Her vitals at the time of ICU admission were stable, and she maintained an SpO_2 of 95% on a non-rebreathing mask at an oxygen flow rate of 15 L/minute. The patient was started on methylprednisolone, enoxaparin, and other supportive treatment. On the 4th day, her SpO_2 dropped to 86%, and her RR increased to 35 breaths/minute. She was then kept on a high flow nasal cannula (HFNC) at 50 L/minute with a fraction of inspired oxygen (FiO_2) of 80%. Her chest X-ray demonstrated hazy bilateral opacities predominantly in the mid and lower lung zone and ill-defined haziness in both upper lung fields (Fig. 1).

We sent sputum culture because of bilateral hazy lung fields suggestive of hospital-acquired pneumonia. There were numerous gram-negative bacilli in sputum on gram staining. So, we escalated our antibiotics to piperacillin-tazobactam and clindamycin; we then discontinued methylprednisolone after giving it for the first 4 days. There was no fetal tachycardia, bradycardia, and signs of late decelerations on electronic fetal heart rate monitoring. We ruled out hemolysis, elevated liver enzymes, low platelets (hemolysis, elevated liver enzymes, and low platelets) syndrome, and preeclampsia. We started remdesivir after obtaining written informed consent from the patient's relative. Remdesivir was initiated on the 4th day of ICU admission as a 200 mg intravenous (IV) loading dose followed by a 100 mg IV daily dose for the next 4 days. We monitored the day-wise laboratory parameters shown in Table 1A. The trend of ABG (arterial blood gas) values after initiating remdesivir is shown in Table 1B. Gradually from the 6th day, the oxygen

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requirement was reduced, and the flow rate of the HFNC decreased to 20 L/minute. The patient was gradually weaned, and on the 12th day of ICU admission, she was maintaining an SpO2 of >95% on 3 L/minute of oxygen flow through by nasal cannula. On the 8th day, inflammatory markers followed a decreasing trend. Liver function tests and kidney function tests were within acceptable limits throughout the ICU stay.

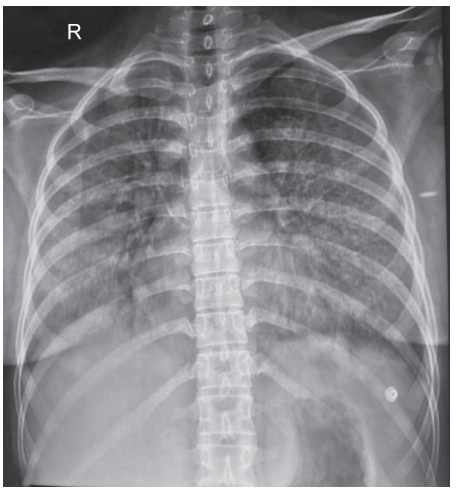

Fig. 1: Chest X-ray suggestive of COVID-19 pneumonia

Discussion

Remdesivir acts by inhibiting the viral nucleic acid synthesis and ribonucleic acid (RNA)—dependent RNA polymerase enzyme.[3] The promising result has been shown by the two major trials, the adaptive COVID-19 treatment trial-1 by the National Institutes of Health,[4] and the phase 3 randomized study to evaluate the safety and antiviral activity of remdesivir in participants with severe COVID-19 (SIMPLE) study by Gilead sciences,[5] for using remdesivir. The United States Food and Drug Administration issued an Emergency Use Authorization for using remdesivir for COVID-19 patients. Remdesivir administration in pregnancy is mainly based on a compassionate use basis. There are no reports of reproductive developmental toxicity in animals at clinically relevant doses of remdesivir (remdesivir investigator's brochure, Gilead sciences).[6]

During the year 2018, at the time of the Ebola crisis, the use of remdesivir was reported in six pregnant patients

Table 1A: Day wise laboratory parameters

Lab parameters	*Day 1*	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Day 6*	*Day 7*	*Day 8*	*Day 12*
Hb (13–16 g/dL)	9.2	8	8.1	8.4	8.8	9.2	9	9.3	10.9
TLC (4–10 × 10^3/µL)	11.37	10.34	12.88	11.83	13.11	13.13	17.52	14.86	8.76
Neutrophils (40–80%)	89.2	85	89.8	90	91.5	92.6	96	95.5	80
Lymphocyte (20–40%)	9.6	12.8	8.5	8.1	7.5	6.3	3.1	3.8	14
Eosinophils (1–6 %)	0	0	0	0	0	0	0.3	0.3	0.6
NLR ratio (<3.5%)	9	7	11	11	12	15	32	25	5.5
Platelet (150–450 × 10^3/µL)	190	186	214	258	321	295	358	307	321
Total bilirubin (0.3–1.2 mg/dL)	0.59	0.51	0.58	0.63	0.60	0.43	0.64	0.69	0.65
Direct bilirubin (0–0.2 mg/dL)	0.19	0.16	0.10	0.23	0.17	0.09	0.18	0.21	0.23
Indirect bilirubin (0–1 mg/dL)	0.40	0.35	0.48	0.40	0.43	0.34	0.46	0.48	0.42
ALT/SGPT (13–40 U/L)	27.2	31	30	47	93	63	135	103.3	67.3
AST/SGOT (0–37 U/L)	60	53	54	72	103	144	78	54.3	44.3
ALP (30–90 U/L)	51	52	62	78	81	35	89.6	110.1	103.1
Urea (13–43 mg/dL)	7.9	18.5	18.4	22.4	27	23	22.5	16	12
Creatinine (0.7–1.3 mg/dL)	0.39	0.38	0.53	0.44	0.48	0.48	0.40	0.40	0.23
Sodium (135–145 mEq/L)	143	141	140	139	139	140	140	137.75	132.45
Potassium (3.5–5 mEq/L)	4.03	4.21	4.45	4.26	4.32	4.65	4.47	4.39	3.25
IL-6 (<6.4 pg/mL)	16.3		31.4		121.2		228.6		14.98
Ferritin (22–325 ng/mL)	400.40	404.3	336.2		365.9		378		239
CRP(0–5 mg/L)	142.40		154.3		165.2		215		95
LDH (230–460 U/L)	705.49		906.20		880.3		1202		459
Procalcitonin (<0.2 ng/mL)	0.238		0.159		0.128		0.370		0.25
D-dimer (<0.2 µg/mL)	0.60	0.68	1.00		2.23		11.27	9.23	0.43
Mode of oxygenation	NRBM 15 L/minute FiO_2 70	NRBM 15 L/minute FiO_2 70	HFNC 80% FiO_2 50 L/ minute	HFNC 70% FiO_2 50 L/ minute	HFNC 60% FiO_2 40 L/ minute	HFNC 40% FiO_2 20 L/ minute	HFNC 40% FiO_2 20 L/ minute	HFNC 40% FiO_2 20 L/ minute	Nasal prong 3 L/ minute

Table 1B: Day wise ABG parameters

ABG	*Day 1*	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Day 6*	*Day 7*	*Day 8*	*Day 12*
pH (7.35–7.45)	7.449	7.453	7.457	7.444	7.436	7.428	7.352	7.36	7.48
PCO_2 (35–45 mm Hg)	27.9	28.1	31.9	33.8	35.4	32.9	31.6	31	28.9
PO_2 (80–100 mm Hg)	56.1	119.4	150.7	85	98.5	116.2	134.7	113.5	109.4
Lactate (<0.9 mmol/L)	0.6	0.9	0.7	0.6	1.1	1.2	2.2	2	1.1
HCO_3 (22–24 mmol/L)	19.5	19.8	22.8	23.4	24.2	21.9	17.7	19	19.8
P/F ratio (mm Hg)	80	199	215	121	164.1	290.5	336.7	283.7	405.1

Hb, hemoglobin; TLC, total leucocyte count; NLR, neutrophil-to-leucocyte ratio; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; ALP, alkaline phosphatase; CRP, C-reactive protein; LDH, lactate dehydrogenase; IL-6, interleukin-6; NRBM, non-rebreathing face mask; HFNC, high flow nasal cannula; NIV, non-invasive ventilation; CPAP, continuous positive airway pressure; P/F ratio, PaO_2/FiO_2 ratio

without evidence of any significant adverse events.[7] Burwick et al.,[8] on a compassionate use basis, administered remdesivir on 67 hospitalized pregnant patients (82% were ≥24 weeks gestation) with COVID-19 and concluded that 93% of patients recovered from their illness despite 67% requiring ICU admission. There may be an increased risk of ICU admission and mechanical ventilation, especially in a pregnant patient with features of COVID-19, as compared with nonpregnant women.

The minimal data available to date suggest that remdesivir is well tolerated in the latter stages (2nd/3rd trimesters) of pregnancy with a low risk of serious adverse events. In our case, we started remdesivir on the 8th day after the initial presentation of symptoms. After completing five doses, there was a marked decrease in O_2 requirement, and the patient was gradually weaned from the HFNC oxygenation. We observed no transaminitis due to remedesivir use. There were physiologic increases in the level of D-dimer from day 5 (2.23 µg/mL) to day 7 (11.27 µg/mL) and returned to below baseline on day 12 (0.43 µg/mL). Several studies demonstrated a steady increase of D-dimer and thrombus formation during pregnancy, primarily if it is associated with COVID-19.[9] Our patient showed no evidence of peripheral thrombus formation, although she had an elevated D-dimer. Thus, remdesivir administration in our patient had favorable clinical recovery. It may be considered a suitable antiviral option under these circumstances by assessing the risk and benefits for both mother and child. Before starting remdesivir, our patient was treated with methylprednisolone 1 mg/kg/day for 4 days, but her respiratory status had not improved, and elevation of inflammatory markers was consistent with cytokine storm. Although, as per our current institute protocol, we used to advise methylprednisolone for 10 days, we discontinued methylprednisolone earlier in our patient due to superimposed bacterial infection, which was ruled out later. We did not restart methylprednisolone as her oxygenation had improved.

Conclusion

Our case describes the role of remdesivir in reducing the inflammatory response and controlling the direct viral damage due to severe COVID-19 pneumonia resulting in favorable maternal and fetal outcomes. However, the results of a single case cannot be generalized, and large clinical trials are required to determine its role as a part of treatment modalities.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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