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The use of convalescent plasma therapy and remdesivir in the successful management of a critically ill obstetric patient with novel coronavirus 2019 infection: A case report

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SUMMARY

Remdesivir is a novel therapeutic with known activity against SARS CoV-2 and related coronaviruses. Remdesivir, as well as convalescent plasma therapy, are currently under investigation as potential therapies for patients with Coronavirus Disease 19 (COVID-19). In this case report we summarize the use of convalescent plasma therapy and then remdesivir as a late addition in the treatment of a critically ill obstetric patient with COVID-19. The patient subsequently improved, was extubated 5 days after initiation of remdesivir, was transitioned to room air 24 h later, and discharged at the completion of remdesivir therapy.

1. Introduction

Since first being identified in December 2019, the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread around the globe and viable therapeutic options are an area of great interest. At present there are nearly 3.5 million global cases of SARS-CoV-2, with nearly 250,000 deaths. Treatments are rapidly evolving during the time of this deadly pandemic and several drugs remain under investigation as potential therapies for critically ill COVID-19 patients. Proposed antiviral treatment options include hydroxychloroquine, remdesivir, and lopinavir/ritonavir, which are all safe in pregnancy [1]. Other potential therapies which are contraindicated in pregnancy include ribavirin and baricitinib [1]. Ribavirin has teratogenic properties; it induces miscarriages and leads to craniofacial and limb defects in mouse models [1,2]. Baricitinib has shown embryotoxicity in mouse models [1,3].

Remdesivir is a nucleoside analog that inhibits RNA-dependent RNA polymerase. Remdesivir has previously demonstrated in vivo activity against both Ebola virus [4] and Middle East respiratory syndrome (MERS-CoV) [5]. Remdesivir underwent in vitro testing early in the SARS-CoV-2 outbreak at the Wuhan Virus Research Institute, and was first used successfully in a US COVID-19 patient in January 2020 [6]. Early data on compassionate use of a 10-day course of remdesivir have shown a significant improvement in rates of extubation and reduction in mortality for COVID-19 patients [7] and randomized controlled trials to assess its efficacy more completely are ongoing both in the United States and abroad.

2. Case

A 35-year-old employee (G7P4115) of an inpatient hospice center presented to the hospital via transfer at 22 weeks and 2 days of gestation with a chief complaint of hypoxia in the setting of known SARS CoV-2 infection. The patient's past medical history was significant for type 2 diabetes mellitus, asthma, and class III obesity. The patient initially presented four days prior to an outside facility with a chief complaint of fever, cough, and myalgias. She tested positive for COVID-19. The patient was managed as an outpatient for four days until development of worsening dyspnea and hypoxia. At this time she was transferred and admitted to the teaching hospital for higher-level care.

On arrival at the hospital the patient was noted to be hypoxic and in respiratory distress with oxygen saturation of 86% on 6 l nasal cannula. The patient was admitted to the intensive care unit (ICU) and placed on high-flow non-invasive positive-pressure ventilation. Chest x-ray on admission showed extensive, bilateral consolidation suggestive of multifocal pneumonia, with more extensive disease visible in the left lung. Repeat chest x-ray performed 24 h later showed interval worsening of consolidation of alveolar opacities, consistent with both COVID-19 pneumonia and acute respiratory distress syndrome.

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Medical therapy was initiated with transfusion of COVID-19 convalescent plasma, rocephin 2 g intravenous (IV) daily and azithromycin 500 mg IV for concern for possible superimposed bacterial pneumonia. Hydroxychloroquine 400 g twice daily was initiated on the day of admission, followed by 400 mg daily for three days.

Given that periods of prolonged immobility, such as extended mechanical ventilation, are associated with increased risk of thromboembolic disease, and that SARS-CoV-2 infection appears to cause a diffuse inflammatory reaction which places patients at an increased risk embolism, this patient was anticoagulated for the duration of her admission with a therapeutic dose of low molecular weight heparin.

Early during the hospitalization a care coordination meeting was held to discuss the plan of care from an obstetric standpoint. The Society for Maternal Fetal Medicine has advised that caution be used when giving corticosteroids for fetal lung development in cases of maternal COVID-19 infection due to possible worsening of pulmonary function and viral shedding [8]. Taking into account this patient's severe respiratory failure, established co-morbidities, and the limited fetal benefit of steroids at 22 weeks of gestation, antenatal steroids were deferred during her admission. It was also felt to be in the best interest of both the mother and fetus to forego delivery for fetal distress until 25 weeks of gestation.

On the morning of hospital day (HD) 2, the patient was intubated and placed on mechanical ventilation for worsening respiratory distress. During the period of mechanical ventilation the patient was noted to have labile blood pressure, with periods of intermittent hypertension and hypotension. Intermittent pressure support with IV ephedrine was provided as needed for hypotension. A trial of prone ventilation was attempted on HD 4 and discontinued secondary to an episode of torsades de pointes. Given this new emergence of a cardiac arrhythmia, hydroxychloroquine was also discontinued at this time.

The use of glucocorticoids for treatment of coronavirus infections remains somewhat controversial, as early use of systemic glucocorticoids has been shown to increase viral load and potentially worsen disease course in patients with SARS, and early data shows that may also be the case in patients with SARS-CoV-2. Specifically, the use of high-dose glucocorticoids have been associated with detrimental effects in both SARS and SARS-CoV-2 patients [9–11]. However, given the correlation of significant cytokine storm with severe disease, the use of low- to medium-dose glucocorticoids may be of use in patients who have already progressed to a critical disease state [11]. As the patient had rapid progression from mild to critical disease, with a known history of asthma, the decision was made to initiate a short course of IV glucocorticoids with hydrocortisone 50 mg IV which was started as a three times daily dose and tapered over the course of five days. Appropriate steps to establish management of hyperglycemia were also initiated at this time.

Application for compassionate-use remdesivir therapy had been completed on admission and the patient was subsequently approved for trial of use. She was started on remdesivir on HD 5 with a 200 mg IV dose. Remdesivir therapy continued with 100 mg IV doses every 24 h for an additional nine days. Daily labs were obtained following remdesivir initiation to monitor for developing renal and/or hepatic impairment. Mild transaminitis was noted with peak aspartate transaminase (AST) and alanine aminotransferase (ALT) values of 49 and 51 on HD 8. The patient was gradually weaned off paralytics with an appropriate response. After passing a trial of spontaneous breathing on hospital day 10 (five days after the initiation of remdesivir therapy), she was extubated and placed on supplemental oxygen via nasal cannula. Oxygen requirements were gradually decreased and on HD 11, the patient was successfully transitioned to room air. Liver enzymes normalized. No renal dysfunction was observed throughout the hospitalization. No further episodes of cardiac arrhythmia occurred during this admission. On HD 14, at 24 weeks and 2 days of gestation, she was ambulating with mild shortness of breath, vital signs remained stable and within normal limits, and the patient was found to be appropriate for discharge following her final dose of remdesivir. At the time of writing, the patient had had no further issues after discharge and was continuing antenatal care with both primary obstetric office and maternal fetal medicine specialists.

3. Discussion

This patient's care was complicated by several factors in addition to her acute SARS-CoV-2 infection, including the potential need for anticoagulation, her existing respiratory disease, the questionable viability of her pregnancy given its early gestational age, and the potential use and efficacy of investigational therapies such as convalescent plasma and remdesivir.

The use of convalescent plasma transfusions for the treatment of acute viral illnesses is an established therapy which has previously shown benefit in the treatment of SARS, MERS, and Ebola virus patients [12]. At present no official recommendations for the use of convalescent plasma as a COVID-19 therapy exist and research is currently ongoing; however, in a limited uncontrolled case series of five critically ill COVID-19 patients who received convalescent plasma therapy, all five patients showed significant clinical improvement [13]. The hospital is currently participating in a trial of convalescent plasma therapy for inpatient management of severe and critical COVID-19 infections, and this patient was deemed eligible for a trial of therapy. As such, this patient was transfused one unit of convalescent COVID-19 plasma on the day of admission.

Remdesivir, a pro-drug nucleotide analog of adenosine, competes for an ATP-binding site on RNA-dependent RNA polymerase and has previously been shown to have activity against both MERS and Ebola virus [4,5]. At present no official guidance has been published for the use of remdesivir in the treatment of COVID-19, but use under compassionate-use protocols it is available as research into the efficacy of this therapy is ongoing. On the date of this patient's admission an application was made for compassionate-use remdesivir therapy, which was subsequently approved. Remdesivir was initiated on day 5 of this patient's hospitalization, by which time the patient's status had deteriorated and she required mechanical ventilation as described. Following initiation of remdesivir the patient improved relatively quickly and was able to be extubated on day 5 of the 10-day course of remdesivir therapy. The patient was able to be transitioned to room air 24 h later, and was subsequently discharged on no supplemental oxygen on day 10 of her remdesivir trial. This result is in line with other such case reports of compassionate-use remdesivir, which, while limited in power and uncontrolled, have shown that initiation of remdesivir may reduce time to extubation, increase the rate of extubation, and decrease mortality in COVID-19 patients requiring mechanical ventilation or extracorporeal oxygen therapy [7]. Randomized controlled trials are ongoing and needed to determine the efficacy of remdesivir in the management of critically ill SARS-CoV-2 infected patients, but this case and other limited case series show promise for remdesivir as a viable therapy for COVID-19.

Contributors

All authors made a substantive contribution to the material submitted for publication.

Conflict of Interest

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

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