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Research letter

Convalescent plasma for COVID-19 in pregnancy: a case report and review

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Conflicts of interest disclosure

The authors declare no conflicts of interest.

Key words: COVID-19, SARS-CoV-2, pregnancy, convalescent plasma.

Introduction

COVID-19 infection in pregnant women shows overall similar clinical features as that in non-pregnant adults, except perhaps for higher risk for admission to intensive care unit and mechanical ventilation[1]. About >85-90% of pregnant women with COVID-19 have no or mild symptoms, 5-10% symptoms severe enough to warrant hospitalization and at times oxygen but not mechanical ventilation, and 1-2% develop critical disease requiring mechanical ventilation, and at times leading even to death.[1] Most promising therapeutic possibilities for COVID infection in pregnancy include currently remdesivir and convalescent plasma (CP). We present a case of a pregnant woman, treated with CP at the city hospital of Mantua in Italy.

Case report

A 29-year-old gravida 2, para 1 (previous preterm birth at 36+4 weeks of gestation), body mass index 31, with a singleton gestation presented at the emergency room on April 9, 2020 at 24+2 weeks of gestation with worsening cough and fever, which started approximately seven days before.

At presentation she was febrile (38 °C), normotensive, with a respiratory rate of 20 bpm and an O_2 saturation (SpO_2) of 95%. Laboratory tests showed normal white blood cell and procalcitonin values, a C-reactive protein concentration of 58.6 mg/L, and normal arterial blood-gas values. The SARS-CoV-2 polymerase chain reaction (PCR) nasopharyngeal (NP) test resulted positive. Initial chest X-ray revealed a parenchymal thickening of the upper right lobe. Foetal wellbeing was assessed by obstetric ultrasound and non-stress test, the latter not detecting uterine contractions. Antibiotic therapy (ceftriaxone and azithromycin) as well as prophylactic low molecular weight heparin (LMWH) were started. The following day, the patient showed a mild clinical worsening, with persistent dry cough, fatigue, dyspnoea, fever (38.5 °C) and lymphopenia; her SpO_2 was 95% on room air. Following a pneumological evaluation, considering gestational age, the patient was

transfused with 300 mL of CP, with no adverse effects. Antepartum testing for foetal well-being was reassuring both before and after the transfusion. The following day, a clinical worsening was observed, with persistently high fever (39.5 °C), tachypnoea (30 bpm), hypotension (90/60 mmHg) and an SpO_2 of 91% on room air. Lymphopenia, elevated interleukin-6 and serum ferritin level were reported too. However, it should be noted that her SARS-CoV-2 PCR NP test resulted negative. Chest ultrasound revealed bilateral pleural thickening with nodulations and several B lines (>4/field). Obstetric ultrasound showed regular foetal biometry with normal umbilical arterial Doppler assessment. Due to the rapid worsening of her clinical condition and laboratory values (Fig. 1), the patient was transferred to the Intensive Care Unit (ICU) were she was given oxygen therapy via a nasal cannula (4L/min). She was initiated on hydroxychloroquine, LMWH at a therapeutic dosage and methylprednisolone. The peak of severity was reached 2 days after admission into the ICU, when she developed acute respiratory distress syndrome (ARDS). The ratio of the partial pressure of arterial oxygen to the percentage of inspired oxygen (PaO_2/FiO_2) fell to a minimum value of 223. She was supported with nasal cannula oxygen non-invasive ventilation (FiO_2 36%) without the need for intubation. Obstetric ultrasound showed a normal umbilical artery pulsatility index (UA-PI) and foetal ductus venous with an observed a-wave. The middle cerebral artery peak systolic velocity (MCA-PSV) was > 1.5 multiples of median, with diastolic reverse flow. Consequently, the patient was again transfused with 300 mL of CP on day 12 from symptom's onset , with no adverse reactions. The patient's clinical condition rapidly improved as shown by normalisation of laboratory tests and vital signs within 3 days of the second CP transfusion (Fig.1). In particular, we observed a rapid normalisation in body temperature and SpO2 and a prompt resolution of dyspnoea. The SARS-CoV-2 PCR NP test was repeated on days 15 and 17 with both negative results. The patient was discharged 13 days after admission. The mother's chest ultrasound showed near-complete resolution of bilateral pneumonia. Foetal Doppler assessment was normal, with UA-PI and MCA-PSV within the normal range for gestational age. The outpatient examinations, performed every week for 1 month, showed a complete recovery of

pulmonary function. Pregnancy continued to be monitored after hospital discharge by foetal ultrasonography with Doppler assessment every 2 weeks. Currently, foetal biometry results are consistent with gestational age (34 weeks).

Discussion

Comparing our patient with those in a US cohort of pregnant women with severe COVID-19 infection,[2] the clinical course was similar, with hospital admission on day 7 after symptom onset, initiation of O_2 therapy on day 9, peak respiratory support on day 10, hydroxychloroquine treatment started on day 9, symptom resolution on day 15. The rationale for the use of CP in our patient was to prevent mother's condition from worsening, to avoid a possible caesarean section at a gestational age of severe prematurity and to reduce potential maternal and foetal risk associated with the administration of various drugs utilised for COVID-19.

There is evidence that CP can be used effectively as a therapy for severe COVID-19 in non-pregnant adults, shortening time to clinical improvement by about 5 days, and with trends for improvement in other outcomes, including death, without causing severe adverse events, in the one RCT published so far.[3] Regarding COVID-19 infection in pregnancy, pregnancy is not a contraindication to blood component transfusion, and two other cases of pregnancies managed using CP have been reported (Table).[4,5] In a single report, CP administration was associated with survival of the mother but newborn's death.[4] In the second case report, CP therapy in association with remdesivir successfully managed a critically ill obstetric patient.[5] The present case is the first treated with CP without antiviral drugs with a favourable outcome for both mother and foetus.

Conclusions

This case report has several limitations, including the short follow-up (the patient is currently 34 week pregnant and well) and the concomitant use of other medications which may confound the evaluation of CP effectiveness. Nevertheless, the close temporal association between CP transfusion and the improvement in clinical and laboratory parameters represent an encouraging finding.

There are several randomized clinical ongoing trials regarding the use of CP in patients with COVID-19, in many of which pregnancy is not considered as an exclusion criterion.[6]

We hope that further studies on plasma administration can be carried out during pregnancy, especially in a gestational age of severe prematurity, with the purpose of prolonging the course of pregnancy as long as possible.

Article contribution

Gianpaolo Grisolia, Massimo Franchini, Paolo Zampriolo, Cesare Perotti and Giuseppe De Donno had the idea for the article. Claudia Glingani, Francesco Inglese, Martina Garuti, Massimiliano Beccaria, Martina Capuzzo, Alessia Pinto, Giorgia Pavan and Lara Righetto performed the literature search and data analysis. Gianpaolo Grisolia and Giuseppe De Donno wrote the case report. Gianpaolo Grisolia, Massimo Franchini, Paolo Zampriolo, Cesare Perotti and Giuseppe De Donno drafted and/or critically revised the manuscript. All authors read and approved the final manuscript.

Figure 1. Case report: graphical course of laboratory and clinical parameters.

Table 1. Clinical course of three pregnant women affected by COVID-19 treated with CP

Author	Gestational age	Severity of disease	Invasive procedures	Comorbidity	CP dose (units)	Other medications	Outcome
Zhang B. et al.[4]	35 weeks and 2 days	Severe ARDS Septic shock MOF	Mechanical ventilation CRRT ECMO Caesarean section	-	1	Lopinavir/Ritonavir Ribavirin Imipenem Vancomycin	Maternal wellbeing Newborn's death due to endouterine asphyxia
Anderson J. et al.[5]	22 weeks and 2 days	Severe ARDS	Mechanical ventilation	Type 2 DM, Asthma Class III obesity	1	Remdesivir Ceftriaxone Azithromycin Hydroxychloroquine Hydrocortisone LMWH	Maternal wellbeing Normal ongoing pregnancy
Grisolia G. et al.	24 weeks and 2 days	Mild ARDS	-	Class I obesity	2	Ceftriaxone Azithromycin Hydroxychloroquine Methylprednisolone LMWH	Maternal wellbeing Normal ongoing pregnancy

Legend: ARDS, acute respiratory distress syndrome; MOF, multi-organ failure; CRRT, continuous renal replacement therapy; ECMO, veno-venous extracorporeal membrane oxygenation; DM, diabetes mellitus.

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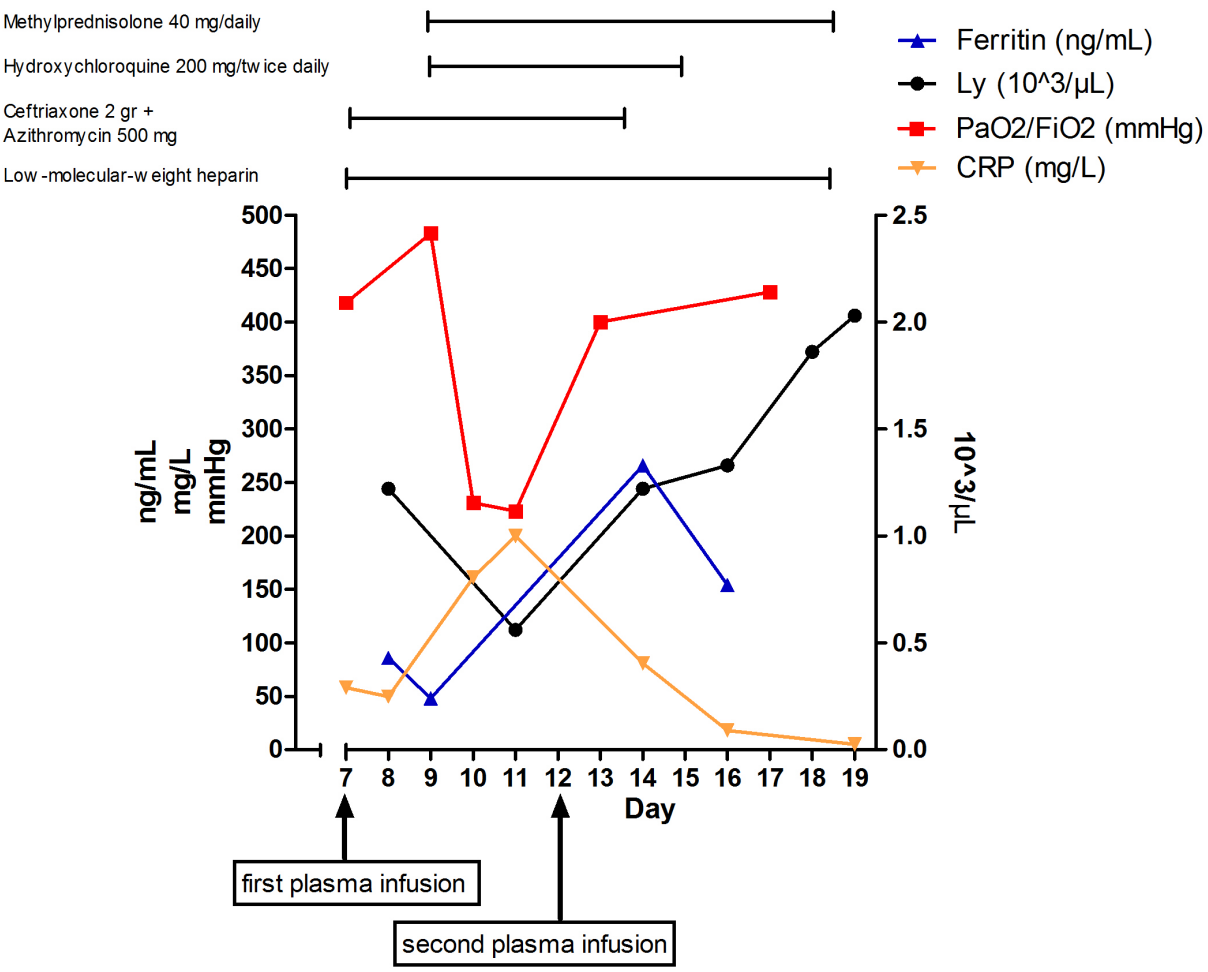

Normal range Ferritin 13 - 150 ng/mL
Normal range C - Reactive Protein (CRP) < 5 mg/L
Normal range Lymphocyte (Ly) count 1.30 - 4.80 *10^3/µL
Acute respiratory distress syndrome PaO2/FiO2 < 300