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CASE REPORT

Treatment of COVID-19 with monoclonal antibodies casirivimab and imdevimab in pregnancy

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Abstract

Propose Pregnancy is a risk factor for severe COVID-19. Treatment with monoclonal antibodies has been shown to decrease the risk of progression to severe COVID-19, but there are few reports on treating pregnant women. Here, we describe the clinical outcome of seven hospitalized pregnant women treated with the casirivimab–imdevimab.

Methods/Results Seven unvaccinated pregnant patients hospitalized due to COVID-19 met the monoclonal antibodies treatment criteria applied at our center. After consultations with obstetricians, the decisions to administer casirivimab–imdevimab to halt the progression of COVID-19 were made by two senior infectious diseases specialists. No patient experienced an adverse drug reaction, and only one patient progressed to severe disease. Two patients had a cesarian section performed during hospitalization, both with delivery of healthy babies. Three patients gave birth to healthy babies at a later time point, while two pregnancies are ongoing.

Conclusion The hospitalized pregnant patients who received monoclonal antibodies due to COVID-19 had favorable outcomes, but further research is recommended to fully assess safety and efficacy of monoclonal antibody treatment in pregnancy.

Keywords Coronavirus disease · COVID-19 · Monoclonal antibodies · Pregnancy

Introduction

Several studies have shown that pregnancy is a risk factor for developing severe coronavirus disease (COVID-19) [1]. The experience of treating pregnant women with monoclonal antibodies is still limited as pregnancy was an exclusion criterion in the studies leading to the approval of emergency use of monoclonal antibodies. However, in May 2021, the Federal Drug Administration recognized pregnancy as a high-risk criterion, granting use of casirivimab–imdevimab in non-hospitalized patients [2]. Since then, results from the DISOVERY group have been presented which strongly suggest that use of monoclonal antibodies in seronegative hospitalized COVID-19 patients decreases mortality [3].

Here, we report the clinical outcome of seven hospitalized pregnant women treated with casirivimab–imdevimab because of COVID-19.

Methods and results

Patient characteristics

This case series included all seven pregnant patients identified from the database of patients treated with monoclonal antibodies at the Department of Infectious Diseases, Karolinska University Hospital, Huddinge, Stockholm, Sweden, during May–November 2021. The study was approved by the Swedish Ethical Review Authority (drn 2020-3139). All seven patients were admitted due to COVID-19 confirmed by a positive nasopharyngeal PCR test. At admission, two patients were in the second trimester and five were in the third trimester, respectively; no one has received any dose of COVID-19 vaccine and all were seronegative (Table 1). Delta strain, B.1.617.2, of COVID-19 was at the time the dominating variant in Sweden. Six of seven women required oxygen supplementation to accomplish peripheral oxygen

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Table 1 Patient´s characteristics at admission and outcome

Patient characteristics	$N=7$
Age, median (IQR), years	32 (30–34)
Co-morbidities	2/7
BMI, median (IQR)	32 (27–35)
Vaccination status	0/7
SARS-CoV-2 IgG at start (U/ml)	0/7
Days from symptom onset until treatment, median (IQR)	8 (6–10)
SARS-CoV-2, CT-values in NPH, median (IQR)	18.5 (16.8–29)
RBC at start (g/L), median (IQR)	111 (14)
WBC at start ($\times 10^9$), median (IQR)	7.9 (4.3)
Lymphocytes at start($\times 10^9$), median (IQR)	1 (0.6)
Neutrophils at start ($\times 10^9$), median (IQR)	6.1 (3.8)
CRP at start (mg/L), median (IQR)	47 (32–101)
Lactate dehydrogenase (microkat/L), median (IQR)	5.3 (3.6–7.1)
D-Dimer (mg/L FEU), median (IQR)	1.12 (0.99–2.2)
Oxygen supplementation at start	6/7
Days of hospitalization, median (IQR)	5 (2–9)
Days for improvement, median (IQR)	4 (2–5)
ICU admission	1/7
Pregnancy outcome	
Cesarian sections at COVID-19	2/7, healthy babies
Later, in-term, births	3/7, healthy babies
Ongoing pregnancy	2/7, no registered complications

BMI Body Mass Index, *IQR* Interquartile range, *NPH* Nasopharyngeal swab specimen, *WBC* white blood cell count, *RBC* red blood cell count, *CRP* C-reactive protein, *ICU* Intensive Care Unit, *MicroKat/L* Micro-Katal/Liter, *FEU* Fibrinogen Equivalent Units

saturation at > 94%. Four of the seven patients had a pulmonary CT performed, all with findings of infiltrates compatible with COVID-19 and without signs of pulmonary embolisms.

All patients met the monoclonal antibodies treatment criteria applied at our center. After consultations with obstetricians, the decisions to administer casirivimab–imdevimab to halt the progression of COVID-19 were made by two senior infectious diseases specialists. The patients received infusion of either 600 mg ($n=4$) or 1200 mg ($n=3$) of casirivimab–imdevimab, respectively.

Follow-up and outcomes

Treatment with casirivimab–imdevimab was well tolerated with no immediate adverse events. Five of the seven patients improved at a median of four days after treatment (as evaluated by WHO ordinal scale) (Fig. 1), with a median hospital stay of 5 days. One patient had a progression of COVID-19 and was admitted to the ICU because of respiratory failure. After receiving invasive mechanical ventilation for six days, the patient could be discharged from the ICU after seven days. Total hospital stay was 22 days, and at discharge, the patient had made a full recovery and still had a viable pregnancy.

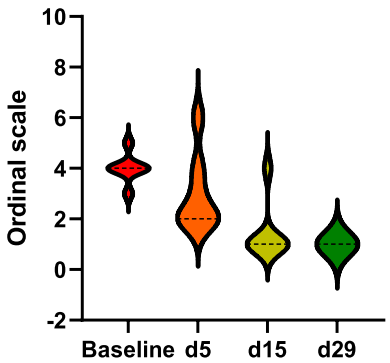

Fig. 1 Clinical improvement described by change in ordinal scale day 0, 5, 15 and 29. Seven-point ordinal scale of the WHO Master Protocol (1) not hospitalized, no limitation on activities; (2) not hospitalized, limitation on activities; (3) hospitalized, not requiring supplemental oxygen; (4) hospitalized, requiring supplemental oxygen; (5) hospitalized, on non-invasive ventilation or high flow oxygen devices; (6) hospitalized, on invasive mechanical ventilation or ECMO; and (7) dead

Regarding outcome of the pregnancies, one patient at 36 weeks of gestation underwent pre-emptive cesarian

section at day three of hospital stay, one day after receiving casirivimab–imdevimab, to avoid a potential progression in COVID-19. Additionally, one patient at 31 weeks of gestation underwent cesarian section due to pathological cardiotocography at day four of hospitalization, 2 days after treatment with casirivimab–imdevimab. Both newborns were delivered healthy. Three patients gave birth in uncomplicated labors in-term pregnancies with healthy babies. Two women are still pregnant with no signs of complications.

Discussion

In this case series, five out of seven unvaccinated pregnant women hospitalized due to COVID-19 infection improved after administration of casirivimab–imdevimab, while one patient needed ICU admittance but survived without severe complications. One patient at 36 weeks of gestation needed a caesarian section performed due to pathological cardiotocography with the delivery of a healthy baby. Treatment was well tolerated in all cases with no adverse events reported. To our knowledge, there are only two earlier published reports on treatment with monoclonal antibodies in COVID-19-infected pregnant patients [4, 5]. Similar to the results in the present work, these reports, including six cases in total, found no adverse effect on the pregnancy.

At the period of patient's admission, the Delta was dominating SARS-CoV-2 variant in Sweden. As Bamlanivimab used in treatment of previous circulating variants has reduced effectiveness to Delta, casirivimab–imdevimab, with remained activity to the Delta strain has been selected for treating these patients. In general, it is of great importance that the choice of the proper treatment is guided by expected neutralization effect of monoclonal antibodies to individual variants—as emerging SARS-CoV-2 variants have potential mutations in spike protein which reduce neutralizing capacity of monoclonal antibodies. [6]

In our case series, all patients receiving casirivimab–imdevimab due to COVID-19 had favorable outcomes with a follow-up time of 90 days. However, further research is needed to fully assess safety and efficacy of monoclonal antibodies in pregnancy.

Declarations

Conflicts of interest The authors declare no conflict of interest that are directly or indirectly related to the work submitted for publication. Piotr Nowak is supported by Region Stockholm / Karolinska Institute research fellowship.

Ethics approval All the work presented in the manuscript was conducted in accordance with the Declaration of Helsinki. The study was approved by the Swedish Ethical Review Authority (drn 2020–3139).

Consent to participate and publish The requirement for patient's consent has been waived by an Ethical Review Board in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Authors consent Not applicable.

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