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CASE REPORT

COVID-19 in a pregnant kidney transplant recipient - what we need to know: A case report

Roberta Angelico, Maria Luisa Framarino-dei-Malatesta, Giuseppe Iaria

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Abstract

BACKGROUND

In the era of the coronavirus disease 2019 (COVID-19) pandemic, kidney transplant recipients are more susceptible to severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection, developing severe morbidity and graft impairment. Pregnant women are also more likely to develop severe COVID-19 disease, causing pregnancy complications such as preterm births and acute kidney injury.

CASE SUMMARY

Herein, we report the case of a pregnant woman with a third kidney transplantation who developed COVID-19 disease. The reduction of immunosuppressive drugs and strict monitoring of trough blood levels were needed to avoid severe SARS-CoV-2-related complications, and permitted to continue a healthy pregnancy and maintain good graft function. In such a complex scenario, the concomitance of COVID-19-related morbidity, the risk of acute rejection in the hyperimmune recipient, graft dysfunction and pregnancy complications make the management of immunosuppression a very difficult task and clinicians must be aware.

CONCLUSION

Tailoring the immunosuppressive regimen is a key factor affecting both the graft outcome and pregnancy safety.

Key Words: Kidney transplantation; Pregnancy; SARS-CoV-2 infection; COVID-19 disease; Immunosuppression; Complications; Case report

Core Tip: Kidney transplant (KT) recipients are susceptible to coronavirus disease 2019 (COVID-19). Pregnant women are more likely to develop severe COVID-19, causing pregnancy complications such as preterm births and acute kidney injury. The management of immunosuppression in pregnant KT recipients with severe acute respiratory syndrome coronavirus infection is crucial for the avoidance of severe morbidity to the patient and the fetus, and to escape renal graft dysfunction.

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INTRODUCTION

Kidney transplant (KT) recipients are susceptible to coronavirus disease 2019 (COVID-19), with an associated 18%-39% intensive care admission rate and 13%-39% mortality[1]. Pregnant women are more likely to develop severe COVID-19, causing pregnancy complications such as preterm births and acute kidney injury[2,3].

CASE PRESENTATION

Chief complaints

In October 2020, a 37-year-old woman at 20 wk of gestation, who had received a third KT 2 years ago, presented with fever, cough, and anosmia.

History of present illness

The patient presented with fever, cough, and anosmia.

History of past illness

Her past medical history consisted of end-stage chronic kidney disease due to focal and segmental glomerulosclerosis, requiring three sequential KTs due to chronic rejections with a panel reactive antibody titer of 100%.

Personal and family history

The patient's personal and family histories were unremarkable.

Physical examination

At presentation, the severe acute respiratory syndrome coronavirus (SARS-CoV-2) polymerase chain reaction (PCR) test was positive.

Laboratory examinations

Biochemical tests showed 7.640/μL white blood cells, C-reactive protein of 10.1 mg/L and creatinine of 1.18 mg/dL (baseline at pregnancy: 1.1 mg/dL). The immunosuppression (IS) regimen consisted of steroids (5 mg/d), once-daily tacrolimus (extended-released Envarsus, target level: 7-8 μmol/L) and azathioprine (1 mg/kg/d), the latter started 1 year previously, replacing mycophenolate acid as she declared the intent to become pregnant.

Imaging examinations

Chest X-ray was negative for pneumonia.

FINAL DIAGNOSIS

SARS-CoV-2 infection in a KT pregnant lady.

TREATMENT

At diagnosis of SARS-CoV-2 infection, azathioprine was suspended, while steroids and tacrolimus were maintained at unchanged doses. During the infection, the patient developed moderate respiratory symptoms and close clinical monitoring was performed, showing persistent stable graft function, steady tacrolimus blood levels and regular fetal growth. One month later, the patient achieved a complete clinical recovery. The SARS-CoV-2 swab became negative after 40 d. At 39 wk of gestation, she had an uneventful delivery of a healthy male infant (weight: 3.2 kg; Apgar score: 9/10) by caesarean section.

OUTCOME AND FOLLOW-UP

At the time of delivery, the placenta and the newborn were not tested for SARS-CoV-2. The patient's renal graft function remained stable throughout the post-delivery period, and after 17 mo of follow-up the creatinine was 1.09 mg/dL (Table 1). During pregnancy, anti-human leukocyte antigen donor-specific antibody (DSA) screening was performed and these antibodies were not detected. In particular, no evidence of post-COVID-19 DSA was identified. Graft biopsy was not done. At the last follow-up, both the mother and the child were in good clinical condition.

DISCUSSION

The reduction of the immune response due to both IS drugs and pregnant status render pregnant KT recipients vulnerable to viral infections such as SARS-CoV-2[1,2]. In our case, this was further enhanced by her non-vaccinated status, since at that time the vaccine for SARS-CoV-2 was not available yet. Therefore, the concomitance of COVID-19-related morbidity, the risk of acute rejection in hyperimmune re-KT, graft dysfunction and pregnancy complications make the management of IS a very difficult task.

In KT recipients, recommendations suggest the modification of IS drugs according to the severity of COVID-19, ranging from no modification in asymptomatic patients, antimetabolite withdrawal in mild/moderate symptomatic disease, to complete drug discontinuation in severely ill patients requiring mechanical respiratory support[4,5]. In this case, we decided to withdraw azathioprine, which inhibits purine synthesis, aiming to avoid the depletion of T- and B-cells during the SARS-CoV-2 infection. Tacrolimus and steroids at low-doses remained the only IS drugs, without increasing their blood target-levels. The extended-released formula of tacrolimus Envarsus, which provides effective and stable blood concentration with less toxic levels compared to other Tacrolimus formulae[6], permitted the safe control of rejection risk and the avoidance of severe COVID-19. Thus, a recent report suggested that a mammalian target of rapamycin inhibitor may have potential antiviral benefits in SARS-CoV-2 infection [7].

In this case, strict monitoring of DSA was performed before and after COVID-19, since the IS regimen had been reduced. Despite the significant decrease of the IS and the high risk of rejection due to the hyperimmune status of third-KT recipients, our patient did not develop new DSA or rejection episodes. These data confirm a recent report investigating the alloreactive immune response during and after SARS-CoV-2 infection in KT recipients, which showed that the incidence of acute rejection is about 1.3% (all in hospitalized patients) and the occurrence of post-COVID-19 DSA is 4% overall, ranging from 0% to 8% in non-hospitalized and hospitalized patients, respectively[8]. Despite the immunosuppressed status of a third KT pregnant lady, our patient was very lucky because she was in this group of patients who do not develop severe COVID-19 disease. Since the stable kidney function and the pregnant status, we did not perform a graft biopsy in order to avoid possible biopsy-related complications. Additionally, venous thromboembolism prophylaxis was not administrated as no evidence was present, but its utility should be explored in pregnant COVID-19 KT recipients.

Pregnancy in KT recipients may be associated with a high-risk of maternal complications and decreased graft function, which could further deteriorate in the presence of COVID-19[9]. In fact, the occurrence of acute kidney injury in infected pregnant KT recipients could be due to the SARS-CoV-2 infection or to other pregnancy-related causes, which need to be differentiated[10]. In immunosuppressed transplant recipients as well as pregnant women, SARS-CoV-2 showed the potently to replicate into the kidney causing renal disfunction[11,12]. Lastly, despite the fact that the risk of acquiring SARS-CoV-2 infection during pregnancy seems to be similar to that of non-pregnant patients, severe maternal COVID-19 is associated with acute kidney injury and preterm birth.

The risk of congenital infection with SARS-CoV-2 to the newborn is still unknown[2,13]. In our case, the placenta and the baby were not tested for SARS-CoV-2 PCR, therefore unfortunately we do not have these interesting data. Moreover, despite KT pregnant recipients are more susceptible to chronic infection such as cytomegalovirus (CMV) infection, we didn't detect any CMV infection during pregnancy. This is the first report focusing on IS management in SARS-CoV-2-positive pregnant KT recipients.

Table 1 Patients' characteristics

Variables at presentation	Values
Demographics	
Age, yr	37
Sex	Female
Race	White
Number of KT	3
Primary nephropathy	Focal and segmental glomerulosclerosis
Causes of previous KT losses	Chronic rejection
Time from last KT	24 mo
Comorbidities	Arterial hypertension
Pregnancy	
Gestation age, wk	20
Fetal grow	Regular
Symptoms/signs	
Fever, T > 37.5 °C	Yes
Dyspnea	Yes
Anosmia	Yes
Myalgias	Yes
SARS-CoV-2 status	
SARS-CoV-2 swab test positive	Yes (positivity for 40 d)
SARS-CoV-2 vaccination	No
Biochemical tests	
At infection diagnosis	
Creatinine, mg/dL	1.18
WBC as × 10^3/mmc	7.640
Lymphocytes, cells/mmc	1.590
PTL as × 10^3/mmc	202
C-reactive protein, mg/L	10.1
Procalcitonin, ng/mL	0.52
Peak during infection	
Creatinine, mg/dL	1.3
WBC as × 10^3/mmc	12.700
Lymphocytes, cells/mmc	3.400
PTL as × 10^3/mmc	250
C-reactive protein, mg/L	20.2
Procalcitonin, ng/mL	2.01
Immunosuppression regimen	
Tacrolimus	Continued at unchanged doses (target levels: 7-8 μmol/L)
Azathioprine	Withdrawal
Steroids	Continued at unchanged doses (5 mg/d)
Outcomes	
Recovery from COVID-19 disease, mo	1

De novo DSA after SARS-CoV-2 infection	No
Rejection episode	No
Delivery	
Time of delivery, wk	39
Newborn status	Healthy, no complication
Time of follow-up after infection, mo	17
Renal function at last follow-up	
Creatinine, mg/dL	1.09

COVID-19: Coronavirus disease 2019; DSA: Donor-specific antibody; KT: Kidney transplant; PTL: Primary testicular lymphoma; SARS-CoV-2: Severe acute respiratory syndrome coronavirus; WBC: White blood cell.

CONCLUSION

We suggest that all efforts should be made to avoid severe maternal COVID-19 disease through tailored adjustment of the IS regimen and close monitoring of calcineurin inhibitor trough-blood levels, graft function and fetal parameters. Currently, mRNA vaccines against SARS-CoV-2 are recommended both in KT recipients and pregnant women, and may help in preventing severe COVID-19 disease[14,15]. However, KT patients have been shown to frequently be poor responders to the vaccines, thus remaining at high risk of developing severe COVID-19[16], especially in pregnancy. In fact, recent data suggest that only selected KT recipients seem to respond to the third booster dose of SARS-CoV-2 vaccine (assessed by anti-receptor binding domain immunoglobulin G titers and/or positive interferon-gamma-releasing assay)[17]. Moreover, in pregnancy, the boosting effect of a third vaccine dose is suggested to have a potential benefit only in those who completed the two-dose vaccine series in early pregnancy or prior to conception[16]. We feel that, although no data are yet available on the efficacy of the vaccine in preventing COVID-19 disease in pregnant KT recipients, a complete vaccine cycle against SARS-CoV-2 with three doses should preferably be performed before pregnancy. In addition, clinicians should be ready to tailor IS drugs when a member of this rare population is infected by SARS-CoV-2.

FOOTNOTES

Author contributions: Angelico R contributed to the study conception and design, writing; Framarino-dei-Malatesta ML was involved in the acquisition of clinical data, analysis, and interpretation; Iaria G contributed to the study conception; and all authors were involved in critical revision.

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