Successful maternal and fetal outcomes in a kidney transplant patient under everolimus throughout pregnancy complicated by pyelonephritis and preeclampsia

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Pregnancy in kidney transplant patients has many risks such as worsening renal function and/or proteinuria, allograft rejection, preeclampsia, spontaneous abortion, premature fetal delivery, and low fetal birthweight. We report a case of a 35-year-old patient with a history of kidney transplant, who received everolimus throughout pregnancy and experienced a successful cesarean delivery with positive maternal and fetal outcomes. Information regarding everolimus use in pregnancy is limited. However, data from animal studies suggest that everolimus may cause fetal harm when administered during pregnancy. In our case, everolimus did not affect the pregnancy of this patient; cesarean delivery was performed without complications. Owing to the increased risks and monitoring required during pregnancy in patients with a previous kidney transplant and limited information regarding the use of antirejection agents during pregnancy, care throughout pregnancy should involve a multidisciplinary team, including transplant, maternal fetal medicine, and nephrology.

Keywords: everolimus, kidney transplant, pregnancy

Introduction

Pregnancy after kidney transplantation poses a high risk for both mother and fetus, yet, more than 2000 successful live births have been reported in the United States, United Kingdom, and Europe combined.[1] Potential drug-related complications include adverse fetal outcomes. Immunosuppressive therapy is required throughout pregnancy to prevent transplant rejection. However, exposure to many of these medications have limited data regarding fetal risk, and others have known fetal risk. Pregnancy in kidney transplant patients has many risks such us worsening renal function and/or proteinuria, allograft rejection, preeclampsia, spontaneous abortion, premature fetal delivery, and low fetal birthweight.[2] We report a successful maternal and fetal outcome in a kidney transplant patient who was administered everolimus throughout pregnancy complicated by pyelonephritis and preeclampsia.

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Case presentation

We report a case of a 35-year-old female patient with a history of a kidney transplant; in 2016, the patient was diagnosed with end-stage renal disease owing to nephritis of unknown etiology despite kidney biopsy. At that time, she was initiated on hemodialysis. After 6 months, she received a living unrelated donor kidney transplant. Postoperatively, the patient did not present any complications; she was on azathioprine 50 mg and everolimus 0.5 mg in the morning and everolimus 0.25 mg in the evening in addition to continuing prednisone 5 mg. The blood pressure and kidney function were normal and creatinine level was 11.4 mg/L.

The patient did not receive care at this facility again until December 2021 when she presented to the obstetrics department with pelvic pain and 6 weeks of amenorrhea; on general examination, the patient was stable with normal vital signs. The patient had a positive blood human chorionic gonadotropin, and ultrasound revealed an intrauterine pregnancy at 7 weeks gestation. At this time, the patient was referred to the transplant center for further evaluation.

Despite the high risk of teratogenicity, the decision was made to continue the everolimus with patient consent (because the patient had toxicity owing to tacrolimus in the past).

At that time, the recipient decided to continue the pregnancy even after being made aware of the potential risk for developing congenital abnormalities related to the exposure of everolimus.

The patient had a stable blood pressure, negative urine protein, and normal liver and renal function throughout the pregnancy.

The patient presented at 22 weeks gestation with a fever and burning with urination. Bloodwork was performed and included the following: hemoglobin 12.6 g/dL; white blood cells: 12,600 elements/mm^3; C-reactive protein (CRP): 75 mg/L; and creatinine: 12 mg/L. A urine

analysis for chlamydia (cytobacteriological examination of urine) was performed, revealing a leukocyte count of 120,000, and bacteriologic exam revealed chlamydiae sensitive to ceftriaxone. Owing to the patient's previous kidney transplant, an abdominal ultrasound was completed and showed pyelocaliceal dilation of the graft. The patient was hospitalized and started on ceftriaxone 2 g daily. Two days after admission, the patient was afebrile. Ceftriaxone was administered for a total of 10 days. Blood analysis made at the tenth day revealed CRP 12 mg/L. At 36 weeks' gestation, the patient presented with severe range preeclampsia, with blood pressures of 170/110 mm Hg and evidence of proteinuria. Laboratory tests confirmed the patient's hepatic and renal function was normal, and the patient was started on nicardipine 50 mg every 12 hours and alfa methyldopa 500 mg every 8 hours. Notably, nifedipine and labetalol were not available at our hospital. Despite antihypertensive therapy, the patient's blood pressure remained in the severe range, so a cesarean delivery with a routine dissection was performed. To avoid any graft lesions, the dissection was performed to the fascia through a Pfannenstiel incision, and the fascia was carefully transected horizontally. A healthy female infant weighing 3260 g was delivered with Apgar scores of 10. The rest of the case was uneventful. The patient's blood pressure returned to normal range on day 3 postpartum, and the proteinuria resolved.The evolution of the patient was favorable, and the child underwent good psychomotor development.

Discussion

The restoration of fertility is one of the many benefits of kidney transplantation. Yet, pregnancy poses risks for the mother, fetus, and allograft.[3] These risks include worsening renal function and/or proteinuria, allograft rejection, preeclampsia, spontaneous abortion, premature fetal delivery, and low fetal birthweight.[4] Everolimus is a macrolide that binds the FK-binding protein and specifically inhibits T and B lymphocyte activation and proliferation.[5] This occurs owing to arrest of the cell cycle in the G1 phase, which leads to decreased interleukin-2 expression[6]. However, this class of medications is currently forbidden during pregnancy because of adverse fetal outcomes observed in animal studies, such as mortality and delayed bone ossification and a high risk of teratogenicity in humans.[7] In our case, everolimus was maintained, because we did not have any other choice. The patient had been informed of the fetal risk of medication, and despite the high teratogenicity risk reported, she consented to keep her pregnancy.

The incidence of miscarriage in kidney transplant patients is similar to that in the normal population, with a better outcome in more than 90% of cases after early pregnancy.[8]

The main maternal complications are infection, hypertension, proteinuria, anemia, and acute rejection. The risk of developing preeclampsia is approximately 4 times higher than that in normal pregnant women, and those with prepregnancy hypertension have 5 times the risk of preeclampsia than transplant patients with normal blood pressure.[9]

It is important to differentiate preeclampsia from transplant rejection in late pregnancy, whereas severe preeclampsia should be distinguished from acute rejection and hemolytic-uremic syndrome.[10] The patient had a stable blood pressure, negative urine protein, normal liver and renal function, and suddenly appeared in late-pregnancy a Preeclampsia with high blood pressure and positive proteinuria.

There are increased rates of cesarean delivery in kidney transplant patients, commonly owing to fetal malpresentation or nonreassuring fetal heart rate tracings in indicated preterm deliveries typically done for hypertensive disorders or fetal growth restriction.[11] Careful delivery planning with particular attention to skin and fascial incisions is imperative. Although several studies comment on the importance of avoiding injury to the graft, no specific recommendations exist on how to prevent this potentially devastating complication.[12] In our case, the cesarean delivery was completed without a graft lesion.

Conclusion

A multidisciplinary team should be involved in the care and delivery planning of a patient with a previous kidney transplant. The transplant surgery team should be present or readily available at the time of delivery, particularly if cesarean delivery is indicated. Ideally, the transplant surgery team should be consulted in the antepartum period to assist with surgical planning with consideration for preoperative imaging to confirm transplant location. ■

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