Consecutive Spontaneous Triplet and Twin Pregnancies in a Woman After Renal Transplantation

João Egidio Romão Junior*, Rolf Passos Lopes, Maria Regina Teixeira Araújo, and Hugo Abensur

Clínica de Nefrologia e Transplantes, Hospital BP—Beneficência Portuguesa, São Paulo, Brazil

ABSTRACT

Background. There are numerous reports of successful pregnancies following kidney transplantation. However, little information is available regarding the management and evolution of multiple pregnancies in a kidney-transplanted woman.

Case report. We report the case of successful consecutive spontaneous triplet and twin pregnancies in a woman who had undergone kidney transplantation at 30 years of age, 12 years before the first pregnancy, as a result of end-stage renal disease secondary to chronic glomerulonephritis due to diffuse proliferative lupus nephritis. An integrated multidisciplinary team closely followed progress during the pregnancies. Maternal complications during the pregnancies included light proteinuria, controlled hypertension, and anemia. No graft rejection episodes or deterioration of renal function was noted during the pregnancies or after the deliveries.

Conclusion. Currently, more than 2 years after her last pregnancy, the mother and all 5 babies are healthy and the mother's renal transplant function is normal.

WOMEN with advanced chronic kidney disease have a fertility rate lower than that of healthy women of childbearing age, and pregnancy in patients with end-stage renal disease (ESRD) carries a high risk of fetal and maternal complications [1,2]. Kidney transplantation is accepted worldwide as the only useful approach to increase the chances of conception in women with chronic kidney disease [3].

Spontaneous twin and triplet pregnancies are uncommon in renal transplant recipients and confer a significant risk in terms of both transplant dysfunction and fetal complications [4]. We present the case of a successful outcome for both mother and babies in consecutive spontaneous triplet and twin pregnancies in a kidney transplant recipient, and the effects of these multiple pregnancies on the mother's transplant function. We performed this study in compliance with guidelines of the Declaration of Helsinki. The Institutional Review Board and Ethics Committee of BP Hospital approved the study.

CASE REPORT

A Brazilian white woman developed ESRD secondary to chronic glomerulonephritis due to diffuse proliferative lupus nephritis. Her past medical history revealed the diagnosis of lupus nephritis when she was 15 years old, which evolved after 5 years into ESRD. After 3 years of being maintained on hemodialysis treatment, the woman underwent kidney transplantation from a living donor (sister; zero HLA mismatch). The woman was treated with immunosuppressive drugs consisting of a combination of tacrolimus, prednisone, and mycophenolate mofetil. At 30 years of age (April 2014), she and her husband presented for advice because they were considering pregnancy. Pre-pregnancy counseling was undertaken, and due to the risk of fetal teratogenicity, mycophenolate was changed to azathioprine. In the past, the woman had had a spontaneous abortion. At this time, there was evidence of good function of the woman's renal allograft with serum creatinine value of 0.9 mg/dL, estimated glomerular filtration rate of 67 mL/min, hemoglobin of 13.0 g/dL, proteinuria of 130 mg/24 h, normal blood pressure, and fasting blood glucose of 91 mg/dL.

First Pregnancy

On August 28, 2014, the woman informed us that she was pregnant. She was not on an assisted fertilization program. Ultrasonography showed triplet gestational sacs in the seventh week of gestation (WG). A multidisciplinary renal and obstetric team was formed,

*Address correspondence to João Egidio Romão Junior, MD, Rua Maestro Cardim, 560/172, São Paulo 01323 000, Brazil. Tel: +55(11) 3283-5304. E-mail: nefrobp@uol.com.br

230 Park Avenue, New York, NY 10169

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Table 1. Clinical and Laboratory Data During the First Pregnancy

	April 14	June 14	July 14	August 14	September 14	October 14	November 14	December 14	April 15
Gestational week	Pre	7th	11th	15th	19th	23rd	27th	31st	After
Blood	100	110	100	110	110	120	110	110	120
pressure (mm Hg)	80	70	70	60	70	80	80	70	70
Weight (kg)	48.0	49.0	52.3	54.4	58.7	59.6	63.7	64.55	57.3
Urea (mg/dL)	41	35	43		50	51		46	45
Serum creatinine (mg/dL)	1.00	1.00	0.98	0.99	1.10	1.20	1.00	1.20	1.10
Hemoglobin (g/L)	13.0	12.8	12.0	12.8		10.0	9.9	8.8	13.3
Serum albumin (g/dL)	4.6		4.8						4.7
Proteinuria (mg/24 h)	<150	<150		<150	<150	494	356	465	<150
Azathioprine (mg/d)	100	100	100	100	100	100	100	100	100
Tacrolimus (mg/d)	4	4	4	4	4	4	4	4	4
Prednisone (mg/d)	5	5	5	5	5	10	10	10	5

and plans were formulated to achieve optimal maternal health and fetal development. The patient presented with a positive antinuclear antibodies test (ANA) (1/320) and a negative anti-DNA antibody. The tests for lupus anticoagulant and anticardiolipin antibodies (IgG and IgM) were negative. Screening for gestational diabetes mellitus was performed in the first trimester, and glycemic control was carried out during the pregnancy. The woman's glycemic control was normal during the course of the pregnancy. There was no change in tacrolimus dosage throughout pregnancy, and low molecular weight heparin was maintained throughout the pregnancy. Clinical and laboratory data obtained during this pregnancy are reported in Table 1.

The woman was diagnosed with pregnancy-induced hypertension (highest blood pressure was 147/91 mm Hg) at 21 WG. Her blood pressure was controlled with pindolol, and blood pressure levels remained within normal range throughout the remainder of the pregnancy. Anemia was detected at 28 WG and was treated by increasing iron and vitamin supplements. Uric acid levels increased late in pregnancy from 2.9 mg/dL to 4.8 mg/dL at 32 WG and to 5.1 mg/dL just before delivery. At 34 WG (January 9, 2015), the triplets (2 boys and 1 girl) were electively delivered by cesarean section. Surgery was performed under epidural anesthesia. The infants weighed 1755 g, 1900 g, and 1505 g (birth weight discordance = 20.8%), had Apgar scores of 8/10, 8/9, and 9/10, respectively, and were cared for in the neonatal intensive care unit. All of the children had respiratory distress syndrome due to hyaline membrane disease and were treated with aminophylline and continuous positive airway pressure as well as prophylactic antibiotics. The 3 infants had mild nonhemolytic neonatal jaundice; blood transfusion was not required. The infants were discharged from the hospital after 19 to 36 days. Maternal complications during pregnancy included proteinuria (494 mg/24 h), anemia, and mild hypertension, all of which resolved after delivery. No graft rejection episodes or deterioration of renal function tests was noted during pregnancy or immediately after the delivery.

Second Pregnancy

Six months after her first delivery, the woman informed us that she was pregnant. One month after this second pregnancy was diagnosed, an ultrasound revealed the approximately 7–2/7 weeks' gestation of 2 viable fetuses (a dichorionic diamniotic twin pregnancy). Ultrasound was repeated after 5 weeks confirming 2 viable fetuses with a posterior placenta and normal amniotic fluid. The gestational age was estimated to be 12–2/7 weeks. The course of the pregnancy was largely uneventful, with normal blood pressure values and no need for antihypertensive therapy. The woman had normal blood glucose levels during the pregnancy, and renal function did not significantly change during the gestational period. Tacrolimus was monitored during pregnancy, and its trough levels remained stable from preconception to the postdelivery period. Clinical data obtained during this pregnancy are reported in Table 2. At 37–4/7 WG, the woman underwent elective cesarean section with the birth of 2 healthy babies, both in cephalic presentation. At this time, the woman underwent tubal ligation. The first twin was a male with a weight of 2295 g, a length of 49 cm, and an

Table 2. Clinical and Laboratory Data During the Second Pregnancy

e	June 15	August 15	September 15	October 15	November 15	December 15	January 16	February 16	March 16	April 16
Gestational week	Pre	7th	12th	15th	19th	23rd	27th	32nd	37th	After
Blood	120	110	100	110	110	110	100	120	100	120
pressure (mm Hg)	70	60	60	70	70	60	60	60	60	80
Weight (kg)	57.4	56.7	55.3	57.0	60.7	61.0	62.6	64.1	64.8	57.1
Urea (mg/dL)	47		24		21		29	23		36
Serum creatinine (mg/dL)	1.10	0.92	0.92	0.90	0.90	1.00	1.00	0.80	0.80	0.90
Hemoglobin (g/L)	12.7		11.9	10.6		10.9		10.8	11.8	12.4
Serum albumin (g/dL)	4.7			4.6			4.5			4.2
Proteinuria (mg/24 h)	<150	<150		<150	<150		<150	<150	<150	<150
Azathioprine (mg/d)	100	100	100	100	100	100	100	100	100	100
Tacrolimus (mg/d)	4	4	4	4	4	4	4	4	4	4
Prednisone (mg/d)	5	5	5	5	5	5	10	10	10	5

Apgar score of 8/10 at the first and fifth minute; the second twin was a female with a weight of 1810 g, a length of 48 cm, and an Apgar score of 8/9 at the first and fifth minute (birth weight discordance = 21.1%). The infants had uneventful evolution, and they were discharged from the hospital after 10 days. Currently, more than 2-years after her last pregnancy, the mother and all 5 babies are healthy, and the mother's kidney transplant function is stable. In her most recent visit, the woman's serum creatinine was 0.90 mg/dL, proteinuria was <250 mg/24 h, and estimated glomerular filtration rate was 62.3 mL/min.

DISCUSSION

This report describes successful consecutive triplet and twin pregnancies in a woman after renal transplantation without assisted fertilization. To the best of our knowledge, there are no similar reports in the literature. Nowadays, fertility is improved within months after successful kidney transplantation [3], and it is not surprising that increasing numbers of pregnancies are reported in patients with transplanted kidneys.

For women with uncomplicated solid organ transplants and good renal function, without proteinuria and without arterial hypertension, pregnancy can be considered safe about 2 years after transplantation, as related in this case. However, pregnancies in kidney transplant recipients can be associated with maternal, fetal, perinatal, and allograft complications [3].

The recommendations just stated were proposed for the management of single pregnancies [3]; but no guidelines concerning the management of twin pregnancies in renal transplant recipient patients have been reported. The main limitations to defining the best obstetrical and systemic follow-up are related to the very low incidence of twin pregnancies in this small cohort of patients and the limited data available in the literature [5].

The first case of a twin pregnancy in a renal transplant woman with a favorable outcome for 1 set of twins was reported in 1975 [3,5], and the first successful triplet pregnancy following renal transplantation was reported in 1980 [4]. Since then, few cases of multiple pregnancies in renal allograft recipients have been reported [4–7], and only 3 successful triplet pregnancies have been described [5,6,8]. In 1980, the Registry of the European Renal Association–European Dialysis and Transplant Association described 4 sets of twins and 1 set of triplets among pregnancies after renal transplantation [6]. Jimenez et al [8] in 1995 and Mahmoud et al [9] in 2017 described successful triplet pregnancies with an excellent outcome without complication for mother or child. Finally, Furman et al [5] reported a triplet pregnancy after induction of ovulation in a renal allograft recipient, but the patient underwent a fetal reduction from triplet to twin, without maternal or fetal complications.

In summary, multifetal gestation in renal allograft recipients represents a high-risk pregnancy; however, the overall outcome in properly consulted patients could be considered favorable. In our report, we have described a case of multiple pregnancies in a renal transplant recipient with good pregnancy course and subsequent optimal maternal/neonatal outcome. Exceptional graft conditions and patient clinical characteristics may have facilitated this success. An integrated multidisciplinary team closely followed progress during the pregnancies. This is believed to be the first reported successful case of consecutive spontaneous triplet and twin pregnancies in a kidney transplant recipient.

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