Asian Biomedicine Vol. 4 No. 6 December 2010; 931-934

## **Clinical report**

# Twin pregnancy after renal transplant: the first case report in Thailand

Suksan Korpraphong<sup>a</sup>, Somchai Tanawattanacharoen<sup>a</sup>, Yingyos Avihingsanon<sup>b</sup> <sup>a</sup>Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, <sup>b</sup>Lupus Research Unit, Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

**Background:** With more advanced technology, the renal transplant women have more chance to get pregnant, even multiple gestations. Obstetricians need the knowledge to provide the better care for these patients. **Objective:** Report the natural course of disease and the intervention for renal transplant woman with twin

*Patient and methods:* A 20-year-old primigravida who underwent living-related renal transplantation eight months before pregnancy with monochrorionic diamniotic twins was treated throughout her pregnancy.

*Results:* At 30 weeks of gestation, the patient was admitted due to rising of creatinine level, high blood pressure, and proteinuria. After conservative treatment for 12 days, the pregnancy was terminated by cesarean section with tubal resection. Both alive twins weighed 1385 g and 1525 g. Allograft kidney biopsy was undertaken, and histologic examination showed acute rejection. The renal function gradually improved after one month of anti-rejection therapy.

*Conclusion:* The complications of pregnancy and poor perinatal outcomes are higher in renal transplant recipients. A multidisciplinary team is required for the management of these patients.

Keywords: Acute graft rejection, renal transplantation, twin pregnancy

The recent advances in surgical techniques and immunosuppressive drugs can improve the outcomes of the graft condition and improve reproductive function. Pregnancy in renal transplant recipient was first reported in 1963 [1]. There have been many case series regarding pregnancy among these patients. In one series, pre-eclampsia occurred in 26.4% and preterm delivery occurred in 26.4% of the recipients [2]. Another series showed that 40.7% resulted in term deliveries, and the rest had preterm deliveries [3].

These patients may have had some problems of infertility, and assisted reproductive technology (ART)

was introduced. The multiple pregnancies after renal transplant have been increasingly reported. These patients carry higher risk for maternal complications such as proteinuria and hypertension as well as poor perinatal outcome. In one study, 13 recipients reported 14 multiple gestations with 32 pregnancy outcomes. Twenty-eight fetuses were liveborns (88%), two were stillborns, and one set had spontaneous miscarriage [4].

The first case of renal transplantation in Thailand was performed in March 1972 at King Chulalongkorn Memorial Hospital. We report the first case of renal transplant recipient with successful twin pregnancy in Thailand. Our patient became pregnant spontaneously with twins, eight months after renal transplantation. We discuss the natural course of disease and the intervention for this patient throughout her pregnancy.

pregnancy.

*Correspondence to:* Somchai Tanawattanacharoen, MD, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Rama IV Road, Patumwan, Bangkok 10330, Thailand. E-mail address: fmedstn@gmail.com

## **Case report**

A 20-year-old primigravida was referred to the Division of Maternal-Fetal Medicine for her pregnancy. Her past medical history revealed chronic renal failure for several years. At the age of 18 years old, her creatinine rose to 13.8 mg/dL, and she was diagnosed as end stage renal disease (ESRD). Ten months later, she underwent living-related renal transplantation at King Chulalongkorn Memorial Hospital. The donor was her 46-years-old biological mother. Histophatologic examination of the failed kidney revealed chronic glomerulonephritis, diffused global sclerosis, and segmental sclerosis with extensive chronic tubulointerstitial change.

The immunosuppressive drug for induction was two doses of 50 mg of daclizumab. Cyclosporine, azathioprine, and prednisolone were selected as the maintenance immunosuppressants. The cyclosporine levels were maintained between 700 and 1,000 ng/ dL. She also needed antihypertensive drugs, atenolol (100 mg/day) and manidipine hydrochloride (40 mg/ day). Trimetroprim was given for the prevention of urinary tract infection. Four months after the transplant, the creatinine level showed clinical improvement, 0.8 mg/dL, and subsequently antihypertensive drugs could be discontinued.

Within eight months of renal transplantation, the patient had an unplanned pregnancy. The first ultrasonography showed a 14-week gestation of twin pregnancy, compatible with her last period. The twins were both female, and a single placenta at the right lateral location of uterus and a T sign of intertwin septum were observed. Therefore, monochrorionic diamniotic (MCDA) twin pregnancy was diagnosed. After counseling at length, the patient decided to continue her pregnancy. She was followed-up at a high-risk antenatal care clinic every two weeks and at a nephrological clinic every four weeks. Ultrasonographic follow-up every four weeks revealed the normal growth of concordant twins. Her blood pressure was normal. Without significant proteinuria, the creatinine level increased to level of 1.36 mg/dL at gestational age of 26 weeks.

At 30 weeks of gestation, the patient was hospitalized due to the rising of the creatinine level to 1.71 mg/dL and high blood pressure (160/100 mmHg). Her 24-hour urine contained 590 mg of protein. Other blood chemistry revealed a BUN level of 43 mg/dL, a uric acid level of 7.8 mg/dL, a SGOT level of 26 U/L, a SGPT level of 25 U/L, and an alkaline phosphatase level of 113 U/L. The cyclosporine level was 719 ng/mL. Ultrasonography of the urinary tract revealed a mild dilatation of the pelvicaliceal system of right upper pole, which was most likely due to the compression of an enlarged uterus. Chronic hypertension with superimposed pre-eclampsia was diagnosed, and graft rejection could not be ruled out.

We decided to terminate the pregnancy in agreement with the nephrologist and the urologist. The patient was counseled, and cesarean section with tubal resection was performed 12 days after admission. Both twins were female. The first twin weighed 1385 g while the second twin weighed 1525 g. Apgar scores at 1, 5 minutes of the first and second twins were 9, 10 and 8, 9, respectively. The post-operative course of the mother was uneventful and her creatinine level was still 1.7 mg/dL at day 2 after delivery. The first neonate needed a continuous positive airway pressure respirator for two days and was discharged at the age of 32 days. The second neonate needed only an oxygen box for one day and was discharged at the age of 26 days. Three weeks after delivery, her creatinine level was still high at a level of 2.25 mg/dL, and proteinuria was persistent. Thus, an allograft kidney biopsy for proving the cause of the deteriorated renal function was undertaken. Histologic examination revealed mild-to-moderate interstitial monomuclear cell infiltration, mild tubulitis, and moderate interstitial fibrosis with tubular atrophy. No endotheliosis was found. The diagnosis was acute rejection. She received 500 mg of methylprednisolone for three days, and the maintenance immunosuppressive regimen was changed to tacrolimus, mycophenolate mofetil, and prednisolone. The renal function became gradually improved. The serum creatinine returned to 1.6 mg/ dL one month after post anti-rejection therapy.

#### Discussion

The reproductive function of ESRD female patients who undergo renal transplantation will eventually improve after surgery. Patients should be counseled, especially, about the opportunity of pregnancy, proper contraception, safety timing for pregnancy, and complications from serious medical condition. Immunosuppressive drugs during pregnancy should be discussed. The contraception of choice in these populations is still inconclusive. Oral contraceptive pills and injections of depot medoxyprogesterone acetate (DMPA) are highly effective but relatively contraindicated in these patients. Intrauterine device should be considered with caution due to the risk of infection in immunocompromised hosts. Barrier methods are more appropriate in terms of patient's safety but may have higher failure rate. Their failure rate is 12%, but can be as low as 2% when used consistently [5]. Each medical center has its individual policy in preconception guidelines. In general, the patient should be in good health within 12-18 months of the procedure with no or minimal proteinuria, absent or well-controlled hypertension, no evidence of graft rejection, a stable renal function with serum creatinine levels of 2 mg/dL or less, and drug therapy should be reduced to maintenance level [6].

The major concern for our patient was the risk of the multiple pregnancies to her health, especially adverse effects on renal function. Two reports revealed the effect on the patient and graft survival after pregnancy; 0-2.9% of graft rejection, 15.3-26.1% of pre-eclampsia, 40.8-60.0% of preterm delivery, and 52% of intrauterine growth restriction [7, 8]. The outcomes of pregnancies were better in the recipients whose transplantation-to-conception interval was greater than two years. The incidence of term deliveries was 82%, compared with 46% in those recipients who became pregnant within one year [9]. Coscia et al. [10] reported the effect of multiple pregnancies to the risk of adverse pregnancy outcome. Of the 14 multiple gestations with 32 pregnancy outcomes (10 sets of twins, four sets of triplets), there were 28 livebirths (88%), two stillbirths (6%), two spontaneous miscarriages (6%). Four out of 14 patients developed pre-eclampsia (29%). There was no report of graft rejection during pregnancy. It was concluded that female renal transplant recipients could successfully maintain a pregnancy with twins or triplets.

At 30 weeks of gestation, the status of this patient became poorer, which was rather difficult to distinguish between pre-eclampsia and graft-versushost rejection. The clinical hallmarks for allograft rejection are fever, oliguria, deteriorating renal function, renal enlargement, and tenderness [6]. Biopsy for proving acute rejections during pregnancy is not common, ranging from 2% to 4% [3, 11]. In this case, pre-eclampsia was more likely to have been the cause of the deterioration in renal function. Our concern was that the renal function would get progressively worse. Therefore, we decided to deliver after consultation with the nephrologist, urologist, and neonatologist. The twin newborns were quite healthy. After delivery, deterioration of renal function persisted for three weeks. Kidney allograft biopsy revealed mild rejection. The possible cause could have been due to her short transplantation-to-pregnancy interval. In the early post renal transplantation period, especially in the first six months, the risk of acute rejection is high. Therefore, the recipient needs potent immunosuppressive drugs and their renal function is not stable. The recipient is not allowed to be pregnant during this period. Previous studies have shown no detrimental effect of pregnancy on long-term renal function in renal transplant recipients [8, 12].

In conclusion, contraceptive methods, proper timing, and risks of pregnancy on renal function, and perinatal outcomes should be discussed with reproductive female recipients after renal transplantation. Not only single pregnancies but also multiple pregnancies can occur in these populations. The effect on allograft renal function, the complications of pregnancies, and a poor perinatal outcome are higher than in the general population. A multidisciplinary team is required for the management of these patients.

The authors have no coflict of interest to declare.

## References

- Murray JE, Reid DE, Harrison JH, Merrill JP. Successful pregnancies after human renal transplantation. N Eng J Med. 1963; 26:341-3.
- Ghafari A, Sanadgol H. Pregnancy after renal transplantation: ten-year single-center experience. Transplant Proc. 2008; 40:251-2.
- Areia A, Galvao A, Pais MS, Freitas L, Moura P. Outcome of pregnancy in renal allograft recipients. Arch Gynecol Obstet. 2009; 279:273-7.
- Schiraldi M, Coscia L, Constantinescu S, Moritz M, Armenti V. National transplantation pregnancy registry (NTPR): in vitro fertilization outcomes in female kidney transplant recipients. Presented at Oocytes, Ovary and Transplantation: New Discoveries Applied to Fertility Preservation, Boston, USA, 2007. p. 28.
- Watnick S, Rueda J. Reproduction and contraception after kidney transplantation. Curr Opin Obstet Gynecol. 2008; 20: 308-12.
- Williams DJ, Davidson JM. Renal disorders. In: Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, editors. Maternal-Fetal Medicines Principle and Practice, 6<sup>th</sup> ed. Philadelphia:Saunder Elsevier, 2009. p. 905-25.
- 7. Al Duraihimh HA, Ghamdi G, Moussa D, Shaheen F, Mohsen N, Shama U, et al. Outcome of 234 pregnancies

in 140 renal transplant recipients from five middle eastern countries. Transplantation. 2008; 85: 840-3.

- Rahamimov R, Ben-Haroush A, Wittenberg C, Mor E, Lustig S, Gafter U, et al. Pregnancy in renal transplant recipients: long-term effect on patient and graft survival. A single-center experience. Transplantation. 2006; 81:660-4.
- Rudolph JE, Schweizer RT, Bartus SA. Pregnancy in renal transplant patients: a review. Transplantation. 1979; 27:26-9.
- Coscia LA, Cardonick EH, Moritz MJ, Armenti VT. Multiple gestations in female kidney transplant

recipients maintained on calcineurin inhibitors. Am J Transplant. 2003; 3 (Suppl 5): 563.

- Armenti VT, Radomski JS, Moritz MJ, Gaughan WJ, Gulati R, McGrory CH, et al. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl. 2005; 69-83.
- Fischer T, Neumayer HM, Fischer R, Barenbrock M, Schobel HP, Lattrell BC, et al. Effect of pregnancy on long-term kidney function in renal transplant recipients treated with cyclosporine and with azathioprine. Am J Transplant. 2005; 5: 2732-9.