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Successful pregnancy in renal transplant recipients.

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Abstract

Three cases of successful pregnancies in renal transplant recipients who had undergone transplantation in the Okayama University Medical School Hospital are reported. Two of the women had received an organ from a living relative and one woman received a cadaveric organ graft. These patients, aged 28-37 at the time of the delivery, had received their transplants 2-5 years prior to their conception. The periods of gestation ranged between 35 and 40 weeks. The weight of the babies at birth ranged from 2,380g to 2,500g and the apgar score at 1 min was 8 or 9. None of the infants showed any congenital abnormalities. Lower-segment cesarean section was performed in all of three cases. Serum creatinine levels, an indicator of renal graft function, did not deteriorate during the pregnancy or after delivery. Although further work is needed to solve problems regarding pregnancy in renal transplant recipients, these results encouraged us to meet their hope for a baby.

KEYWORDS: pregnancy, renal transplantation, immunosuppression

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Successful Pregnancy in Renal Transplant Recipients

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Three cases of successful pregnancies in renal transplant recipients who had undergone transplantation in the Okayama University Medical School Hospital are reported. Two of the women had received an organ from a living relative and one woman received a cadaveric organ graft. These patients, aged 28–37 at the time of the delivery, had received their transplants 2–5 years prior to their conception. The periods of gestation ranged between 35 and 40 weeks. The weight of the babies at birth ranged from 2,380g to 2,500g and the apgar score at 1min was 8 or 9. None of the infants showed any congenital abnormalities. Lower-segment cesarean section was performed in all of three cases. Serum creatinine levels, an indicator of renal graft function, did not deteriorate during the pregnancy or after delivery. Although further work is needed to solve problems regarding pregnancy in renal transplant recipients, these results encouraged us to meet their hope for a baby.

Key words : pregnancy, renal transplantation, immunosuppression

Most women with chronic renal failure during their reproductive years usually experience amenorrhea and consequently are infertile even if they are treated with regular dialysis. However after renal transplantation, their reproductive function is often restored and conception becomes possible. It is thought to be a great event for these patients to be blessed with children. Three cases of successful pregnancies in renal transplant recipients who underwent their transplantation in the Okayama University Medical School Hospital are described in this report.

Case Report

Case 1. The patient was a 25-year-old woman, who received a kidney transplant from her mother in March, 1985 after completing donor specific transfusion (DST).

She was treated with conventional immunosuppression therapy consisting of Azathioprine (AZ; 1.5mg/kg/d) and Methylprednisolone (MPS; 8mg/kg/d). She became pregnant in May, 1987 against the obstetrician's advise. Her first pregnancy was terminated at 10 gestational week by therapeutic abortion. The patient eagerly desired a baby and again became pregnant in April 1988. Her obstetricians and we, transplant surgeons decided to accept pregnancy and to proceed under careful control. Her renal function maintained well and there was no acute rejection. In December, 1988, she delivered via cesarean section a healthy boy weighing 2,440g, whose apgar score at 1min was 9 (37th week of pregnancy).

Case 2. A 34-year-old woman had received a cadaveric kidney in March 1989, and was treated with triple drug immunosuppression consisting of cyclosporine (CyA), MPS and AZ. She became pregnant 2 years and 5 months after the transplantation. Her pregnancy proceeded smoothly with the immunosuppression therapy of 4mg/kg/d of CyA, 10mg/d of MPS, and 50mg/d of

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Table 1 Clinical data of three pregnancies and deliveries in renal transplant recipients

Case	Type of transplant	Age at transplant	Age at delivery	Immunosuppressive drug	Average CyA trough level (ng/ml)	Serum creatinine (ng/dl)			Infant maturity (weeks)	Birth weight	Apgar score (1 min)	Cesarian section	Congenital abnormality
						Before pregnancy	During pregnancy	After delivery					
1	Living-related	25	28	MPS 8mg AZ 75mg	—	0.9	1.1	1.1	37	2,440g	9	Yes	No
2	Cadaver	34	37	CyA 4mg/kg MPS 10mg AZ 50mg	33	1.3	1.4	1.5	35	2,500g	8	Yes	No
3	Living-related	30	35	CyA 3mg/kg MPS 8mg	52	1.2	1.1	1.0	40	2,380g	9	Yes	No

CyA: Cyclosporine; MPS: Methylprednisolone; Az: Azathioprine.

AZ. Serum creatinine levels were 1.40, 1.37, and 1.37 mg/dl at the first, second, and third trimester, respectively. An ultrasonogram during the 35th gestational week, revealed mild hydronephrosis of the transplanted kidney, which appeared to press the fetal head and contraindicated a vaginal delivery. She delivered a healthy boy weighing 2,500 g via cesarean section. The apgar score at 1 min was 8 and no congenital abnormalities were found. The patient was advised against breast feeding.

Case 3. The patient, a 30-year-old woman, had suffered from chronic renal failure secondary to disseminated intravascular coagulopathy (DIC) caused by placental abruption and been treated with hemodialysis for 2 years. She had received a kidney from her mother in June, 1986 and was treated with double drug immunosuppression consisting Cyclosporine (CyA) (4 mg/kg/d) and MPS (8 mg/d). She became pregnant 4 years after transplantation and showed a stable renal function during the pregnancy. The patient delivered a healthy boy weighing 2,380 g at 40 weeks of the gestation via cesarean section. Breast feeding was not allowed in this case, either. Clinical data of the above mentioned cases are listed in Table 1.

Discussion

Since the first successful pregnancy of a woman after receiving a kidney from her identical twin sister was reported in 1958 (1), more than 2,000 cases of pregnancies in renal transplant recipients have been reported (2). In our country, 55 cases of successful pregnancies

after renal transplantation have been reported (3). For most transplant surgeons in Japan who have to treat the renal transplant recipients even after the transplantation, pregnancy counseling is not an avoidable issue because it is estimated that one among 50 women of childbearing age with a functioning graft become pregnant (4). To address this delicate issue, some maternal as well as fetal aspects of pregnancy in renal transplant recipients are discussed.

Due to the immunosuppressive state, renal transplant recipients are more susceptible to various infections during pregnancy (2). Although our three cases did not suffer from any infection, patients should be carefully monitored for all types of infection and prophylactic antibodies should be administered before and after even trivial surgical procedures.

Pregnancy is regarded as an immunologically privileged state (5) and no rejection episode was encountered in our experiences during pregnancy.

It is reported that in about 15 per cent of pregnant recipients significant impairment in renal function develops during pregnancy and persists in the postpartum period (5). Serum creatinine levels, used as an indicator of the renal graft function in our patients, did not deteriorate during gestation (average: 1.2 mg/dl) and after delivery (1.2 mg/dl), and compared well with preconception levels (1.1 mg/dl).

According to the Davison's review (2), cesarean section is necessary for obstetric reasons only and vaginal delivery should be the aim. Cesarean section was chosen for all three cases for various reasons. In the case 2 (hydronephrosis of the allograft caused by a fetal head oppression) and case 3 (CPD: Cephalopelvis disproportion-

tion) there were absolute indications for the cesarean section, but case 1 was thought to be a relative indication.

The three babies did not show any congenital abnormalities at birth, but effect of the immunosuppressive drugs on the fetus is a concern of the patients and the physicians. Corticosteroids have been reported to be associated with an increased incidence of cleft lip and cleft palate in animals, but not in humans (6). Small doses of the azathioprine readily transferred to the fetus, but reported anomalies were appeared random at a rate of about 3% (7). Uncertainty remains regarding long-term effects, particularly with reference to reproductive potential and risk of malignancy. CyA was introduced to the clinical field so recently that enough data to permit discussion of its effect on the fetus has not yet accumulated. One hundred sixteen pregnancies have been reported to the manufacturer with isolated cases of abnormalities, none reported more than once, although intrauterine growth retardation was frequently observed (7). According to previous reports, such small doses of immunosuppressive drugs as used in maintaining therapy after transplantation do not seem to evoke congenital abnormalities much more frequently than those observed in normal pregnancies (7). The two patients who were treated with CyA were advised against breast feeding because of high concentration of the CyA in the breast milk (8).

Some guideline for permitting pregnancy should be followed when transplant surgeons counsel the patients. Famous guidelines proposed by Davison (4) are as follows: a) good general health for about 2 years after transplantation; b) stature compatible with good obstetric outcome; c) no or minimal proteinuria; d) no hypertension; e) no evidence of graft rejection; f) no pelvicalyceal distention on a recent intravenous urogram; g) stable renal function with plasma creatinine of 2.0 mg/dl or less, preferably less than 1.5 mg/dl; h) drug therapy reduced to maintenance levels (prednisone, 15 mg/d or less, and azathioprine, 2 mg/kg body weight/d or less has been

quoted). Several points of this criteria, however, seem to be out of date because it was established before the cyclosporine era. We, therefore, modified this guideline based on recent reported findings. We are employing the following guideline to decide whether to support or advise against pregnancy: a) Stable for 2 years after transplantation; b) Serum creatinine level is less than 2.0 mg/dl; c) no proteinuria and no hypertension; d) no sign of rejection; e) immunosuppressive therapy can be kept as low as preconception maintenance doses (aiming doses; CyA: 4 mg/kg/d, MPS: 8 mg/d, AZ: 1 mg/kg/d).

It is natural that these patients may want to become mothers after their reproductive function is restored. Transplant surgeons should give appropriate counseling and try to accept their desire for pregnancy under the supervision of experienced obstetrician if the patient's condition meets the criteria. The previous reports and our results encourage a positive attitude towards pregnancy in renal transplant recipients.

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