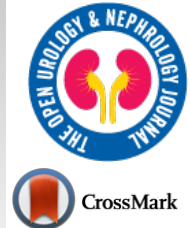




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## CASE REPORT

### The Treatment of Male Infertility After Allograft Renal Transplantation: A Case Series

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#### Abstract:

##### Background:

Renal transplantation is a useful option for allowing female renal failure patients of childbearing age to achieve pregnancy. However, there have been a few reports on the effects of renal transplantation on infertility treatment in male renal failure patients. We herein report two cases in which male patients underwent infertility treatment after renal transplantation.

##### Case Presentation:

Case 1: A 51-year-old Asian (Japanese) man underwent transplantation (the donor was his wife) for renal failure due to Autosomal Dominant Polycystic Kidney Disease (ADPKD). At two years after transplantation, he visited the reproduction center in our institute due to infertility. A semen analysis revealed oligoasthenozoospermia. He ultimately failed to achieve pregnancy and gave up on infertility treatment.

Case 2: A 47-year-old Asian (Japanese) man underwent renal transplantation (the donor was his sister) due to renal failure caused by diabetes mellitus. At three years after renal transplantation, he visited the reproduction center in our institute for infertility. Due to ejaculation disability and the absence of sperm in the patient's urine after masturbation, he was diagnosed with anejaculation. Thus, testicular sperm extraction (TESE) was performed. Twenty-three motile spermatozoa were successfully retrieved by microdissection TESE (micro-TESE). ICSI was subsequently performed and a good embryo was transferred. His wife achieved pregnancy and is expected to deliver this October.

##### Conclusion:

We report two cases of male infertility treatment after renal transplantation.

**Keywords:** Male infertility, azoospermia, oligospermia, Renal transplantation, Spermatozoa, Kidney disease.

#### Article History

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## 1. BACKGROUND

Renal transplantation is a useful option for female renal failure patients of childbearing age who wish to achieve pregnancy. Previous studies have confirmed that the fertility of some female renal failure patients was improved by renal transplantation [1 - 3]. However, there are a few reports on the effects of renal transplantation on male infertility. We herein report two cases in which male infertility treatment was performed after renal transplantation.

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## 2. CASE PRESENTATION

### 2.1. Case 1

The patient was a 53-year-old Asian (Japanese) man who had received hemodialysis due to autosomal dominant polycystic kidney disease (ADPKD) for 12 years (Table 1). He underwent renal transplantation (the donor was his wife). At that time, neither the patient nor his wife intended to have children. Immunosuppressive treatment was initiated with Tacrolimus (Tac), Mycophenolate Mofetil (MMF), Methyl Prednisone (MP), and Basiliximab (Basi). He experienced no graft rejection and favorable control with Tac (1.5 mg/day), MMF (1.5 g/day), and MP (2 mg/day). At two years after renal transplantation, the patient indicated that he and his wife

wished to have children and the patient visited the reproduction center in our institute with the chief complaint of infertility. At this time, his wife was 40 years of age.

**Table 1. Patient characteristics and the clinical course.**

Case	1	2
Underlying Disease	ADPKD	DM
Age	53	50
Duration of HD(years)	12	3
Immunosuppressive Tx.	Tac+MMF+MP+Basi	Tac+MMF+MP+Basi
After Transplantation(yr.)	2	3
Age of Wife	40	38
PRL(ng/mL)	9.7	20.9
Testosterone(ng/mL)	5.03	5.96
LH(IU/mL)	4.8	9.1
FSH(IU/mL)	8.4	6.8
Passage	ICSI, IVF-ET	mTESE, ICSI, IVF-ET
Pregnancy	(-)	(+)

A semen analysis revealed that the patient's sperm concentration was  $3.69 \times 10^6$ /mL and the motile sperm count was 6.67%. According to semen analysis, zoospermia was observed, therefore TESE was not performed. The bilateral testicular volume was 18 ml and no varicocele was seen. Hormone analysis revealed the following findings: prolactin, 9.7 ng/mL; testosterone, 5.03 ng/mL; LH, 4.8 IU/mL; and FSH, 8.4 IU/mL. Due to the low motile sperm count, IVF, ICSI and subsequent embryo transfer were performed. However, pregnancy was not achieved.

## 2.2. Case 2

The patient was a 50-year-old Asian (Japanese) man who had received hemodialysis due to diabetes mellitus for three years (Table 1). He underwent renal transplantation (the donor was his sister). Immunosuppressive therapy was initiated with Tac, MMF, MP, and Basi. He experienced no graft rejection and favorable control with Tac (4 mg/day), MMF: (1.0 g/day), and MP 5 (mg/day).

At three years after renal transplantation, he visited the reproduction center in our institute due to infertility. He had two children with his former wife before renal failure. At that time, he was fertile and the two children were conceived naturally. He had no varicocele and seminal tract obstruction. A laboratory examination revealed the following findings: prolactin, 20.9 ng/mL; testosterone, 5.96 ng/mL; LH, 9.1 mIU/mL; FSH, 6.8 mIU/mL. He had an ejaculatory disorder during masturbation, despite the presence of orgasm. Retrograde ejaculation was suspected; however, no sperm was found in the patient's urine after masturbation. Thus, with a diagnosis of anejaculation due to diabetic neuropathy, 23 motile spermatozoa were successfully retrieved by micro-TESE. ICSI and embryo transfer were subsequently performed. Implantation and pregnancy were successfully achieved. His wife is expected to deliver this October.

## 3. RESULTS & DISCUSSION

One in 6 couples complains of infertility. Approximately half of such cases involve male infertility [4]. Infertility among

female patients with end-stage renal disease has been extensively investigated. The male reproductive function in such patients is less well-characterized. Recently, some cases have been reported that showed that the genesis of the male sexual function is multifactorial [5].

In renal failure patients, various factors result in infertility, including endocrinological abnormalities (*e.g.*, hyperprolactinemia), decreased spermatogenesis through the Sertoli cells, ejaculatory disorder and erectile dysfunction, autonomic neuron dysfunction, iatrogenic infertility related to hemodialysis or immunosuppression, impeded blood flow due to arteriosclerosis, and primary disease. The most commonly accepted hypothesized mechanism of infertility in renal transplantation patients is that hypergonadotropic hypogonadism occurs due to the disturbance of the hypothalamic-pituitary-gonadal axis, resulting in the suppression of spermatogenesis [6]. After renal transplantation, the improvement of the endocrine environment results in improved fertility [7].

Generally, immunosuppressive agents do not induce spermatogenesis or teratogenicity. On the contrary, some reports have shown that cyclosporine A has a negative impact on spermatogenesis and oogenesis [8]. Eid *et al.* reported that phthalic acid from the dialysis circuit reduced sperm motility in patients undergoing long-term dialysis [9]. These findings suggest that male infertility has a multifactorial etiology; thus, it is difficult to detect specific factors causing male infertility.

In case 1, we investigated ADPKD-induced infertility. ADPKD is one of the most common monogenic human disorders and causes renal failure in a significant number of patients who require dialysis or renal transplantation. ADPKD is an inborn disease in which cysts arise in the bilateral kidneys and various organs, suppressing the renal function. Although ADPKD does not reduce infertility in comparison to the general population, male infertility has been reported to occur due to seminal vesicle cysts and azoospermia [10].

Diabetes mellitus also affects infertility. Majzoub *et al.* showed that more than half of diabetes mellitus patients showed ejaculation disability [11]. Based on these findings, it is difficult to detect the causes of infertility before renal transplantation. A hormone analysis or semen examination might help in the pre-transplantation diagnosis of male patients with infertility.

Age also affects fertility in renal male transplantation patients. Generally, the quality of sperm gradually decreases after 35 years of age [12]. However, it is more difficult to set a cut-off age for male infertility than it is for female infertility.

We experienced and treated two cases of male infertility after renal transplantation. In one case, assisted pregnancy was successfully achieved.

## CONCLUSION

We reported two cases of male infertility treatment after renal transplantation.

## LIST OF ABBREVIATIONS

- ADPKD = Autosomal Dominant Polycystic Kidney Disease
- TESE = Testicular Sperm Extraction
- MMF = Mycophenolate Mofetil

**MP** = Methyl Prednisone

**Basi** = Basiliximab

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval and consent to participate & consent for publication were obtained.

The present study was approved by the IRB of Yokohama City University Medical Center and written informed consent was obtained from the patients. The Editor-in-Chief of this journal has a copy of the written consent available for review.

### HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

### CONSENT FOR PUBLICATION

Written informed consent was obtained from the patients for the publication of this case report and any accompanying images.

### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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### AVAILABILITY OF DATA AND MATERIAL

Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

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### AUTHORS CONTRIBUTION

DT, TK, TT, TM, YH, JT SK and ST conceived and designed the experiments. DT, TK, TT, KS, YH, YM and HU analyzed the data. ST, TT, KU, KS, YH, TM, DT, YH, JT,

YM, MY, YI, YY, and HU performed the experiments. KK, YY, YM, JT and HU critically revised the manuscript for important intellectual content. DT, TK and TT wrote the paper.

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