Live birth after in vitro fertilization and single embryo transfer in a kidney transplant patient: a case report and review of the literature

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Abstract

Background To present a successful case of in vitro fertilization (IVF) and single embryo transfer (SET) in a kidney transplant (NTX) patient and review of the literature.

Methods Case report and review of the literature.

Setting IVF-Unit in a university medical center.

Patient(s) A 31 year-old nulliparous woman with primary infertility and a history of two kidney transplants.

Intervention(s) IVF-SET

Main outcome measure(s) Live birth, renal transplant function.

Results(s) IVF-SET resulted in a pregnancy with labor induction and cesarean delivery in the 37th week of gestation due to rising serum creatinine. There was no significant maternal or fetal morbidity.

Capsule Assisted reproduction by in vitro fertilization/embryo transfer is feasible in kidney transplant patients. To date, including this case, five cases have been reported in the literature.

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Conclusion(s) Successful IVF-SET is possible in NTX patients. To date, including this case, five cases of IVF in NTX patients have been reported in the literature without an apparently increased renal morbidity.

Keywords Kidney transplant · In vitro fertilization · Single embryo transfer

Introduction

The first successful pregnancy in a kidney transplant (NTX) recipient was reported in 1963 by Murray et al. [1]. In 2004, the US National Transplantation Pregnancy Registry (NTPR) listed 1480 pregnancies in NTX patients [2], supporting the notion that pregnancy does not compromise the function of the kidney transplant. In 1995, Lockwood et al. performed the first successful IVF attempt in a NTX patient [3]. Subsequently, four reports of IVF in NTX patients have been reported, as presented in Table 1 [4–7] (PUBMED literature search on July 5, 2010; search terms: kidney transplant, renal allograft, in vitro fertilization, IVF, assisted reproduction, ART, pregnancy). To our best knowledge, the present case is the fifth reported successful pregnancy after IVF in a NTX patient and the first using single embryo transfer (SET).

Case report

A 31-year-old G0 P0 was referred to our infertility center because of primary infertility based on a male factor, ie teratozoospermia. She had undergone her first NTX for reflux nephropathy in 1991 at the age of 14 years. In 2001, she experienced a transplant rejection. The transplant was removed and she subsequently underwent dialysis. One year later, a second kidney transplan-

Table 1 Case reports in the literature of pregnancies after IVF/ICSI^a in renal transplant patients

Author	Year	Age of Patient	NTX ^b	Period between NTX ^b and IVF ^a (Years)	Protocol	Gonado-tropin	E2 ^d on Day of OI ^e	No of O ^g	IVF/ ICSI ^a	FR ^h	CRYO ⁱ	No of LB ^k TE ^j			
Lockwood et al.	1995	36	Kidney graft	10	Long	rFSH ^l (Metrodin 75 IU ^c)	n.a.	HCG ^m (Profasi)	10000 IE ^f	2	IVF ^a	2	no	2	1
Furmann et al.	1999	31	Kidney graft	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	2
Khalaf et al.	2000	28	Kidney graft	10	Long	rFSH ^l (Gonal F IU ^c)	4086 pg/ml	HCG ^m (Profasi)	10000 IE ^f	22	ICSI ^a	12	11	2	2
Tamaki et al.	2003	32	Kidney graft	1	n.a.	n.a.	n.a.	n.a.	13	ICSI ^a	7	no	3	1	1
Nouri et al.	2010	31	Kidney graft	10	Antagonist	Puregon 150 IU ^c	3726 pg/ml	rHCG ⁿ (Ovitrelle)	15	IVF ^a	6	0	1	1	1

^a IVF/ICSI = in vitro fertilization/intracytoplasmic sperm injection; ^b NTX = renal transplantation; ^c IU = international units; ^d E2 = estradiol; ^e OI = ovulation induction; ^f IE = international units; ^g O = oocytes; ^h FR = Fertilisation Rate; ⁱ CRYO = cryoconservation; ^j TE = transferred embryos; ^k LB = live birth; ^l rFSH = recombinant follicle stimulating hormone; ^m HCG = human chorionic gonadotropin; ⁿ rHCG = recombinant human chorionic gonadotropin

tation was performed with an uneventful course. At the time of presentation, her serum concentrations of urea and creatinine were 7.4 mg/dl and 0.99 mg/dl, respectively. Anti-muellerian hormone (AMH) was 4.51 ng/ml. Her medication included azathioprin (Imurek[®] GlaxoSmithKline Healthcare, Austria), which was switched to Cyclosporine A (Neoimmun[®] Kwizda Pharma GmbH Vienna, Austria), after she declared her intention to become pregnant.

The first IVF attempt was made in November 2008 using an antagonist protocol, which was not successful resulting in a biochemical pregnancy with subsequent spontaneous abortion. The second IVF attempt took place in February 2009. On day three of the menstrual cycle, we started with 150 international units (IUs) of recombinant follicle stimulating hormone (FSH) (Puregon[®]; Organon Germany) for 11 days. On day five of the stimulation, the serum estradiol (E2) concentration was 1114 pg/ml. Transvaginal sonography on day 9 revealed 15 follicles. The E2 concentration rose to 3726 pg/ml. The leading follicles did not reach a diameter of 17 mm. Because of the risk of developing of ovarian hyperstimulation syndrome (OHSS), we decided to perform coasting until the E2 concentration fell below 3000 pg/ml. The patient did not have any pelvic pain or abdominal distension. Both ovaries were enlarged (70×65 mm and 73×58 mm). She had no ascites. The patient did not inject any gonadotropins on day 9 and day 10, and she received ganirelix (Orgalutran[®] 0.25 mg/0.5 ml, Organon, Germany). After administration of recombinant hCG (Ovitrelle 250 mg; Serono, Germany) on day 10, we performed transvaginal oocyte retrieval 36 h later. Fifteen oocytes were retrieved. Six oocytes were fertilised. On day 3 after retrieval, we transferred one embryo in the cleavage state. A qualitative urine hCG pregnancy test two weeks later was positive and on day 35 after SET, we observed a single embryo in the uterine cavity with a positive heart beat.

The patient was monitored weekly throughout pregnancy. The early course of pregnancy was uneventful with a creatinine of 0.82 mg/dl and urea below 7 mg/dl at 12 weeks gestation. Renal function at the end of the first trimester was normal. The 14 weeks scan was normal. There was no proteinuria on weekly urine monitoring and ultrasound examinations showed regular fetal growth. At 37 weeks gestation, there was a rise of serum creatinine with 1.07 mg/dl and of serum urea with 8.6 mg/dl. Based on the rise of creatinine and urea indicating deterioration of the renal transplant, it was decided to start labor induction with vaginal dinoprostone (Prostin[®] E2; Pharmacia Upjohn, Erlangen, Germany) 2×3 mg in an interval of 6 h on two consecutive days without success. We performed a cesarean section at 37+6 weeks gestation. A healthy boy (weight 2630 grams; length 50 cm) was delivered. Creatinine and urea decreased to normal levels within 24 hrs. Renal function remained stable throughout the patient's stay in the maternity ward (serum creatinine 0.9 mg/dl and urea 7.7 mg/dl on day five after delivery). Blood

pressure and diuresis were daily monitored and were satisfactory. The patient returned home on day 7 after delivery.

Review of the literature

Table 1 lists four cases of IVF in NTX patients. The first IVF in a NTX patient was reported by Lockwood et al. in 1995 [3]. After a long protocol and the transfer of two embryos, the patient had a twin pregnancy complicated by deep venous thrombosis and premature rupture of membranes (PROM) with a subsequent vaginal delivery in 29 weeks gestation. Her renal function was stable throughout pregnancy. Furman et al. reported another twin pregnancy in a NTX patient after IVF with a stable renal function and cesarean delivery in 33 weeks gestation subsequent to the development of therapy-resistant pregnancy-induced hypertension (PIH) [4]. Also in 2005, Khalaf et al. reported on a NTX patient with renal obstruction, presumably due to enlarged ovaries after controlled ovarian hyperstimulation. Three months later, a twin pregnancy after transfer of two thawed frozen embryos was achieved [5]. This pregnancy was complicated by preterm labor and spontaneous delivery in 30 weeks gestation. Tamaki et al. reported on a successful singleton pregnancy after IVF and transfer of three embryos with a cesarean section in 35 weeks gestation. In this case, renal function was stable throughout pregnancy [6].

Discussion

This case report is, to the best of our knowledge, the fifth case of a successful IVF in a NTX patient resulting in a live birth and the first reported case of SET in this patient population. The impact of pregnancy on the kidney transplant in NTX patients is still a matter of debate. The developments in the field of transplantation medicine have led to a better and longer functioning of renal allografts, which subsequently led to a higher quality of life in these patients. One of the most controversial aspects in this population remains the concern regarding reproductive health in general and the use of assisted reproduction in particular. Both impaired graft dysfunction and graft rejection have been previously described in non-IVF pregnancies. It was reported that only 40% of conceptions in NTX patients will progress beyond the first trimester [7]. As pregnancy advances, there is a 26–30% risk of developing hypertension, proteinuria, and pre-eclampsia with a potentially increased risk of transplant failure [8]. Compared to normal pregnancies, an increased risk of intrauterine growth retardation, low birth weight, and prematurity have been suggested in pregnant NTX patients [9]. This is in accordance with the data reported in four

cases of pregnancies after IVF in NTX patients in the literature. In all four cases, pregnancy resulted in premature delivery and was complicated by PE, PIH or PROM in three cases. One may therefore also consider alternatives to assisted reproduction such as a gestational carrier in those women with NTX and further relative contraindications to pregnancy.

Regarding the functionality of the renal transplant, however, the NTPR reported a graft rejection rate of 6% in pregnant NTX patients, which hardly differs from that found without pregnancy [10]. This finding is also in accordance with the reports on pregnancies after IVF in NTX patients, which consistently experienced stable transplant functions throughout pregnancy.

In summary, NTX patients with infertility can successfully be treated with IVF and deliver healthy children without compromising the transplant function. To date, including this case, five cases of IVF in NTX patients have been reported in the literature without an apparently increased renal morbidity. However, pregnancy was complicated by PE, PIH, PROM, and premature delivery in four of five cases.

Conflict of Interest Disclosure The authors declare no conflict of interest.

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