

## Successful pregnancy outcome after in vitro fertilization in a pancreas-kidney recipient

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**Objective:** To describe the first case of IVF pregnancy in a pancreas-kidney recipient.

**Design:** Case report.

**Setting:** Reproductive Medicine Department, Hôpital Edouard Herriot, Lyon, France.

**Intervention(s):** In vitro fertilization in a pancreas-kidney recipient.

**Patient(s):** A 39 year-old nulliparous woman, with primary infertility and a history of pancreas-kidney transplant at 29 years of age.

**Main Outcome Measure(s):** Multidisciplinary agreement for the couple to be managed by IVF. Follow-up of pregnancy and delivery.

**Result(s):** Singleton IVF pregnancy in a pancreas-kidney recipient, maintained up to 34 weeks. Cesarean delivery ahead of labor. No severe maternal or fetal complications. Live birth. Normal postpartum renal function and glycemia.

**Conclusion(s):** An IVF pregnancy is feasible in a pancreas-kidney recipient. Such treatment should follow agreement by all the medical teams following the patient. Pregnancy in a pancreas-kidney recipient is at-risk, requiring close monitoring. (Fertil Steril® 2008;90:849.e1–e3. ©2008 by American Society for Reproductive Medicine.)

**Key Words:** IVF-ET, pancreas-kidney recipient, pregnancy, multidisciplinary team

The first pregnancy in a kidney recipient was achieved in 1956 and reported in 1963 (1). There have been several subsequent reports of full-term pregnancies after pancreas-kidney transplant. The National Transplantation Pregnancy Registry (NTPR) compiles such cases and, in 2004, analyzed a series of 56 pregnancies in 38 pancreas-kidney recipients (2). The first IVF pregnancy in a kidney recipient presenting with secondary infertility was reported by Lockwood et al. in 1995 (3). There have been subsequent reports, notably by Furman et al. in 1999 and Tamaki et al. in 2003, describing pregnancies after IVF or induced ovulation in kidney recipients (4, 5).

We here report a successful IVF pregnancy in a pancreas-kidney recipient.

A 39-year-old woman was referred for primary infertility of 6 years' standing, with a history of abortion. She had suffered insulin-dependent diabetes since the age of 7 years and had received a pancreas-kidney graft in 1997, at the age of 29, which restored normal renal function and glycemia. In 1999, she underwent vitrectomy followed by enucleation of the left eye, due to glaucoma, with concomitant right

eye vitrectomy and laser treatment for diabetic retinopathy. In 2002, her immunosuppression treatment was complicated by an infiltrating keratinizing differentiated malpighian left carcinoma of the labia minora (T1b, N0, M0, according to FIGO staging classification), managed by in sano surgical resection. Her first request for IVF was in 2004. When she first began to be followed in our department, her immunosuppression treatment included azathioprine (Imurel; GlaxoSmithKline, Marly-le-Roi, France), tacrolimus (Prograf; Astellas Pharma, Levallois-Perret, France), and prednisolone (Solupred; Sanofi-Aventis France, Paris, France). Hormonal status was normal. Hysterosalpingography showed bilateral hydrosalpinx.

Initial management comprised treating a *Ureaplasma urealyticum*-positive spermoculture with doxycycline (Vibramycine; Laboratoires CS, Paris, France) and adapting the husband's antidepressant treatment, notably by stopping the neuroleptics, so as to restore ejaculation. Multidisciplinary coordination between the Reproductive Medicine Department and obstetrics, nephrology, oncology, anesthesiology, and ophthalmology teams led to IVF management being authorized for the couple's infertility.

The protocol was a long protocol, with LHRH analog blockade (daily decapeptyl 0.1 injection; Beaufour Ipsen Pharma, Paris, France) and ovarian stimulation by recombinant FSH

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(Puregon; Organon, Puteaux, France). A first attempt was made in October 2005; 20 oocytes were recovered, 12 of which were fertilized by intracytoplasmic sperm injection and 8 by classic IVF. Ten embryos were obtained and two 4-cell embryos transferred; no pregnancy was obtained, and no embryos were frozen. A second attempt was made in January 2006; 21 oocytes were recovered, and 11 embryos obtained by classic IVF, 2 of which were transferred. No pregnancy was obtained, and no embryos were frozen. At the end of this second attempt, spermatozoid DNA fragmentation was assessed at 7.6%. In May 2006, a third attempt involved 17 oocytes fertilized by classic IVF, giving 13 embryos. Ovulation induction was induced on day 12 (peak E<sub>2</sub> level: 5,605 pg/mL on day 11) by recombinant hCG (Ovitrelle 250 µg; Serono France, Boulogne, France). Two blastocyst-stage embryos (A/A and B/A according Gardner and Schoolcraft's classification [6]) were transferred, and an evolutive singleton pregnancy was obtained with a vaginal progesterone supplementation: progesterone 200 mg (Utrogestan; Laboratoires Besins International, Montrouge, France) twice a day for 3 months.

Early course was without incident, with glycemia at 3.73 mmol/L and creatinemia at 68 µmol/L at 12 weeks of gestational age. After consultation with the hospital's Antenatal Diagnosis team, the couple decided against the amniocentesis indicated for the patient's age. Renal function at the end of the first trimester was normal. Morphologic ultrasound scan showed a biometry of 25th percentile. At the beginning of the second trimester, there was onset of elevated blood pressure, well controlled by clonidine (Catapressan; Boehringer Ingelheim, Paris, France). Proteinuria never exceeded 0.32 g/L on weekly monitoring, and glycemia was consistently satisfactory. Ultrasound check-ups showed regular growth, with a biometry of 25th percentile. At 34 weeks of gestation, the patient was admitted for abnormal fetal heart rate. Cesarean section was performed at 34 weeks post-menses + 2 days following cervical bleeding and abnormal fetal heart rate. A 1,630-g boy was delivered and transferred to Neonatology. Renal function and glycemia remained normal throughout the patient's stay in the maternity ward (glycemia and creatininemia on day 4 after delivery were 3.3 mmol/L and 78 µmol/L, respectively). Blood pressure and diuresis were daily controlled. Patient returned home on day 5 after delivery.

This case report is, to the best of our knowledge, the first of an IVF pregnancy in a pancreas-kidney recipient leading to live birth. Such management raises several questions. It is relevant to only a small number of patients, i.e., pancreas-kidney recipients of child-bearing age and wishing a pregnancy.

The graft impact of pregnancy is a matter of debate (7). Impaired renal function or even graft rejection can be observed, especially when uncontrolled vomiting in the first 3 months hinders intake of immunosuppressants. Immunosuppression needs to be stepped up during the second trimester owing to increased distribution volume. Finally, certain cases of

pregnancy-linked kidney obstruction have been reported (8). The NTPR, however, reported 56 pregnancies in 38 pancreas-kidney recipients for 2004, with 46 live births and a graft rejection rate during pregnancy of 6%, which hardly differs from that found without pregnancy (7).

Pregnancy in pancreas-kidney recipients is especially at-risk and requires close monitoring. The NTPR reported a 14% spontaneous stillbirth rate and 2% extrauterine pregnancies. Infection is a frequent (55%) complication, and urinary infection in particular is to be screened for and treated owing to the potential renal impact. High blood pressure is found in 75% of cases, and preeclampsia in 34% (2).

Seventy-eight percent of live births are preterm (delivery <37 weeks of gestation), and 63% show delayed intrauterine growth (birth weight <2,500 g) (2). The present case showed both these features.

The originality of the present case report lies in the pregnancy's having been obtained by IVF. Such an attitude in managing a pancreas-kidney recipient raises certain problems (3). First, ovarian hyperstimulation causes hyperestradiolemia and increases the risk of thromboembolism, especially in case of ovarian hyperstimulation syndrome. Antiplatelet or anticoagulant therapy may be envisaged, although not implemented in our present case. Lower recombinant FSH doses may also be used; in the present case, we never exceeded 200 IU Puregon. Second, there is a danger of damaging the ectopic kidney during ovarian puncture, although ultrasound guidance should avoid this. Finally, IVF entails a risk of multiple pregnancy (4), particularly unwelcome in such patients; we nevertheless chose to implant two embryos, because, having agreed to include the patient in an IVF protocol, it seemed only logical to give her every chance of success.

An IVF pregnancy involves a risk of certain maternal and/or fetal complications in pancreas-kidney recipients. The treatment decision must therefore be made conjointly by the medical team and the couple, whose informed consent is essential. The medical team needs to be multidisciplinary, with all parties—Reproductive Medicine, obstetrics, anesthesiology, the transplantation team and, in the present case, the oncologists and ophthalmologists—in full agreement. Once obtained, pregnancy requires close monitoring, as in spontaneous pregnancy in pancreas-kidney recipients.

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