Birth of a Healthy Baby 9 Years After a Surgically Successful Deceased Donor Uterus Transplant

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Objective: To describe surgical procedures, previous failed pregnancies, methods for overcoming pregnancy failure and, most importantly, birth of a healthy infant, in a uterus transplantation from a deceased donor.

Background: Majority of uterus transplants have involved live donors, but several advantages make deceased donor transplantation a practicable option, principally by eliminating surgical risks to the live donor.

Methods: Uterus transplantation from a deceased donor was performed in September 2011 in Turkey. After 5 miscarriages, perfusion computed tomography revealed an obstructed blood-outflow. To overcome this blood flow obstruction, a saphenous vein graft was anastomosed between utero-ovarian and left ovarian vein with laparotomy. Follow-up computed tomography confirmed resolution of venous congestion and a decrease in uterine volume.

Results: Following vascular augmentation surgery, fetal cardiac activity were observed 28 days after the first embryo transfer attempt. Preterm premature rupture of the membranes was diagnosed at 19 weeks' gestation. Cesarean section was planned at 28 weeks' gestation due to intrauterine growth restriction and suspected preeclampsia. A healthy 760 g male baby was delivered. The baby was discharged from the neonatal intensive care unit 79 days after delivery in good condition weighing 2475 g.

Conclusions: Deceased donor uterus transplantation is a reasonable approach for treating uterine factor-related infertility. In case of recurrent miscarriages, regional vascular augmentation by arterial or venous supercharging may be required to overcome regional misperfused regions determined by imaging studies.

Keywords: deceased donor, live birth, repeated miscarriages, uterus transplantation, vascular revision

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Absolute uterine factor infertility affects 3% to 5% of all reproductive women, and no treatment for this condition has been available until recently.[1] Surrogacy and adoption are alternative methods for overcoming uterine-related infertility, although surrogacy is not legal in many countries, and adoption does not establish a genetic link between mother and child. After the successful uterus transplantation in Turkey on September 2011, studies in this field accelerated significantly, and successful transplantations and consequently live births were reported from different parts of the world.[2–4] Most uterus transplants involve live donors, although several advantages make deceased donor transplantation a reasonable option, mainly by eliminating surgical risks to the live donor. This report describes in detail the surgical procedures, previous failed pregnancies, methods for overcoming pregnancy failure and, most importantly, the birth of a healthy infant, in this uterus transplantation from a deceased donor.

METHODS

Our institution is a highly specialized referral center for microsurgical procedures, including traumatic extremity autotransplantations and a number of successful composite tissue transplantations (face, double hand, and lower extremities), and numerous solid organ transplantations.[5–7] We also receive significant patient numbers and have considerable experience of surgical treatment of vaginal agenesis.[8] A special patient registry had already been established for women with Mayer–Rokitanski–Kuster–Hauser syndrome. Patients eligible for the uterus transplantation project were selected from this registry, and pretransplantation work-up was carried out for each candidate, as previously reported.[2,9]

Case

The uterus transplantation from a deceased donor performed in Turkey in September 2011 was the first such procedure in the world, and only the second trial after the failed attempt in Saudi Arabia, as previously reported.[2,10] The recipient was 21 years old female with Mayer–Rokitanski–Kuster–Hauser syndrome without any chronic disease. Two years before the transplantation she had a vaginal reconstruction with jejunal segment. Preoperatively she had normal blood tests (including normal renal function, normal Follicle stimulating hormone, Estradiol (E2), Anti-mullerian hormone levels). The renal function and anatomy was normal before the transplantation procedure. Basic fertility work-up for the patient and her spouse was all within normal limits. Her ovarian reserve was evaluated by measuring her Follicle stimulating hormone, E2, and Anti-miillerian hormone (1.9 ng/mL) levels and her total antral follicle count (13). The sperm analysis for her husband was normal according to World Health Organization 2010 criteria. The result of her karyotype analysis was 46, XX. She was a nonsmoker with a BMI of 21 kg/m^2. Her screening tests were negative for infection with

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human immune deficiency virus, hepatitis B and C virus, toxoplasma, rubella, and cytomegalovirus. In psychiatric examination, counselor found her to be stable. She was selected to be first among the 3 candidates because of the match with the donor's blood group and HLA. The patient underwent 2 in vitro fertilization cycles, which yielded 8 grade-1 embryos.

The donor was a 22-year-old nulliparous brain-dead woman who had cerebral trauma in a traffic accident. She was pretested for blood group type, human leukocyte antigen (HLA) matching, and screening for toxoplasma, rubella, cytomegalovirus, human immunodeficiency virus, and hepatitis B and C. She revealed no signs of latent or acute infection. The donor's and recipient's blood groups were the same, and they shared 3 HLAs (donor: HLA-A∗03, HLA-A∗11; HLA-B∗08, HLA-B∗51; HLA-DRB1∗03, HLA-DRB1∗15; recipient: HLA-A∗03, HLAA∗ 32; HLA-B∗08, HLA-B∗18; HLA-DRB1∗03, HLA-DRB1∗11). Anti-HLA reactive antibodies and retrospective crossmatching were negative. Transabdominal ultrasound performed in the intensive care unit revealed the uterus had no structural abnormalities such as myoma uteri or uterine anomaly. A cervical smear was inspected for the presence of cervical lesions and human papillomavirus types 16, 18, 31, 33, and 45 using the nucliSENS Easy Q HPV v1 assay (BioMerieux) to get a reliable and prompt result.

The uterine retrieval was performed as the first procedure from the donor including long vascular pedicles of common iliac artery and veins. The retrieval process took 120 minutes. Transfer time was 30 minutes. Regarding the recipient surgery, a median incision was performed. The external iliac artery and vein were dissected. After back-table preparation of the uterine graft, the uterus allograft was placed in the orthotopic position. Vaginal part of the graft was sutured to the apex of previously created jejunal neovagina. Sacrouterine ligaments were secured to sacrum to create a three-dimensional stable neo-uterus. After the positioning and securing the ligaments, vascular anastomosis was performed between the recipient's external iliac vessels and the donor's hypogastric vessel pedicle, as end-to site anastomosis. During the back-table preparation and positioning of the uterine graft, the length of the hypogastric artery pedicle (including uterine vessel pedicle) was adjusted and a smooth curve (3 cm length longer than the straight distance) was created in order not to cause a tension in anastomosis but also to avoid a loose vessel graft. After vascular anastomosis, round ligaments were sutured to inguinal ligament of the recipient. A wide anterior bladder peritoneal flap retrieved generously from donor was sutured to parietal peritoneum of the recipient. Bilateral salpingectomy was also performed to prevent any possible ectopic pregnancy. The fixation of the anterior bladder pillar is an important step of the procedure to tailor and to position the uterine graft properly in a three-dimensional manner. We described and published this part of the surgery previously and our technique was also adopted by the Swedish team who visited our clinic after our successful uterus transplantation procedure.[2,11] Right after the declamping of the arterial bulldogs, the perfusion of the uterus was observed both clinically with the change of the color from pale yellow to red and also confirmed by intraoperative color-Doppler ultrasonography scan. We also retrieved a rectangular sentinel skin graft from the donor and transplanted this onto the anterior thigh of the recipient to monitor any possible rejection externally (Fig. 1A). The patient experienced the first menstrual cycle 20 days after the procedure. The first embryo transfer attempt, performed 18 months after the transplantation, yielded an increase in human chorionic gonadotropin (hCG) up to 35IU/L with no ultrasonographic sign of pregnancy. At the second embryo transfer trial, a viable fetal pole confirmed by transvaginal ultrasound was achieved for the first time. Unfortunately, embryonic cardiac activity ceased at 8 weeks' gestation. Cytogenetic analysis of the abortus material of the second pregnancy trial confirmed normal karyotype (46, XX).



FIGURE 1. (A) Sentinel skin graft from the donor transplanted onto the anterior medial thigh of the recipient in order to monitor any possible rejection externally. (B) Gradual rejection of the skin after delivery, and cessation of the immunosuppressants.

Following an abortus at 7 weeks in June 2013, 3 failed Embryo transfer (ET) attempts in 2014, another abortus at 7 weeks in January 2015, we experienced 3 more failed ET attempts in 2015. The tenth ET revealed a viable pregnancy that aborted at 8 weeks of gestation in March 2016. The 12th ET in March 2017 resulted a viable pregnancy that aborted again at 8 weeks of gestation. After these failed attempts and 5 pregnancies all concluded with miscarriages at 7 to 8 weeks, the ET attempts were suspended and the underlying etiology was investigated. Repeat transvaginal ultrasonography revealed no anatomical pathology, and the uterine dimensions were 103 mm × 65 mm × 42 mm in sagittal, coronal and transverse sections, respectively. The couple's peripheral blood karyotypes were analyzed, and both were reported as euploid. Diagnostic hysteroscopy was unremarkable. Endometrial biopsy was obtained to rule out chronic endometritis. Increased CD56 was observed in endometrial tissue, a predictor of immunological factors, and tacrolimus levels were adjusted. Endometrial receptivity array (Igenomix; Spain) was performed and reported to be receptive 120 hours following the progesterone administration. Interestingly, the growth of the gestational sac always lagged behind the normal fetal pole, and all 5 pregnancies resulted in miscarriages at nearly 8 weeks gestation, all of which suggested a possible placentation problem and/or blood outflow obstruction. The nongravid uterus was observed to be relatively enlarged between pregnancies. Static magnetic resonance imaging of the uterus revealed normal anatomic findings. Perfusion computed tomography (256-slice helical SOMATOM Definition Flash CT, Siemens Medical Solutions, Erlangen, Germany) revealed an obstructed blood-outflow, particularly in the left anterolateral part of the uterus (Fig. 2). To overcome this blood flow obstruction, we planned to create a new venous outflow from the uterus to the central venous pool. Following receipt of informed consent and a detailed discussion with the patient, we planned to perform a vascular venous revision to overcome this obstructed, misperfused area. The plan for vascular augmentation surgery was reported to both Turkish Ministry of health authorities and Akdeniz University Ethical commitee and IRB approval was obtained. On November 2018 an exploratory laparotomy was performed, followed by dissection of a vein originating from the left utero-ovarian pedicle. A saphenous vein graft (4 mm in diameter and 13 cm in length) was retrieved and used as an interpositional vein graft between one of the branches of the

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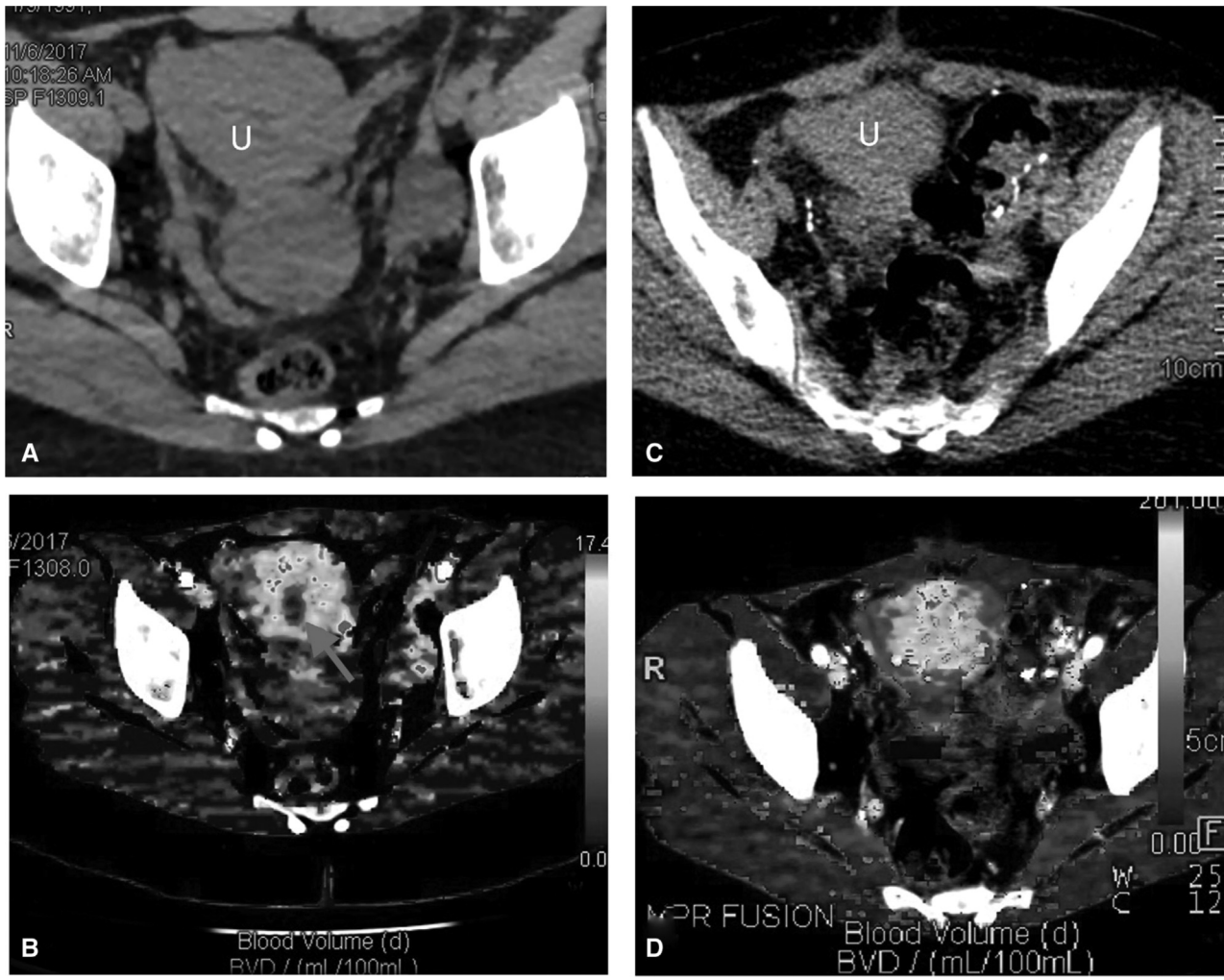


FIGURE 2. (A and B) Preoperative axial unenhanced computed tomography (CT) image (A) and (B) axial CT perfusion image (U uterus). Perfusion deficit areas secondary to venous congestion can be seen in the left part of the uterine fundus (Grey arrow). (C) Postoperative axial unenhanced CT image (D) postoperative CT perfusion image showing improvement of perfusion deficit areas.

uteroovarian veins (end-to-end) and the left ovarian vein (end-to-side) (Fig. 3). After the anastomosis of the saphenous vein graft to the utero -ovarian vein, the left ovarian was clamped and end to side anastomosis was performed. Total clamping time and anastomosis to left ovarian vein was 15 minutes. After the anastomosis, the patency of the vessels on both sides (both vein and artery) was checked with intraoperative Doppler ultrasonography. During the operation, apart from relative enlargement, the location and blood flow of the uterus were normal. The anastomosis worked well, both intraoperatively and postoperatively which all confirmed with intra-operative Doppler ultrasonography during the operation and in the early postoperative phase. Follow-up perfusion computed tomography performed 3 months after the operation confirmed the resolution of venous congestion on the fundal side and a significant decrease in uterine volume (154 cm^3) compared to the preoperative period (280 cm^3) (Fig. 2). Three months after surgery, the patient underwent 3 cycles of controlled ovarian stimulation with a fixed antagonist cycle starting on the second day of period without pretreatment. Ovulation was triggered by injection of 250 μg recombinant human chorionic gonadotropin (Ovitrelle; Merck Serono). Oocyte pick-up was performed with transvaginal ultrasound guidance. The oocytes were all fertilized by intracytoplasmic sperm injection. PGT-A was performed employing NGS technology (Igenomix; Spain). In the last ET attempt, endometrial preparation for the frozen-thawed cycle was initiated on the second day of the period using oral estrogen with a step-up regimen. On the 13th day of period, endometrial thickness was 8.8 mm, the E2 level was 446 pg/mL, and the P4 level was 0.2 ng/mL. On December 2019 120 hours after the administration of intramuscular progesterone (100 mg) single euploid embryo transfer (embryo grading 6BC, according to the Gardner & Schoolcraft classification) as 14th attempt was performed under ultrasonographic guidance. Blood β-hCG level was 923IU/L 13 days after the embryo transfer.

Course of the Pregnancy

Following total of 8 controlled ovarian hyperstimulation cycles and 14 embryo transfers (yielding 5 miscarriages and 1 chemical pregnancy), clinical pregnancy and fetal cardiac activity were confirmed 28 days after the last embryo transfer. The first trimester was uneventful, and for the first time after 5 miscarriages,

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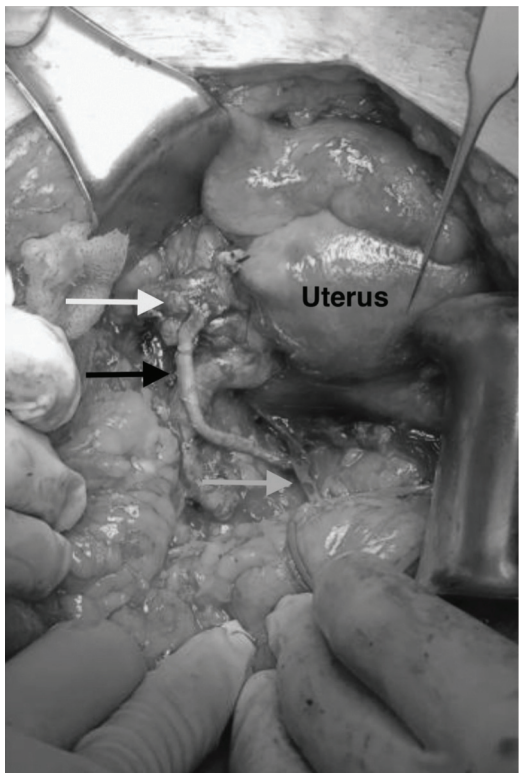


FIGURE 3. Saphenous vein graft between the left utero-ovarian vein and the ovarian vein. White arrow; a branch of left utero-ovarian vein, black arrow; saphenous vein graft, grey arrow; left ovarian vein.

this index pregnancy continued well beyond 8 weeks. The patient received prednisolone (5 mg/day), azathioprine (50 mg/day followed by 100 mg/day in the second trimester), and tacrolimus (2 mg/day, target serum dose 5–7 ng/mL) treatments throughout the pregnancy. First trimester screening was within normal limits. At 19 weeks' gestation the patient expressed a significant gush of vaginal fluid, and preterm premature rupture of membranes was diagnosed. The cervical length was 45 mm, and no signs of infection were observed. Vaginal culture was negative, and infection markers (leukocyte count, C-reactive protein, and sedimentation rate) were all within normal limits. The patient was hospitalized, and a double antibiotic regime was initiated (ceftriaxone 2 g/day iv and metronidazole 1500 mg/day iv) for 10 days. Our perinatology team monitored the patient closely. Fetal growth and gross anatomy were both normal. The amniotic fluid index was 11 mm on the deepest pocket. The possible consequences of preterm premature rupture of membranes before the time of viability and of infectious morbidity were discussed in detail with the patient, who opted to continue the pregnancy.[12]

The cervical length remained stable all through the pregnancy and was 40 mm at 24weeks of gestation (Fig. 4A). The patient's kidney functions also remained stable and were within normal limits all through nongravid phase and the pregnancy as well. We regularly checked renal functions during the index pregnancy (Supplemental Digital Content Figure 1, http://links.lww.com/SLA/D589). We also checked regularly for symptoms of rejection (a watery, foul smelling discharge). The sentinel skin graft from the donor implanted on the recipient's anterior thigh during the time of uterus transplantation served as a means for observing a possible rejection episode (Fig. 1A). To note, no clinical rejection episode occurred in the period from uterus transplantation to hysterectomy. In the first trimester, gross examination of the cervix was considered to be adequate for the follow-up of rejection, and cervical biopsy was planned for the second trimester. However, this could not be performed because of the preterm premature rupture of membranes and potential risk of infection. Serial sterile speculum examination of the cervix was normal (Fig. 4B), and complete blood counts, particularly eosinophil counts, were within normal limits. The dosage of tacrolimus was adjusted according to the blood levels. As we could not monitor rejection with serial cervical biopsies, we did not decrease the doses of immunosuppressive drugs in the second trimester. Intramuscular corticosteroid (12 mg betamethasone, 2 doses i.m. 24 hours apart) was administered at 24 weeks' gestation. Follow-up with Doppler and gray scale ultrasonography was performed twice weekly, and cardiotocography tests were carried out twice daily. At 26 weeks' gestation, the middle cerebral artery Doppler findings revealed an increased end-diastolic flow and 1-week growth

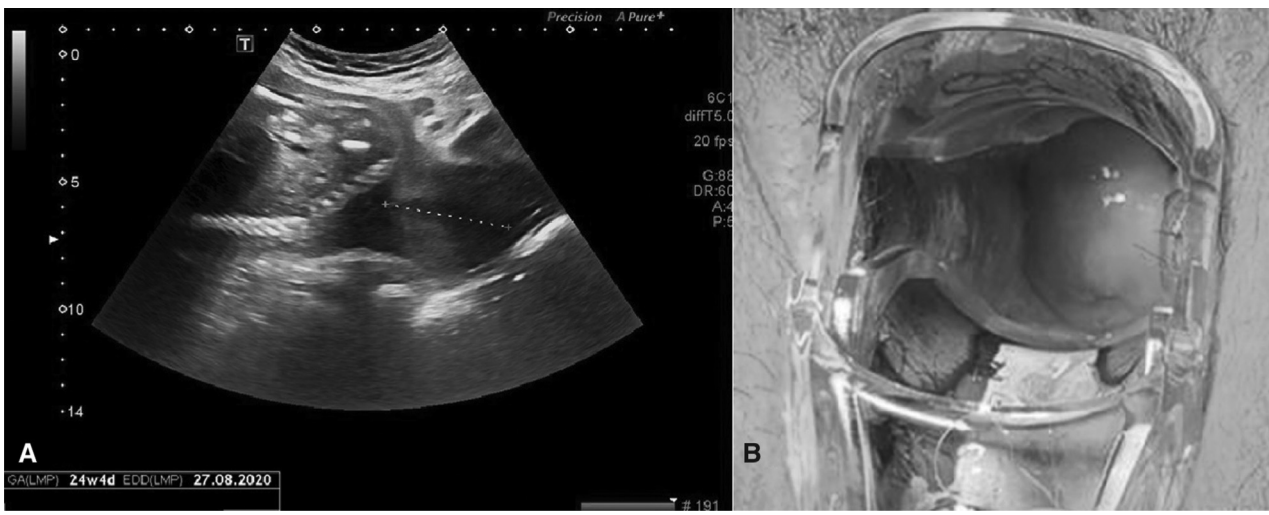


FIGURE 4. (A) Transvaginal measurement of the cervix at 24 weeks' gestation (40 mm) (B) Speculum examination and appearance of the cervix at the same week of gestation without any sign of rejection.

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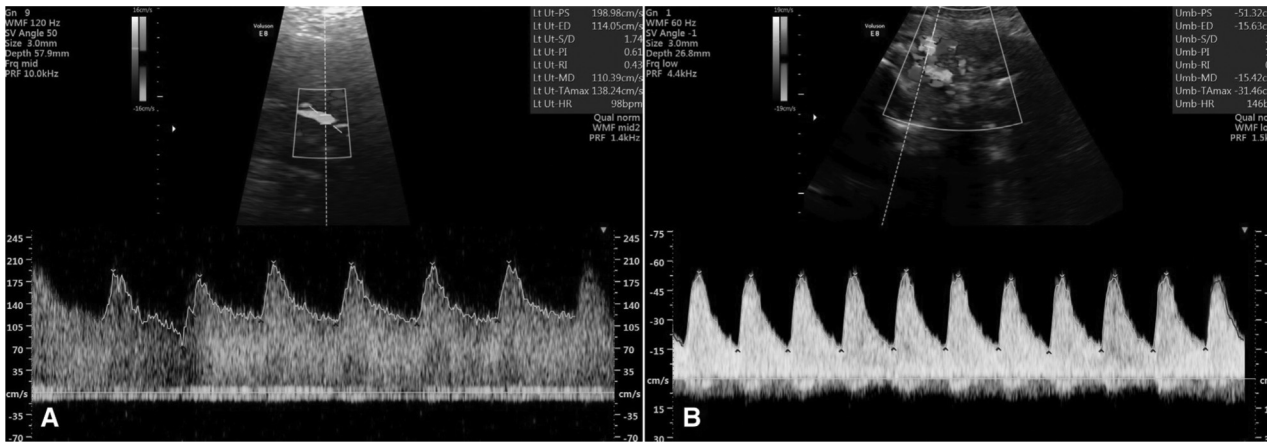


FIGURE 5. (A) Left uterine artery Doppler ultrasonography at 26 weeks 6 days. Note the low to normal resistance in the measurements. (B) Umbilical artery Doppler ultrasonography 8 days before delivery at 26 weeks 6 days.

retardation, which were all attributed to the beginning of intrauterine growth restriction. To note, uterine artery and umbilical artery Doppler measurements were within normal limits with low to normal resistance (Fig. 5). Cardiotocography follow-up was uneventful except for occasional variable decelerations. Based on these findings, a rescue dose of corticosteroids was administered at 27 weeks' gestation. Doppler ultrasound was performed daily and cardiotocography every 4 hours. Blood pressure was approximately 140/90 mm Hg at that time, but 24-hour urine protein was within normal limits (137 mg/day). Due to the intrauterine growth restriction, deteriorated Doppler ultrasonography findings and suspected preeclampsia (according to International Society for the Study of Hypertension in Pregnancy criteria), cesarean section was planned at 28 weeks' gestation.[13] After detailed discussion with the patient, hysterectomy was planned, and informed consent was obtained. Expectations with respect to neonatal survival and morbidity of a 28 weeks fetus were all discussed with the patient and her spouse (92% crude survival and more than 50% intact survial in 28 weeks of gestation in highly specialised NICUs).[14]

Six hours before the planned cesarean section $MgSO_4$ (2 g loading dose, 1 g/h maintenance) was initiated for neuroprotection. On June 4, 2020, operation was initiated with a midline incision after the onset of regional anesthesia. Adhesions were lysed. The bladder peritoneum was close to the lower uterine segment, and the planned uterine incision site was vascularized, and a classical vertical fundal incision was therefore made. A 760 g male fetus with Apgar score of 7-8-8 was delivered (Fig. 6). A true knot was observed at gross examination of the umbilical cord, together with a succenturiate appearance in the placenta (Fig. 7). After delivery, the umbilical cord was sutured, the fundal incision was closed, and we proceeded with hysterectomy. The patient's position was changed to low-lithotomy from supine. Adhesions were lysed, and normal anatomy was restored. Round ligaments were divided, the retroperitoneum was entered, and ureteral traces were visualized. The bladder peritoneum was dissected off, while the ovaries were left in situ. Salpingectomy had been performed previously in the first uterus transplant surgery. The uterine arteries were ligated close to the entrance to the uterus. The venous anastomosis between left ovarian vein and utero-ovarian vein was subsequently ligated. The sacrouterine ligaments were ligated and cut. A sponge was introduced from the neo-vagina. The previous line of the vaginal-neovagina lining was identified, and a circumferential colpotomy was carried out. The uterus was then removed along with recipient's vagina. Every effort was made to excise the whole length of donor's vagina. The cuff of neovagina



FIGURE 6. (A and B) Midline skin incision and classical incision of the uterus. (C) Delivery of the baby. (D) The baby at 4 months of age.

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(jejunal graft) was sutured and closed. Surgicells were applied, and 2 drains were left in place after hemostasis. Total operative time was 130 minutes, and total blood loss was 400 mL. Two units of packed red cells were transfused intraoperatively. Postoperative broad-spectrum antibiotics (ceftriaxone 2 g i.v. and metronidazole 1500 mg i.v.) together with low molecular weight heparin (enoxaparin 4000 IU s.c./day) were administered. Intra-abdominal drains were removed on the third postoperative day. Immunosuppression treatment was tapered and finally stopped on the postoperative seventh day.

After delivery, the baby was transferred to the NICU. Surfactant was administered using the LISA method 1 time, and iv antibiotics (penicillin and gentamycin) were given for 7 days. The baby received nasal Continuous positive airway pressure therapy for 15 days and oxygen support for 45 days. Minimal enteral feeding was initiated on day 1 and full-enteral feeding by day 13. The infant was successfully discharged from the NICU 79 days after delivery in good condition, weighing 2475 g.

The recovery phase of the recipient was uneventful. She experienced a watery vaginal discharge 2 weeks after the graft hysterectomy. A granulation tissue on neo-vaginal cuffwas identified on examination and this was excised under local anesthesia after which she was symptom free. Moreover, sentinel skin graft from the donor was gradually rejected after delivery and cessation of the immunosuppressants (Fig. 1B).

Pathologic evaluation of uterus revealed normal findings without any signs of histologic rejection including chronic cervicitis, normal vaginal epithelium and hydropic villi with gestational decidua. Histopathologic evaluation of placental revealed hypoplasia and infarction with hydropic villi. It has been 16 months since the birth of baby. Both mother and baby were all in good condition. At

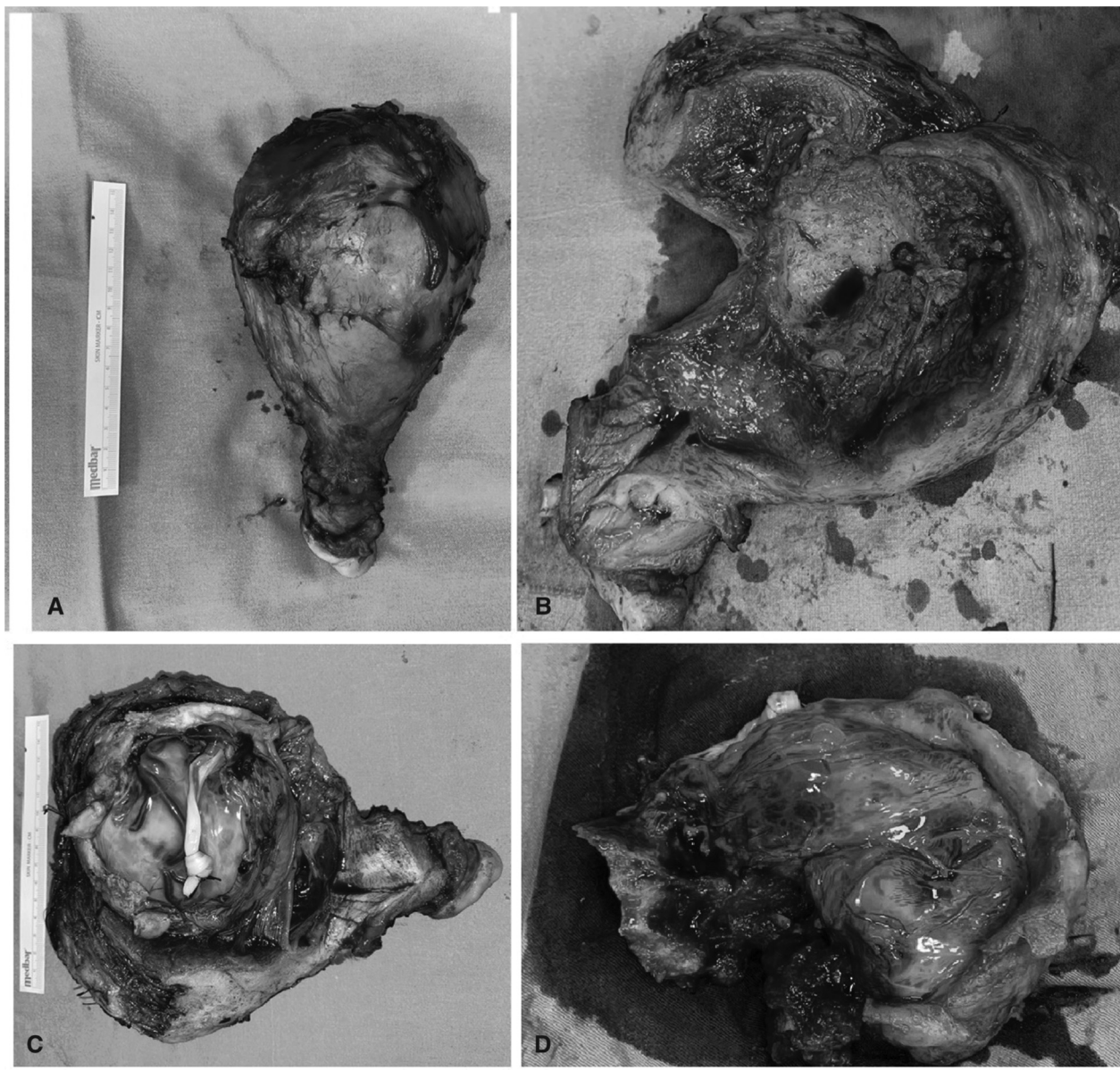


FIGURE 7. (A and B) hysterectomy specimens;(C and D) cut surface of the uterus and gross appearance of the placenta.

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the last visit the baby weighed 9100 g (5–10 p) and his height was 76 cm (5–10 p) with a normal mental and motor development. The renal functions of the mother was also normal (creatinine 0.69 mg/dL, BUN 15 mg/dL and creatinine clearance 117 mL/min).

DISCUSSION

This report describes the course of the first long lasting uterus transplantation from a deceased donor. This case possesses a number of important and unique features, including the use of a deceased donor and live birth after failed attempts handled with the use of vein graft to restore venous outflow. This was also the first case of uterus transplantation with a live birth after jejunal vagina construction. Following this first long-lasting case, experience in uterus transplantation has increased exponentially, and this has now become a reality rather than merely an experimental concept. In the writing of this manuscript, 65 such transplantations have been reported to date, and 22 infants have been successfully delivered, 4 from cadaveric donors.[15] The importance of deceased donor uterus transplantation lies in the fact zero harm occurs to the donor and in the possibility of retrieval of long vascular pedicles, thus improving the chances of vascular anastomosis. The first donor surgeries in Sweden lasted more than 10 hours, and the donors were transferred to ICU units after the procedures.[16] Recently, minimally invasive surgery has been adapted to uterine retrieval surgery, although operative times are still long. In a report by a team from Sweden, part of the donor surgery commenced with robotic surgery lasting 360 minutes.[17] For safety reasons, due to the extended time spent in the Trendelenburg position (360 minutes), the surgery was converted and completed with laparotomy. The total duration of donor surgery was 12 hours, with 400 cc blood loss. The same group recently published their experiences with 8 more robotic donor surgeries. However, the median duration of surgery was still 10.5 hours, the final parts still being completed with median laparotomy.[18]

A number of complications such as ureteric injuries, ureterovesical fistula formation, and vaginal cuff dehiscence have been reported from live donor surgeries.[16,19] To retrieve longer vascular pedicles, donor surgeries in China and India included the removal of the ovaries, thus putting young donor women into a menopausal state requiring prolonged exogenous estrogen use and involving a possible increased future cardiovascular risk and mortality.[20,21] In the light of all these drawbacks of live donor uterus transplantation, deceased donor transplantation can avoid potential harm to the donor and increase the chance of successful vascular anastomosis with the help of longer vascular grafts.

Another important aspect of the present case is the previous history of repeated miscarriages. After 5 failed pregnancies, investigation of the etiology involved revealed an area of venous congestion in the fundal region of the transplanted uterus. The previous pregnancies had resulted in miscarriages at exactly the same gestational time (7–8 weeks). We observed faulty growth of the gestational sac inappropriate for the gestational age. Uterine enlargement in the nongravid phase also indicated a vascular insufficiency, particularly a venous problem. The first static radiological studies including magnetic resonance imaging revealed no anatomical problem, but perfusion computed tomography subsequently revealed venous congestion and an area of venous pooling in the fundal area of the uterus. A vascular venous graft was performed to overcome this venous congestion. The resolution of the previously congested area and a relative decrease in the size of the uterus at follow-up perfusion computed tomography were all possible hints of a real venous insufficiency. The underlying condition could be a mechanical obstruction due to a kinking or a thrombotic event but during the revision surgery the gross venous outflow and arterial vasculature were all checked with intraoperative Doppler ultrasonography and the uterine venous and arterial vasculature were normal.

Embryo implantation in a hypoperfused or hypercongested endometrial area might lead to miscarriage. The timing of the miscarriages at around 8 weeks of gestation, corresponding exactly to the time of luteo-placental shift, may also indicate a possible venous outflow obstruction that was unable to keep up with increased blood flow.[22] To the best of our knowledge, there is no data regarding the relationship with regional uterine perfusion defects and recurrent pregnancy loses either in normal pregnancies or in uterine transplant patients. The importance of this case is the presence of regional venous congestion area that was treated with vascular augmentation and presentation of a new exit strategy to establish a health pregnancy before removing uterine graft after failed pregnancy attempts. By this way an important cause of infertility was eliminated by improving vascularity in a small regional area of the uterus with the help of vascular augmentation.

Achieving pregnancy is an important step in uterus transplantation trials but the real success and proof of an established treatment of uterine-related infertility is the birth of a healthy baby. Previous reports have described a number of patients with pregnancy attempts resulting in recurrent miscarriages, without successful delivery of a baby.[23–25] To the best of our knowledge, this is the first uterus transplantation case involving birth after vascular revision of uterine venous outflow following recurrent miscarriages. In case of recurrent pregnancy failures in uterine-related infertility, in addition to routine evaluation of recurrent pregnancy losses, the presence of a venous outflow obstruction could be checked before removing the graft. Perfusion computed tomography may serve as a good tool for evaluating blood in- and outflow characteristics of the transplanted uterus. Vascular revision in these patients may increase the possibility of ongoing pregnancies. We should also stress that the results of the surgical revision is highly speculative which should be supported with further studies.

The drawbacks of the deceased uterus transplant are a relatively low number of multiorgan donors, a shorter time for preoperative evaluation of the donor, logistic problems concerning organ transfer, and that less experience has been achieved with this procedure.[26] Adapting the organ retrieval order without impairing vital organ outcomes will shorten the cold ischemia duration of the uterus.[27] As the number of live births from deceased uterus transplants increases, the opportunities to compare both live and deceased donor transplants will also increase.

One possible criticism of this case may involve the follow-up of the recipient for 9 years without removal of the uterus. There is an increased risk of infections in the course of treatment, malignancy even after discontinuing immunosuppression and a potential risk for nephrotoxicity. However, post-transplant malignancy rates in renal transplant recipients are comparable to those of the nontransplanted population, particularly for recipients aged 20 to 30 years and receiving immunosuppression for less than 10 years.[28,29] This was the first long lasting uterus transplant and there was no index case that the authors could follow and all interventions were not relied on solid data. Removal of the uterus was discussed with the patient after failed attempts during the course of follow-up. All the risks were explained in detail, but the patient opted to keep the uterine graft. Interestingly, the patient stated that she felt positive about herself due to experiencing menstrual cycles despite previous unsuccessful embryo transfer attempts. To note, as the guidelines suggest, the maximal time to keep the transplanted uterus should be limited to 5 years.

In conclusion, deceased donor uterus transplantation is a reasonable approach for treating uterine factor-related infertility. Even in the absence of blood flow disorder under normal physiological conditions, in case of recurrent miscarriages, regional vascular

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augmentation by arterial or venous supercharging may be required to overcome regional misperfused regions determined by imaging studies.

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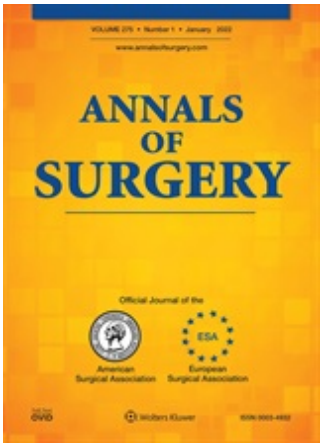
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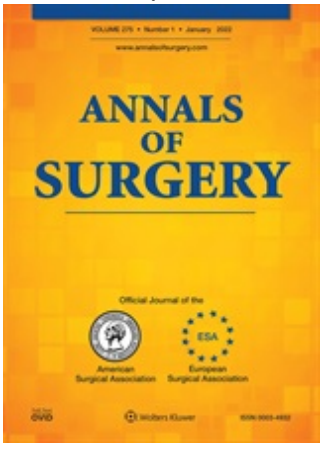
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