Section 11-c

Uterus Transplantation

Wafa Fageeh, Giovanna Lucchini

Introduction

Uterine transplant is at a crossroads. It is possibly the best solution for approximately 4% of infertile women who undergo the frustration of being unable to conceive due to the absence of a uterus. In some cases, this absence is due to congenital abnormality (e.g. Rokitansky's syndrome). In other cases, it is due to surgical removal of the uterus at a relatively young age due to clinical emergencies, such as obstetric uterine rupture.

Until recently, only life and death situations warranted organ transplantation. Nonvital transplantation simply to fulfill a patient's wishes or goals was not considered justified. It can be argued, however, that this distinction is not morally significant. Patients with kidney failure, for example, can be kept alive by dialysis, but their quality of life can be greatly enhanced by kidney transplant, which is thus considered a justified procedure. So a spectrum of rationales may justify transplantation. Therefore, the only chance for women without a uterus to have babies was by resorting to surrogate gestation. In many countries, this procedure is prohibited by the law. In some other countries, surrogate mothers are registered as legal mothers of babies born through surrogacy. Another problem that parents may face if they decide to try surrogacy is that they have no control over the course, care or outcome of such pregnancy. These and other ethical, moral and religious issues surrounding surrogacy have left these women to hope for the possibility of uterine transplant. Transplantation of the uterus would relieve the anguish of women who greatly desire to conceive a child and allow them hope for an opportunity to become pregnant.

A clinical milestone was made by Dr. Wafa Fageeh and her team when they successfully transplanted a human uterus in Saudi Arabia in the year 2000 although the transplant lasted only 99 days [1]. The furor that followed this partial success reveals the range of views of the scientific community and the public at large. Of course, the concerned women were enthusiastic and delighted at the potential for progress in this technique. Sceptical scientists raised the question as to whether this "non-life-saving transplant" was necessary at all? Only further progress in transplant science can shed more light on the answer to this critical question. Antirejection drugs are nonetheless becoming safer, and patients with cardiac and renal transplants have had successful pregnancies. Thus, in the progress of the development of nonessential human transplants, the uterus seems to be leading the way because of the successful, if only temporary, transplant in 2000. The three menstrual cycles that followed indicated functionality of the uterine endometrium but the unfortunate incident of thrombus was a drawback.

While other organ transplant donations most often come from cadavers and less often from living donors (kidney or partial liver), the donor

source for a uterus may be an otherwise healthy living patient who requires uterus removal as a care procedure. Furthermore, it should be mandatory to remove the transplanted uterus from the recipient after successful pregnancies so the patient need not be subjected to lifelong antirejection medications.

Since animal uterus transplantation has been done successfully, human uterine transplantation could be considered for select cases.

The interest in uterine transplantation has been increasing in the scientific community since the mid-twentieth century, with the aim of overcoming infertility problems linked to uterine absence or uncorrectable anomalies. It has been stated that 5–10% of cases of infertility are caused by either congenital or acquired uterine disorders, among which are Müllerian agenesis, Mayer-Rokitansky-Kuster-Hauser syndrome, leiomyomas, Asherman's syndrome and hysterectomy are the most common [2]. New reproductive procedures are of no help in these situations. The only chance for women affected by these problems to give birth is to rely on gestational surrogacy, which consists of using gametes of a genetic couple to produce embryos that are then transferred to the womb of a woman who agrees to act as a host for the pregnancy [3]. The technique is legally approved in Canada, UK, Brazil, South Africa, Israel, Hungary, the Netherlands, Australia and some states in the USA. Other countries have no specific legislation on the practice of surrogacy (Greece, Argentina, Belgium, Finland and India). In most Muslim countries and some Asian territories, it is strictly forbidden on the basis of religious or ethical grounds. Even in nations that have accepted this procedure by law, scattered incidences of resistance based on ethical, psychological, religious and economical issues have been reported [4, 5].

Around 15% of all couples are infertile. Most resistant cases have been helped by assisted reproductive technologies, such as in vitro fertilisation (IVF) and intracellular sperm injection (ICSI). However, for women who have healthy ovaries but have had a hysterectomy or serious uterine problems due to injury or congenital conditions, a transplant could provide their only hope for experiencing a pregnancy of their own. At present, they can choose IVF, in which their own egg and their partner's sperm can be used for gestational surrogacy. Technically, this is straightforward, but it may not always be suitable for many couples. Uterine transplants could help up to 47% of infertile women. The surgery would be comparable to a kidney transplant and would offer advantages over surrogacy, especially in countries where it is not allowed.

With a uterine transplant, any health risk of pregnancy, such as high blood pressure, are taken by the genetic mother, which makes it acceptable from an ethical point of view. There is also no financial consideration, a situation often criticised with surrogacy. It also clears up complications regarding who is the legal mother. In some countries, the legal mother is the woman who gives birth regardless of who is the biological mother. With transplantation, the biological mother would be the legal, social and gestational mother.

Since a uterine problem is a factor in 3–4% of infertile women, there would probably be no shortage of women willing to try the technique because according to Dr. Mats Brännström of the Sahlgrenska Academy at Göteborg University in Sweden, he has received hundreds of enquiries from women who have read about his pregnancy success with uterine transplants in mice. Several volunteers contacted Fageeh's team to be donors, and several others as would be recipients, indicating that there is definitely a demand for this procedure even though the numbers may be small.

Landmarks in Organ and Uterine Transplantation

The advent of organ transplants began with that of the kidney in the early 1960s. Inspired by the success, transplantations of other vital organs, such as liver, heart, lung and pancreas, followed. In the beginning, azathioprine (Imuran) and prednisone were the only available immunosup-

pressive agents. In 1980, with the introduction of cyclospine therapy, the prognosis for transplanted organs became better. Progress in safer and more easily tolerated immunosuppressive therapy has opened the doors for the transplant of nonvital organs, such as the uterus.

The first study of ovarian transplantation was published as early as 1896 by Knauer. However, attempts at uterine autotransplantation did not begin until 1918 [6]. Autotransplant of a uterus in a dog by Eraslan, Hamernik and Hardy in 1964 and 1966 was the first to end in a successful delivery [7]. Confino, Vermesh and Gleicher introduced the use of cyclosporine therapy for uterine allotransplantation in rabbits in 1986 [8].

In 2000, a human uterine transplant was performed in Saudi Arabia by Fageeh et al. [1]. Postoperatively, the patient had three spontaneous menstrual cycles followed by amenorrhea. Exploratory laparotomy confirmed uterine necrosis due to vascular thrombosis. There was no evidence of rejection. The attempt, however, raised discussions on many moral and ethical issues. The scientific community, although deeply divided, consider this as the only reference to a human success. Recently, interest has fallen on further exploring the feasibility of human uterine transplantation as a replacement for surrogate gestation.

Work on Animal Models

The story of experimental animal models used for the purpose of uterine transplantation begins in the early 1960s [7–14]. Sheep, dogs, macaques, rabbits and rats were used in both autologous and homologous transplantations. The intention was to understand two main areas of this technique: (1) recreation and stable vascularisation of the uterus, with anatomical network of small vessels, and (2) modulation of immunosuppressive treatment in order to avoid rejection, prevent toxicity for the mother and eliminate teratogenicity for the foetus. Vascular support of the pelvic region was crucial to graft survival and was therefore the most studied element in the first proposed animal models. This led to the development of different techniques to obtain good viability of the transplanted organ. Among these, omentopexy has been commonly used to obtain a milieu that supports spontaneous revascularisation, fixation of the uterus to the broad ligament has been tested with good results and the more classical vascular anastomosis has been improved to the point of becoming the most efficient surgical option. All these studies proved the surgical feasibility of the transplantation and even attempted to recreate the function of the normal uterus by producing some examples of pregnancies and deliveries in the grafted animals. From an immunological point of view, experimental models using azathioprine and prednisolone were tested but never achieved outstanding results in avoiding rejection and because close monitoring of serum drug levels was not easily carried out.

More recent epidemiologic and experimental studies have underlined the effect of some immunosuppressive drugs on the foetus. Azathioprine has proven to be mildly teratogenic on rats whereas corticosteroids seem to be linked to a general augmented risk of cleft palate development [15, 16]. Cyclosporine has shown to restrict foetal growth, resulting in low birth weight. However, these data were collected in a population of patients suffering from autoimmune diseases, and therefore the role of these diseases on gestation is still to be clarified [17].

Fageeh performed 16 autologous orthotopic uterine replantation on baboons and 2 on goats. After a midline abdominal incision, hysterectomy was done so as to preserve tissue and vascular integrity. The uterus was then flushed with Euro-Collins solution and replanted in the same animal with cervico-vaginal anastomosis. The first 8 animals had end to end uterine vascular anastomosis but occlusion and vascular thrombosis was observed in 12 out of the 16 vascular connections. It was therefore decided to change to an end to side anastomosis between uterine vessels and internal iliac vessels, which offered better results (18 out of 20 vessels remained viable). After 6 to 12 weeks the animals underwent abdominal exploration that showed survival of the uterine graft and good vessels patency [1].

To complete the history of experimental surgery in uterus transplantation we need to quote the most recent animal model of this kind. The researcher leading the work on mice, Dr. Mats Brännström of the Sahlgrenska Academy at Göteborg University in Sweden and his team proposed a mouse model for homologous uterus transplantation. They had seen pregnancies in mice with donor uteruses which resulted in healthy babies. The mice used were syngenic (inbred strain) and the vascular technique used was that of end to side anastomosis between donor uterine vessels and recipient inferior cava vein. The viability of the uterus was sequentially examined and proved to be good for 8 weeks post operatively. The function of the transplanted uterus was evaluated inducing pregnancies with good results. This model is still under development [18].

In their original work, the team took a uterus from a donor mouse and transplanted it alongside the recipient mouse's own uterus. This meant they could compare how both worked.

The team led by Mats Brännström grafted one arm of the V-shaped mouse uterus from a donor mouse into another's abdomen, alongside its existing uterus. The implanted partial uterus was connected to the mouse's blood supply. Several days later, tests demonstrated that blood flow in both organs was similar, the team says. Three fertilized embryos were then transplanted into each of the uterus.

Their report, published in the Journal of Endocrinology (V 174, Pg 157), reveals that one of the three in the donor organ, and all three in the mouse's native uterus, developed into healthy fetuses. The experiment was terminated after 13 days, two-thirds of the way through the pregnancies, due to ethical restrictions placed on the research.

The reason their experiment on mice worked is because they connected the vascular system of the implanted uterus directly to the existing blood supplies, rather than using stents which have caused other transplants to fail.

As predicted by the Swedish researchers, the procedure conducted in mice would be easier to repeat in humans. In a woman, the procedure would involve removing the existing organ completely and replacing it by the donor uterus.

The First Human Uterine Transplant

The first human uterine transplant is reproduced in its entirety here to shed clarity on this very important landmark in uterine transplantation.

Introduction

During the past three decades, scientists have made tremendous efforts to solve infertility problems; indeed, the achievements and developments that have occurred in this field have had a considerable clinical impact [18]. Infertility due to the absence of a uterus or to a congenitally malformed uterus with normally functioning ovaries, has remained an obstacle to pregnancy, however, especially in communities where surrogate gestational carriers are approved by neither religious nor ethical authorities.

Uterine transplantation could provide a solution to this problem, but its feasibility, safety and reproducibility remain to be proven. To evaluate the potential for safe, successful, uterine transplantation in humans, we reviewed earlier animal experiments and clinical trials. The main difficulty was vascular anastomosis between uterine vessels of donor and recipient [20]. Unlike other organs where large vessels are the source of blood supply, in the uterus, the blood supply and drainage occur through a net of tiny vessels. Most earlier animal experiments were performed with avascular techniques that led to failure and the formation of pelvic abscesses [8]. Human trials were limited to transplantation of endometrial tissue [21], and no documentation of successful uterine transplantation was available in the English literature.

The Islamic religious position on uterine transplantation was clarified in March 1990, before initiation of this project, when the Islamic Jurisprudence Council approved the transplan-

tation of reproductive organs that do not transfer genetic coding.

Experimental Animal Studies

The project conformed with the Guiding Principles in the Care and Use of Laboratory Animals approved by the authorities of the King Fahd Medical Research Center. Previous experiments had proven the feasibility of uterine transplantation in animals, with successful pregnancy [7]. As the main difficulties lay in uterine vascular connections, some researchers performed avascular uterine transplantation in the animals, which resulted in failure and in the formation of pelvic abscesses. We, therefore, decided to concentrate our animal studies on uterine reimplantation rather than transplantation. We focused on the vascular surgical anatomy and its variations [22], the physiology of the uterine blood flow and mastery of microvascular techniques of uterine arterial and venous anastomosis.

Autologous orthotopic uterine reimplantation was performed on 18 virgin female animals (16 baboons and two goats). The baboons' average age, weight and height were 2–4 years, 15.6 kg and 37 cm, respectively; the goats' average age, weight and height were 2–3 years, 20–30 kg and 60–71 cm, respectively. Surgery was performed with the animals under general anaesthesia without muscle relaxation. Prophylactic antibiotics (tetracycline, 20 mg/kg body weight) were given for 5 days. In each animal, a midline abdominal incision was made. Hysterectomy was modified to preserve tissue and vascular integrity. The extirpated uterus was flushed in both the antegrade and retrograde manner with 60 cm^3 of cold Euro-Collins solution then reimplanted orthotopically in the same animal by doing cervicovaginal anastomosis. The first eight animals underwent end-to-end uterine vascular anastomosis, but anastomotic occlusion and pelvic abscesses occurred due to graft failure and vascular thrombosis in 12 of the 16 (75%) vascular connections. Therefore, the technique was modified so that the anastomosis was performed between the uterine vessel and the internal iliac vessels in an end-to-side fashion using monofilament, nonabsorbable polypropylene sutures. This modification was technically easier to accomplish. It also provided wider anastomotic stoma and a higher success rate in the remaining ten animals, with proven vascular patency in 18 of 20 (90%) vascular connections. All animals underwent abdominal exploration after 6–12 weeks to evaluate survival of the reimplanted uterus, and the following steps were taken:

- assessment of vascular patency by visualising emptying and refilling of veins and pulsatility of arteries, and by palpation of the arteries for presence or absence of thrill

assessment of uterine and fallopian tube viability by evaluation of their color and texture

- observation of bright red fresh bleeding from the tissue on abrasion or puncture
- determination of pelvic infection.

Our animal studies demonstrated survival of the uterine graft and indicated that good mid- and long-term vessel patency could be achieved using skillful microvascular techniques for uterine arterial and venous anastomosis in an end-to-side fashion.

After reviewing the earlier reported experimental work by other researchers [6] and our satisfactory results, we decided to prepare for a human trial. Protocols for human uterine transplantation were designed detailing indications, contraindications, selection criteria, surgical techniques, immunosuppression regimen and clinical follow-up. Detailed informed consent forms were prepared for the donor and recipient according to the guidelines and regulations of the Food and Drug Administration (FDA).

Materials and Methods

The potential recipient was a 26-year-old woman who had undergone a hysterectomy in 1994 because of massive bleeding following a cesarean section. She had consulted us concerning the possibility of uterine transplantation and after thorough evaluation was found to be eligible. The donor was a 46-year-old woman who presented with bilateral multiloculated ovarian

cysts measuring 8×6 cm on the right side and 3×2 cm on the left side. Hysterectomy with bilateral salpingo-oophorectomy was planned, as this patient agreed to donate her uterus. ABO compatibility, human leukocyte antigen (HLA) tissue matching and negative cytotoxic antibodies in the recipient were confirmed.

The Procedure

The Donor

On 6 April, 2000, uterine extirpation was carried out with the patient under general anesthesia. The donor's abdomen was opened through a midline incision; bilateral en-block oophorectomy was performed, and the ovaries were sent for frozen section, which confirmed the benign nature of the cysts. Uterine removal was accomplished using a technique modified so as to maintain the vascular pedicle of the uterus as long as possible and thus maintain tissue integrity. The long vascular pedicle was maintained by transecting the round ligaments as far laterally as possible. Ureters were identified and protected. Infundibulopelvic ligaments were clamped, divided and sutured. Pararectal and paravesical spaces were developed with care to avoid traumatising the numerous small veins in the broad ligaments and paravesical space. Uterine arteries were then encircled with vessel loops. Uterosacral ligaments were serially divided and sutured. The uterovesical peritoneum was incised, and the bladder was separated from the cervix and vagina. At that stage, methyl prednisolone (500 mg) and heparin (20,000 IU) were given IV. Uterine arteries were clamped 1 in. away from the uterine body (Fig. 1). The vagina was entered by circumferential incision and the extirpated uterus immersed in cold saline for topical hypothermia. The graft was flushed with modified, cold (4°C), Euro-Collins solution, antegrade through uterine arteries and retrograde through uterine veins, to ensure removal of all white blood cells and fibrin and to induce central core cooling for tissue preservation during the ischaemia period. The uterosalpingeal graft was additionally trimmed to ensure removal of any remnants of unwanted tissue (Fig. 2). A 6-cm-long segment of the great saphenous vein and an 8-cm-long reversed segment were anastomosed to each uterine vein and artery, respectively, with 6×0 nonabsorbable polypropylene suture (Prolene Ethicon) on a sterile side bench to extend the length of vascular pedicles (Fig. 3). The eight vascular grafts were flushed again with Euro-Collins solution to check for any anastomotic leaks. A small laceration of the anterior wall of the donor's left ureter was found and was splinted with a double J tube and sutured by the urologist.

The Recipient

A preoperative oral dose of cyclosporine (4 mg/kg body weight) was administered 6 h prior to surgery, and methyl prednisolone (500 mg i.v.) was administered to the patient at induction of anaesthesia. The recipient's laparotomy was started when donor uterine extirpation was imminent. A midline subumbilical incision was selected, and intra- and retroperitoneal adhesions were lysed. Internal and external iliac vessels were dissected bilaterally. The bladder and rectum were dissected from the cervical stump, and the latter was excised. The donor uterus was placed in orthotopic position, and the cervix was then sutured to the recipient vaginal vault by single, interrupted, nonabsorbable 2×0 Ti-Cron (Ethicon) sutures. Uterosacral shortening was accomplished using two nonabsorbable 2×0 Ti-Cron sutures. The extended uterine veins and arteries were then anastomosed to the external iliac veins and arteries, respectively, with 6×0 Prolene. No ovarian arterial or venous anastomosis was performed. Five hundred milligrams of methyl prednisolone was given IV on releasing the iliac clamps and reestablishing uterine perfusion. The abdomen was closed in layers after complete homeostasis. The recipient made an uneventful recovery with good wound healing. White blood count, cyclosporine level and creatinine phosphokinase enzyme levels were checked twice a week. Immunosuppression consisted of oral cyclosporine (4 mg/kg body weight) divided into two doses to assure a serum trough level of 200 ng%, azathioprine (Imuran) (1 mg/kg body weight) and prednisolone, with a maintenance dose of 0.2 mg/kg body weight. The adequacy of immunosuppression was monitored by measuring the lymphocyte subpopula-

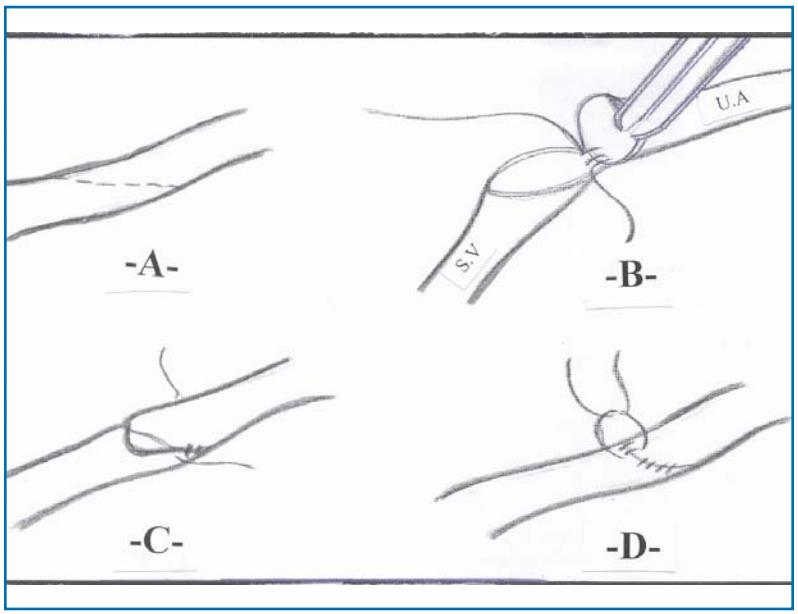

Fig. 1. Preparation of vascular pedicles

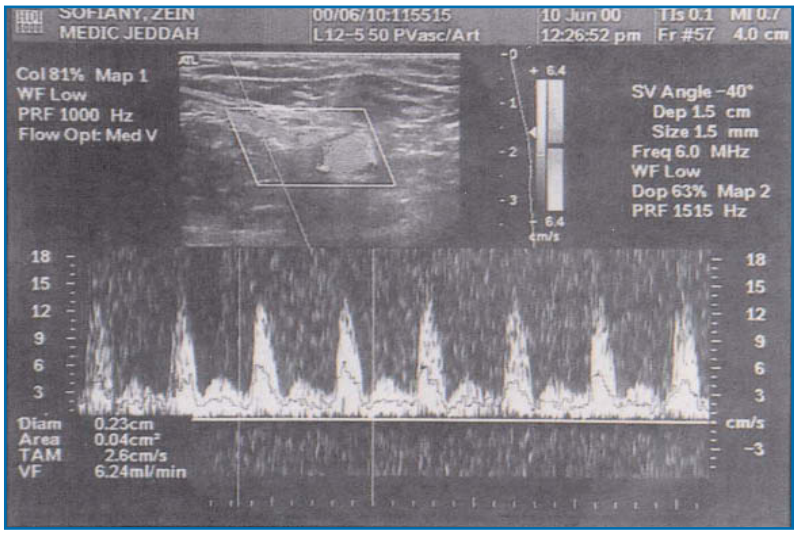

Fig. 2. Doppler ultrasound with excellent uterine artery filling

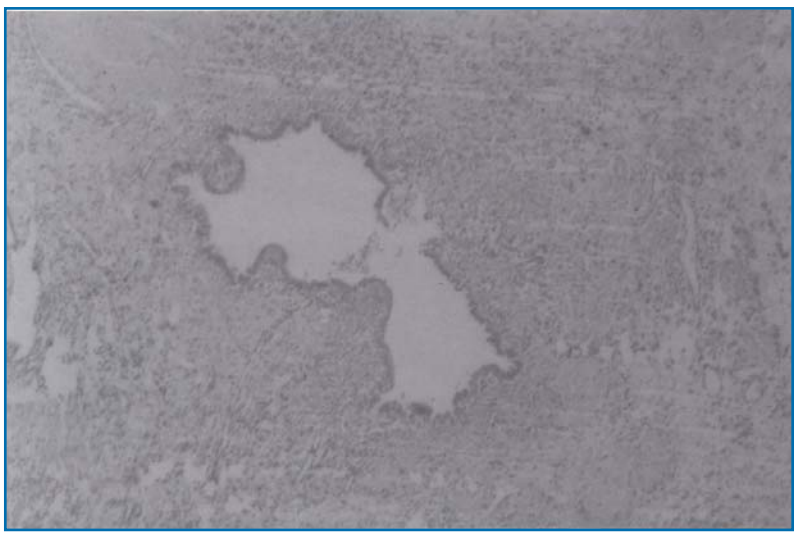

Fig. 3. Tubes with patency and no rejection

tion (CD4/CD8 = helper/suppressor) cell ratio by cytoimmunological cytometer (FACS Scan) and Doppler ultrasound to study flow volume, pulsatility and resistance index [23]. On the ninth postoperative day, the patient complained of low abdominal and back pain, general fatigue, malaise and body aches. She had minimal serosanguineous vaginal discharge, low-grade fever and tachycardia, indicating acute rejection. The CD4/CD8 ratio was found to be reversed to 3.4. Abdominal Doppler ultrasound showed increased brightness due to myometrial oedema. The patient was treated by increasing the oral doses of cyclosporine and azathioprine and administering an intravenous pulse of methyl prednisolone. The rejection did not resolve, however. Antithymocytic globulin (ATG) (2.5 mg/kg body weight) was given, controlling and resolving the rejection phenomenon. Cervical inspection on the 12th day revealed good healing of the cervicovaginal anastomosis, with some venostasis of the lower one third of the ectocervix. Biopsy was not attempted so as to avoid anastomotic disruption. The symptoms of rejection disappeared after 2 days, and the CD4/CD8 ratio was 1.3. Doppler ultrasound revealed excellent bilateral uterine arterial perfusion, with low resistance indices (Fig. 4). Hormonal therapy with oestrogen and progesterone (Progyluton) was given for the first 3 months to build up the atrophic endometrium. Two withdrawal bleedings occurred promptly after cessation of hormonal therapy. These were considered to reflect good blood perfusion and viability of the transplanted uterus.

Removal of the Transplanted Uterus

On the 99th day, the patient experienced a sudden feeling of heaviness, with a foul-smelling vaginal discharge on straining. Speculum examination revealed a dusky-coloured cervix prolapsing into the vagina. Immediate Doppler ultrasound confirmed cessation of uterine blood flow. A diagnosis of mechanical occlusion of the uterine vessels with resulting uterine infarction was made, and the need to perform a hysterectomy became obvious. At surgery, the uterus was found to be infarcted, and the uterine arteries, veins and their supplying grafts were thrombosed. Both fallopian tubes remained pink and viable, however. Histopathologic microscopic examination confirmed the above findings as well as the viability of both tubes and absence of any rejection (Fig. 5).

Discussion

Advances in immunology make organ transplantation for end-stage organ failure a clinical reality [24]. Advances in microvascular surgery and tissue preservation as practiced in ovarian transplantation [25] provide support for major steps in the new era of the surgical management of infertility [26]. Such advances can be applied

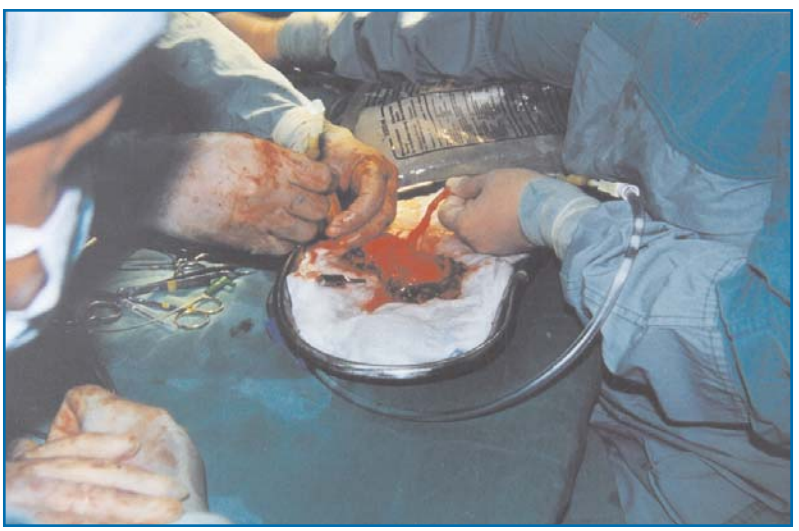

Fig. 4. Irrigation of donor vessels

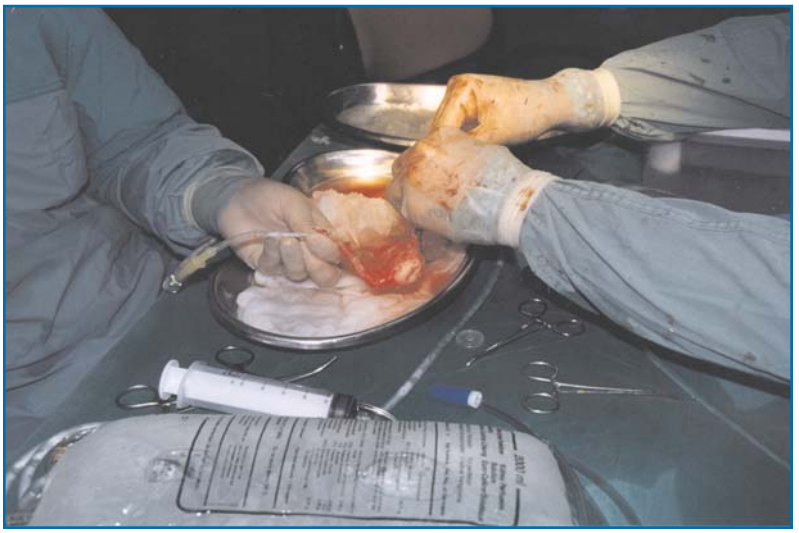

Fig. 5. Preparation of donor uterus

successfully in uterine transplantation, and indeed, our experimental work with microvascular uterine vessel anastomosis provides ample clinical evidence of good mid- and long-term vascular patency and graft survival.

Simple noninvasive techniques, such as Doppler ultrasound, to monitor and detect early rejection are essential. Cytoimmunological monitoring for activated lymphocyte subpopulation (CD3/CD4) cell ratio using monoclonal antibodies is a simple, noninvasive technique to monitor rejection, with sensitivity and specificity approaching 96% and 88%, respectively [27]. Punch biopsy from the endocervix to detect and histopathologically grade rejection seen as myocyte necrosis and perivascular infiltration of lymphocytes is an invasive procedure that could be associated with certain risks. It was, therefore, not applied in our patient.

Modification of the hysterectomy technique in the donor is essential to promote preservation of a longer vascular pedicle and application of a gentle, atraumatic technique to preserve the uterus and differs from conventional hysterectomy. Extension of the vascular pedicle for a required length using a conduit such as the great saphenous vein or the radial artery may be advantageous in selected patients, and application of microvascular techniques by an experienced vascular surgeon is mandatory. The use of fine polypropylene monofilament, nonabsorbable sutures is required. Suspension of the uterus to the anterior abdominal wall (ventrouteropexy) and by uterosacral shortening is essential to avoid displacement of the uterus with consequent tension, torsion or kinking on the vascular pedicle and anastomosis, with obstruction of blood flow and vascular thrombosis.

Conclusion

Our clinical results with the first human uterine transplantation confirm the surgical technical feasibility and safety of this procedure in gynaecologic, surgical and vascular terms. Acceptable short- and midterm outcomes were documented by good endometrial proliferation on hormonal therapy and the occurrence of two withdrawal bleedings in the transplanted menopausal donor uterus.

An understanding of the surgical vascular anatomy and physiology of uterine blood flow and the application of microvascular techniques in uterine vessel anastomosis solved the earlier reported difficulties encountered in that aspect. Cytochemical and cytoimmunological noninvasive techniques for monitoring graft rejection are useful and reliable. Preservation of tissue and vascular integrity during uterine extirpation

is essential. A vascular pedicle of good length with the possible use of an extension conduit, such as the radial artery or the great saphenous vein, could be required. Strong fixation of the transplanted uterus to the anterior abdominal wall and the sacral promontory is required, as the uterus lacks the support of the uterosacral ligaments and could develop slow progressive or acute prolapse with consecutive thrombosis, infarction and loss of the uterus.

Further clinical experience and additional development of the surgical techniques could make uterine transplantation useful in the treatment of infertility, especially in communities where the surrogate mother concept is unacceptable from a religious or ethical point of view.

Controversies

Unlike other organs, which are supplied by large blood vessels, the uterus receives its blood supply from a network of tiny vessels. This means that establishing a blood supply for the transplanted organ is extremely complex and prone to problems. In addition, blood vessels supplying the uterus must be able to expand to three times their normal size during pregnancy if they are to support a developing foetus.

The Future

Uterine transplantation is still supported by gynaecologists who believe that advancement in microsurgery and immunology may allow the achievement of good results without major side-effects or risks for the transplanted mother and her foetus. Two frontiers clearly lie in the path of progress of further development in uterine transplant. One is improving and optimising immunosuppression techniques. The second is to develop an ideal vascular model for uterine transplant, its survival and functionality and subsequent pregnancy.

According to Brännström: “Suitable donors could be either a sister after she has had her own children or a mother since the chance for a good immune and blood type match would be high. It would be possible to carry your own child in the same womb [donated by mother] as you developed during your growth as a foetus” [18]. Commenting on the work by Brännström and his team, Dr. John Mills, chairman of the British Fertility Society and a consultant obstetrician and gynaecologist at Ninewells Hospital, Dundee, UK, said: “This paper has described successful pregnancies in the mouse, at least to the early pregnancy stage, and will obviously give hope to those surgeons who are interested in carrying out a similar operation in humans. More evidence of success in other animals will be required before it is justified to make such an attempt.” He said there was a huge difference between mice and humans, which meant much more work was needed. He also said the Swedish work and successful pregnancies in women who had taken immunosuppressant drugs after kidney or heart transplants showed that progress is being made on the issue of reducing the rejection of transplants.

US experts Dr. Louis Keith and Dr. Guiseppe Del Priore described transplantation of the reproductive organs as the “last frontier” in the field of organ transplantation. To some individuals, childbearing is the greatest event of a lifetime. To such persons, transplantation of organs of reproduction would not be considered frivolous or unnecessary even though these organs do not sustain life [31]. Further clinical experience and additional development of the surgical techniques could make uterine transplantation useful in the treatment of infertility, especially in communities where the surrogate mother concept is unacceptable from a religious or ethical point of view.

Dr. Richard Smith from the Chelsea and Westminster Hospital in London, who has been carrying out laboratory experiments to test the feasibility of a uterus transplant, says that a similar operation should be possible in the UK in 2 years. According to him ,there is a small group of women who are very keen to have children and who would be prepared to undergo that sort of surgery to achieve that end [31]. Peter Bowen-Simpkins, from the Royal College of Obstetricians and Gynaecologists, said he believed the develop-

ment would eventually lead to women without a uterus being able to give birth. "This shows it is technically possible. The womb survived for more than two menstrual cycles, so the first crucial hurdles have been passed" [31].

The Web to Assist the Progress of this Procedure

Web and Internet-based activities have shown an ability to bring together persons keen on further development of techniques as well as clientele looking for venues to discuss their experiences and other cooperative efforts. In relation to uterine transplantation, these sites include:

- www.uterinetransplant.com
- www.uterinetransplant.net
- www.uterinetransplant.org

The latter two were under development at the time of publication of this material. Monitoring contemporary views and progress will continue on www.uterinetransplant.net, which will also provide a platform for publications. Researchers and clients will use the forum available at www.uterinetransplant.org to continue exchanging views and cooperate with each other.

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