Uterus Transplantation

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- five face transplantations
  - (four total and one partial)
- two extremity transplantations
- More than 400 kidney transplantations/y
- 100 liver transplantations/y
Uterus Transplantation

History

- 1896, Knauer
  - Ovary transplantation
    - uterine ototransplantation research
- 1964, Ersanl, Hamernik and Hardy
  - First autotransplantation model in animal (dog, uterine)
- 2000, Saudi Arabia
  - uterine transplantation
    - Recipient; Hysterectomy after Postpartum hemorrhage
    - Live donor: Oopherectomy
- 99 day
  - Occlusion in anastomotic sides
- Animal model research
- Cadavary study
- Ethical evaluation
- Indications
- FSH, LH, and E2 levels
  - Normal and no difference in transplant patients
- 1958
  - First pregnancy in transplant patient
- Renal, liver, pancreas, cardiac, lung
  - Patient
  - Fetus
- Gonadal dysfunction
  - 6 months
  - Waiting period
    - 2 years, 1 year
    - Stable transplanted tissue
    - CMV infection
## Table I. Preconceptional Counseling Issues

- Contraception and counselling optimal timing for pregnancy
- Continuation of immunosuppressant medication
- Folic acid* and calcium# supplementations
- Performing rubella and varicella vaccination, if required
- Cervical cytology for screening cervical cancer
- Screening and treating anemia and infections

*: 400 microgram/day
#: 1000 mg /day
<table>
<thead>
<tr>
<th>Table II. Pregnancy complications</th>
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<tbody>
<tr>
<td><strong>Maternal complications</strong></td>
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<tr>
<td>Chronic Hypertension</td>
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<tr>
<td>Preeclampsia/Superimposed Preeclampsia</td>
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<tr>
<td>Infection</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Graft rejection and dysfunction</td>
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<tr>
<td><strong>Fetal complications</strong></td>
</tr>
<tr>
<td>Fetal growth restriction</td>
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<tr>
<td>Preterm labor</td>
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<tr>
<td>PROM</td>
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<tr>
<td>Low birthweight</td>
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<tr>
<td>PROM: Preterm rupture of membranes</td>
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</tbody>
</table>
- Spontan abortus
- Preterm delivery (%50, before 37 hf week)
  - Preterm membran rupture
- Intrauterine growth retardation
• Pregnancy
  • Immunosuppressive state
  • Systemic immunity
Table 3. FDA category of Immunosuppressive Agents Used in Transplant Recipients

<table>
<thead>
<tr>
<th>Immunosuppressive Agents</th>
<th>FDA category</th>
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<tbody>
<tr>
<td>Corticosteroids</td>
<td>B</td>
</tr>
<tr>
<td>CyA</td>
<td>C</td>
</tr>
<tr>
<td>Tacrolimus (FK 506)</td>
<td>C</td>
</tr>
<tr>
<td>AZA</td>
<td>D</td>
</tr>
<tr>
<td>MMF</td>
<td>C</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>C</td>
</tr>
<tr>
<td>ATG</td>
<td>C</td>
</tr>
<tr>
<td>Muromonab-CD3</td>
<td>C</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>C</td>
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</tbody>
</table>

FDA: Food and Drug Administration (United States)
CyA: Cyclosporine-A
AZA: Azathioprine
MMF: Mycophenolate mofetil
ATG: Antithymocyte globulin
Composite Tissue Transplantation Centers Registry

(SB 29.03.2011 and 13984 number established)
This registry is maintained for the regulation of transplantation centers

The duty of the stuffs of this tx centers is regulated by this registry

The tissues which originated from any embriologic layers like intestine, trachea, larinx, are included in this registry

Liver, kidney, lung, pancreas, heart, cornea and bone marrow tx are excluded from this registry
Criteria for donor selection

- Healthy volunteers younger than 45 years old
- Multipar, carries similar criterias for kidney transplantation donor volunteers
- Brain death with hemodynamic stability
- Minimal comorbidity before death
- Normal level in routine blood tests
- Matched blood type/ HLA type
- Human Papilloma Virus (HPV) Negative
- Cytomegalovirus (CMV) negative
- HIV (AIDS) Negative
- Negative viral hepatitis
- Identification of absence of myoma or vascular anomaly
Indication for uterine transplantation

- Infertility related to uterus
- Desire for uterine transplantation
- Medically Impossible to have a baby
- Congenital uterine agenesis
- Resection of uterus because of hemorrhage, trauma except malign tumors
- Be aware of long time postoperative rehabilitation
- 18 – 45 age
- Have no major trauma or surgery for negative effect of outcomes
- Healthy organs and systems
- Psychosocial stability
- Whole healthy who has no limitation for taking immunosuppressive agent
- Informed concern about all adverse effect of immunosuppressive agents
Recipient

- 21 y f
  - RKMHS
    - Vagina reconstruction with intestine segment 2,5 years ago
- Rutin pretransplantion evaluation
- Embrions obtained before tx
- Stabile family life
- Mental stability
- Good general condition
- Informed consent
Donor

- August, 2011
- 21y
- Traffic accident
- Multiorgan cadaver donor
- Donor-recipient matched blood type
- 3 HLA A, B, DR matched
• Eksternal iliac arteries and veins and Uterine arteries and uterin veins
  End to side anastomoses
• Sakrouterine ligament
• Round ligament
• Vagino-neovaginal anastomoses
• Vesicouterine peritoneal reflection
Immunosuppressive protocol

- Induction phase
  - ATG: 100-300mg/day for 10 days
    - prednisolone: 1000 mg IV on day 1; then slowly tapered to 20 mg/day
- The maintenance
  - tacrolimus (Prograf, 0.2 mg/kg/day with blood levels between 15 and 20 µg/ml in the first month, 12-15 µg/ml in the second month)
  - Mycophenolate mofetil (Cell Cept, 2 g/day)
  - prednisolone: 10 mg/day
• Wide spectrume AB
  first 10days
• sulfadoxine pyrimethamine
  *Pneumocystis carinii* pneumonia.
• CMV profilaxis
• Valgancyclovir
• GVH (-)
• Complication due to surgery (-)
• Wound healing
• Circulation
• Sentinel skin
• Rejection (-)
• Skin bx
  normal histopathological findings
• Metabolic or inf compication (-)
Conclusions

- use of immunosuppressive drugs
  - Malignancy
    - non-melanoma skin cancers
      - squamous cell carcinoma
      - closely associated with level of immunosuppression
      - withdrawal or decrease in immunosuppression
  - Post-transplant lymphoproliferative disorders (PTLD)
    - more aggressive behavior
    - less responsive to conventional treatment
    - outcomes are generally poor
    - wide spectrum of disorders ranging from benign hyperplasia to aggressive non-Hodgkin's lymphoma (NHL).
    - Mostly associated with Epstein Barr virus (EBV).
    - Proper match of the EBV is crucial to reducing the risk of PTLD
    - reducing or withdrawing immunosuppression
Five months after face tx,
- SCC on the dorsum of the left hand and the right pretibial regions.
One month later (6 months postoperatively)
- rapidly growing 2x2 cm ulcerative nodule (lymph node) in the left preauricular region
  - CD-20 positive diffuse large B cell lymphoma
  - PET-CT scan and bone marrow biopsy
    - unilateral inguinal lymph node.

Chimerism analysis revealed fully autologous signals of recipient origin.
Stage IIIA non-Hodgkin lymphoma (NHL)
- Reduction of immunosuppressive treatment
- R-CHOP regimen (rituximab, cyclophosphamide, adriamycin, vincristine and prednisolone)
- Control PET scanning
  - A high active area in the right cerebellum
  - MR imaging
    - cerebellar aspergillosis (central nervous system lymphoma??)
    - developed ataxia during walking concordant with the cerebellar lesion

- The immunosuppressive agents were stopped completely
● The dosage and length of ATG

● Informed of the greater risk of opportunistic infections and malignancies
High risk of life-threatening fungal infection
- Candida
- Aspergillus
  - involve nearly all organs
  - nonspecific clinical manifestations
    - early detection is almost impossible
  - usually diagnosed when it is already well disseminated
    - associated mortality rates can be as high as 100%.
  - early detection is crucial for the administration of effective antifungal treatment
  - removal of infected original lesions.
  - The risk is especially high in patients using steroid therapy
  - Adjustment of immunosuppressive drugs
    - lowering or even stopping them entirely may be life-saving.
- Unidentified clinical signs or pathological findings in system investigations
  - pulmonary
  - central nervous system
  - renal involvement
Semra Kahraman
Ozlenen Ozkan
Munire E. Akar
Batı Aydınuraz
Okan Erdoğan
Mehmet Şimşek
İnanç Mendilcioğlu
Necmiye Hadimioğlu
Ömer Geçici
Ayhan Dinçkan
Huseyin Koçak
Filiz Günseren
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Thank you