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, Erslan, Hamernik and Hardy
 - First autotransplantation model in animal (dog,uterine)

• 2000, Saudi Arabia

- uterine transplantation
 - Recipient; Hysterectomy after Postpartum hemorage
 - 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 disfunction

- 6 months
- Waiting period
 - 2 years, 1 year
 - Stabile 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 vacciniation, if required Cervical cytology for screening cervical cancer Screening and treating anemia and infections

*: 400 microgram/day

#: 1000 mg /day

Table II. Pregnancy complications

Maternal complications

Chronic Hypertension

Preeclampsia/Superimposed Preeclampsia

Infection

Diabetes

Graft rejection and dysfunction

Fetal complications

Fetal growth restriction Preterm labor

PROM

Low birthweight

PROM: Preterm rupture of membranes

- 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

Immunosuppressive Agents	FDA category
Corticosteroids	В
CyA	С
Tacrolimus (FK 506)	С
AZA	D
MMF	С
Sirolimus	С
ATG	С
Muromonab-CD3	С
Daclizumab	С
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 rutine blood tests
- Matched blood type/ HLA type
- Human Papilloma Virus (HPV) Negative
- Cytomegalovirüs (CMV) negative
- HIV (AIDS) Negative
- Negative viral hepatitis
- Identification of absence of myoma or vascular anomally

• Indication for uterine transplantation

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



- 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 histopatological findings

• Metabolic or inf complication (-)











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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
 - aassociated 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
- Nilgün Keçecioğlu

Thank you

