Conference & Workshop on Human Transplants Identification and Monitoring in European Union

Serious adverse events and reactions in organ transplantation

Janusz Wałaszewski,

Zbigniew Włodarczyk

Katowice, 6-7 October 2011

Risk of transplantation

- Safety in solid organ transplantation depends on most common complications related to transplantation and immunosupressive therapy to more specific issues as those related to the use of organ from NSRD

  (non –standard risk donors)

Organ transplant complications

- Main complication : organ rejection
- Complication related to donated organ itself *(with correct protocol without any negligence or malpractice the organ might fail)*
- Complication arising from preexisting conditions: *(high blood pressure ,high cholesterol, diabetes affect the success of organ transplantation)*

Evaluation of deceased potential donor

General evaluation

- Interview with the family
- Detailed review of the medical notes
- Assessement of the donor's medical history
- Full physical examination
- Postmortem examination
- Laboratory tests including all microbiologial

Major risk factors

- transmission of non detected and untreated malignancies
- transmission of infections including v.rare *(ie. West Nile Virus inf.)*
- Wrong evaluation of disease transmission leading to unnecessary discarding

Non- standard risks deceased donor

- Donors with past or present history of malignancy
- Donors with positive serology for HCV,HBV,HIV
- Donor with risk behavior for viral infectious diseases or pitfalls in serology screening
- Donors with developing infectious diseases

Pitfalls of serologic screening

- Hemodilution – tests should be repeated
- False- negative test does not detect existing infection *(hemodilution, windows period, incorrect sampling)*
- False –positive results wrongly indicates reactivity to infection ,contamination , inappropiate test quality

Measures in case of serological pitfalls

- Donation procedure must be interrupted until test results are available
- Donation may be continued under assumption that appropiate recipient is selected (e.g D+/R+)
- Donation may be continued ,including procurement , under assumption that infection can be managed (CMV)

Most common organ transplant errors sued in Courts

- Receiving diseased organs – ex: cancer
- Receiving infectet organs – ex : HIV, hepatitis
- Receiving organs that are not compatible - ex : blood type not a match
- Receiving organs from non standard risk donor
- Post transplant malpractice - ex: failure to control infections
- *www.floridalawsuits.com/Personalinjury/MedicalMalpractice/Organ Transplant)*

Risk levels and risk assessment (Alliance-O)

- Unacceplable (RL1) - absolute contra-indication with the exception of life -saving procedures
- Incrised but acceptable (RL2) - transmissible diseases identified ,but utilisation of organ justified by recipient clinical condition
- Calculated risk (RL3)accepts some transmissible diseases for recipients with the same disease
- Not assessable (RL4) evaluation does not allow an appropriate risk assessement
- Standard (RL5)

Probability of donor's neoplasias transmission

- ONT Registry (1990-2006) – **undetectd tumors 5.8/1000 donors .Only 5 or 2.9/10,000 donors tumors were transmitted** to the recipient, **10 out of 155(6.4%) or 2.2 per 10,000** recipients who received graft with a tumor developed tumoral transmission
- UNOS Registry (1994-1996) -**1.7% history of cancer 4.3% of tumor transmission**

  (1994-2000) - **14 out of 35,500 or 4/10,000 donors possessed tumor. Tumor transmission occurred in 15 of 110,000 recipients or 1.3/10,000 transplants**
- Danish Registry - **13 malignant tumors among 626 donors (2%) during 27 y.** 8 were detected after organ transplantation (1.3%) but only one transmitted neoplasia

Recommendation to prevent transmission of neoplasias

- Clinical history of a donor and physical examination (including xR and CT)
- Histopathological examination of a donor and organ during procurement (especially ISOL)
- frozen section of suspected lesion before organ tranasplantation
- Routine screening of tumor markers is not recommended except confirmed malignancy donor history *(false positive results lead to unnecessary discarding)*

Infection transmitted with organs or tissues

- **Pathogens**

-viruses,latent infection in the tissue/viremia

-**bacteraemia /**inf.tissues

-fungaemia /tissues colonosation

-parasites latent /acute infection

-prion infections

- **Primary infections –**

- before hospitalisation (CMV, tuberculosis)

-shortly before hospitalisation no clinical symptoms or serological response

- during hospitalisation/ procurement/transplantation

Medical errors : ABO incompatible heart transplantation

-After first 10,000 heart TX in US the blunder rate 1/1000. Errors occured in typing the donor or the recipient in transcription or communication, mistaking the organs when two donors were involved.

(Paul I.Terasaki NEJM 1991;325 December 12,1991)

-UNOS → Probabilistic Risk Assessment (PRA)

pre- march 2003 - predicted 1:72000 explants

JS event-2003 a Duke Univ.Hosp.

*1995 -2*003 - 1: 28,625 explants

PRA after October 2004 – predicted 1:320,000 explants

PRA current process predicts such events every 1,251 y.

(Transplantation vol.84,Number 12,Dec.2007)

Probabilistic Risk Assessment(PRA) of accidental ABO incompatible thoracic organ transplantation

The faults model includes events reflecting :

- Acceptance of a conventional match-list directed offer versus an open offer
- Local procurement versus transfer of the organ
- Use of the recipient identified at the time of match versus some other recipient
- Determination that the organ is suitable for use versus declining to use the organ
- Confirmation testing of ABO compatibility versus no confirmation

(Transplantation vol.84,Number 12, Dec.2007)

Medical error :lungs „size error”

- A nurse put in wrong figure into computerised organ matching service : donor -156 cm tall,recipient 151cm
- Surgeon was forced to compress oversized lung into the chest.Transplant team discovered later that the donor was 165 cm tall.
- Recipient developed pneumonia and died two months later. The surgeon attributed the death of the patient to the wrong size of transplanted lungs.

Medical error: inadvertent incompatible ABO cadaveric kidney transplantation (2 cases)

1-Recipients O Rh+; graft A Rh+

-Cross match negatif

-No hyperacute reaction after revascularisation

-Recipients accepted : plasmaferesis,immuno globulins, escalation of immunosupression

-Results - R.kidney- IF (-) after 1m graftectomy (no fuction)

L.kidney- IF+ ; 12m F+ ok.!

2-Recipients A Rh+; graft B Rh-

- Cross match ?

-No hyperacute reaction after revascularisation.

-IF of both grafts 0

-After discovering the error graftectomies during the first 24h performed

Histo –path – acute rejection

Medical error :inadvertent incompatible ABO living donor kidney transplantation (1 case)

- Compatible blood group determined in the country of donor and recipient origin (enclosed in medical files !)
- Cross match before transplantation twice negative
- May 9 - kidney transplantation from mother to daughter
- 15 min after reavascularisation suspicion : intravascular coagulation? hyperacute rejection ? Post-op biopsy – hypetracute rejection. Intervention –bolus ATG ,antycoagulants
- May 11 - graftectomy – hyperacute rejection
- Epicrisis : verification of blood group discovered the error. Kidney (B+) from mother was transplanted to (A+) daughter

Is nighttime organ transplant surgery an important factor ?

- In general opinion nighttime medical care has been associated with worse outcomes in general surgery and abdominal organ transplantation
- UNOS study (2000-2010) of 27118 thoracic organ transplantations patients were stratified by operative time : day -7am to 7 pm night - 7 pm to 7 am
- Survival time was similar for patients with organ transplants performed during the day and night

JAMA,2011;305[21]

Medication errors in organ transplantation

- **149 errors in 93 patients** in one year (Yale Univ.)

- 56% patient error

- 26 % prescription/ delivery / availability errors

- 8% patient could not give enough information

- **Adverse events(AE) were associated in 32 %** of errors with : 17 hospitalisations ,9 episosodes of rejection, **6 failed transplants**

- **Roots of error: patients 68 %, health care providers 27% (10% caused by transplant team !!)**

Arch.of Surg.2007 Mar;142((3)

WHO Guiding Principle Number 10

- „the level of safety, efficacy and quality of human cells, tissues and organs for transplantation, as health product of an exceptional nature, must be maintained and optimized on an on-going basis
- This requires implementation of quality system including traceability and vigilans , with adverse effects (AE) and reactions (AR) reported nationally and for exported human product”

Principle Number 10 provides

- … first overview of the current situation of vigilance system (V-system) applied to human organs intended for transplantation *(a summary of the provision of the **Directive 2010/53/EU** and update of the lessons learnt from the developement of vigilance in the EU applied to tissues and cells.*

Vigilance system of human organs transplantation

- Main objective of a vigilance is immediate preventive action on affected or potentially affected patients
- Additional preventive strategy : survillance, analyisis of data provide indicators and information on stratification of risks, systemic follow up of recipients grafted from non standard risk donors
- A **V-system should aim at the prevention of SAE and /or SAR** thereby protecting the health of all organ recipients and the living organ donors

Definitions SAE , SAR

- SAE serious adverse events – any unforseen occurrance associated with procurement, testing, processing ,storage and distribution of organs
- SAR serious adverse reaction – an unintended response or effect that occurs after transplantation and immuno-suppressive therapy

SAE & SAR examples

SAE :

-mistake of blood group in donor/recipient

-lack of confirmity of donor selection ((HLA, serology)

-tumor diagnosed in donor organ after transplantation

-preservation fluid contamination

- other

SAR in a recipient :

-death or removal of graft

-infectious disease

-viral seroconversion

-tumor diagnosed in a recipient

-other AR i.e. allergic reaction in a recipient

SAR in living donor :

-unexpected clin. reaction

Serious Adverse Effects

- **Errors** : failed identification of potential donor or failed transplantation due to organizational logistic issues
- **Medical errors** : missed or inappropriate intervention (clinically significant AE derivated)
- **Minor adverse event** conected with any phase of procedure leadindg to undesirable damage to the patient
- **Sentinel event** potentially highlighting malfunctioning of the system
- **Near miss** –error has potential to provoke a SAR

Serious Adverse Reactions

- **Unexpected primary infections** transferred from the donor
- **Transmitted infections** due to contamination on the procured organ or associated material
- **Hypersensivity reactions** allergy/anaphylaxis
- **Malignant disease** transferred by the organ
- **Immunological reactions** –unexpected delayed or absent engraftment, graft failure including mechanical failure

Unexpected SARE

- **Graft-related complication** arises despite all safety precautions.
- Examples :

  - donor derivated de novo HCV (not known at procurement)

  - metastasis detected in recipient related to donor with history of malignancy

Expected SARE

- **Recipient related complications** occur as a part of the transplantation process
- Examples :

  - graft rejections

  - reactivation of CMV infection

Potential SARE

- **Cases with adequate assessment and awareness**
- Example

  -donor derivated disease transmission were known and subsequently occured in the recipient HCV or HBV

Reporting SARE (Directive 2010/53/EU)

- **Life threatening complication** to other recipients ,SARE must be reported immediately to CA (competent authority)
- **Unexpected or potential SARE,** institution detecting SARE must immediately report this to the CA
- **CA must record all** unexpected or potential SARE
- **An annual SARE report** must be produced by CA of each member state and published by Council of Europe
- **All SARE data should be shared** by all CAs in European SARE registry

Organisation /Team working

- **Communicating the other partners** of health problem detected in one recipient would improve diagnostic/terapeutic capacity of the team treating other recipients from the same donor
- **Establishing a system for reporting** and managing information as well as alerting other centers concerned
- **To keeping traceability** of organs from donor to recipient in all phase *(this information must be stored)*

Organisation/ Team work

- **The form of organisation** specific for donation and transplantation system becomes a network of every team recovering,allocating or transplanting .
- **Particularity of this network** is that the teams involved in one donation share a group of factors that might influence the results of transplantation and the appearence of SAE and /or SAR may be submitted to similar risks as their transplanted organs from the same donor

Remarks

- Only organs recovered under high quality management of the donation process are likely to function satisfactorily.

- There is no perfect system for tracking

  all donors risk factors but careful evaluation of donors should keep the risk level as low as possible

Conclusions

- „the most important risk factor in transplantation for the patienton Waiting List is the risk of death because not getting an organ in time”

- gap between the supply and demand of organ for transplantation,requires individual case-by-case risk/benefit analysis produced for each patient enrolled on a Waiting List