

Supporting solid organ transplants: *Challenges for Blood Transfusion Labs*

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Addenbrooke's Blood Bank

- 1. Bone Marrow Transplant Program
- 2. Renal transplants
 - ABO/RhD incompatible
- 3. Liver transplants
 - Some ABO/RhD incompatible
- 4. Multiple visceral transplants
 - Immediate and longer term implications for blood transfusion

- 45 year old Caucasian male
- Diagnosis: MM
- Underwent unrelated BMT
- Reduction/discontinuation of immunosuppression
- Anaemia
 - Bone marrow examination
 - Absent erythroid precursors
 - Chimerism:95%

Admitted to oncology ward following 3 unit transfusion

Clinical symptoms were suggestive of an acute HTR
(rigors, tachycardia, hypertension & hypoxia, bright red urine)

Post-transfusion group: A RhD positive

Pre-transfusion results the same

- Antibody screen – pre = negative,
- post = weakly positive
- DAT: 2+ C3d positive (1+ pre-transfusion)
- Anti-E only found by IAT
- Eluate negative

- 10 days later
- 3 units ordered
 - (E negative cross match compatible)
- Severe reaction at end of 1st unit
 - Temperature
 - rigors
 - chest pain
 - Haemoglobinuria

- Eluate negative
- DAT = C3d 3+ positive
 - Anti-E

Investigations repeated at NHSBT- RCI

- **Pre-transplant**

- Fya POSITIVE
- Fyb POSITIVE
- Fy GATA mutation NEGATIVE
- Jka POSITIVE
- Jkb POSITIVE
- K (KEL1) NEGATIVE
- k (KEL2) POSITIVE
- M POSITIVE
- N POSITIVE
- S NEGATIVE
- s POSITIVE

- **Donor's sample**

- Fya POSITIVE
- Fyb NEGATIVE
- Fy GATA mutation NEGATIVE
- Jka POSITIVE
- Jkb NEGATIVE
- K (KEL1) POSITIVE
- k (KEL2) POSITIVE
- M POSITIVE
- N POSITIVE
- S POSITIVE
- s POSITIVE

- **Pre-transplant**

- Fya POSITIVE
- Fyb POSITIVE
- Fy GATA mutation NEGATIVE
- Jka POSITIVE
- Jkb POSITIVE
- K (KEL1) NEGATIVE
- k (KEL2) POSITIVE
- M POSITIVE
- N POSITIVE
- S NEGATIVE
- s POSITIVE

- **Post transplant**

- Fya POSITIVE
- Fyb NEGATIVE
- Fy GATA mutation NEGATIVE
- Jka POSITIVE
- Jkb NEGATIVE
- K (KEL1) POSITIVE
- k (KEL2) POSITIVE
- M Undetermined
- N Undetermined
- S Undetermined
- s Undetermined

- Transfused uneventfully S(-) and K(-) blood
- Re-start immunosuppression
- Currently transfusion independent
 - *?Antibody mediated haemolysis*
 - *If yes, why we can not detect it?*

Renal transplants

- Historically only ABO compatible
 - Graft viability
 - Haemolytic reactions/side effects
- Increasing number of ABO incompatible renal transplants from live donors
- Pre-selection of donor/recipient
- Preparation of the donor (reduction of anti-A-anti-B)

ABO-incompatible renal transplants

Blood Bank

- Addenbrooke's protocol 2006
- Titration at presentation
- 4 days prior to the intended day of transplantation
- Monitor rate of reduction
- Urgently if rejection is suspected

ABO-incompatible renal transplants

Blood Bank

anti-A **IgG** and IgM

Anti-B IgG and IgM

titration reagent red cells
donor red cells

ABO-incompatible renal transplants

- *Accommodation*
- *Anti-A and –B titres post transplantation*

Recipient Group	Donor Group	Group of FFP 1 st choice / 2 nd choice	Group of Cryo 1 st choice / 2 nd choice
A	O	A then B	A
A	B	AB then HTN B	B
A	AB	AB then HTN A	A
B	O	B then AB	B
B	A	AN then HTN A	A
B	AB	AB then HTN B	B
O	A	A then AB	A
O	B	B then AB	B
O	AB	AB then HTN A	A
AB	O	AB then HTN A	A
AB	A	AB then HTN A	A
AB	B	AB then HTN B	B

HLA sensitisation

- Renal transplantation
- Possible link to red cell transfusions
- Transplantation 2012 Feb 27;93(4)
 - RR 4.1 ($p=0,02$)
- Transplantation 2012 Dec 15;94(1)
 - HLA selected red cells offers protection($p=0.002$)

Transfusion support for liver transplantation

- History of significant number of transfusions
 - Antibodies present
 - -limiting factor for transplantation
- Often coagulopathic
- Time restrictions for optimisation
 - Cell savers
 - Near patient testing

Transfusion support for liver transplantation

- Blood Bank input at liver transplantation MDT (weekly)
- Presence of antibodies
 - (validity of samples)
 - no atypical antibodies detected
 - no atypical antibodies detected. Had red cell transfusion therefore please monitor antibody status.
 - No recent transfusion samples received
- Anticipated time for preparation of blood

Transfusion support for liver transplantation

- Blood availability
 - Anti-E
 - Please allow an additional 2 hours for blood availability
 - O RhD positive female patient
 - Anti-C, K, Jkb, Fya

Transfusion support for liver transplantation

- Patient's with complex antibodies:
 - Minimise unexpected patients with complex antibodies:
 - Communication with shared care hospitals for transfusion history
 - Pre-transfusion samples
 - Transfer of stocks(10-15 units)
 - Prioritisation for transplantation

ABO incompatible liver transplants

In the past

- Error
- Emergencies
- Paediatric practice

ABO incompatible liver transplants

- Emergencies
- No previous preparation
- Possible some titration prior to transplant

- 55 year's old female patient
- Blood group O RhD positive
 - » Antibodies negative
- Urgent liver transplant
- Donor's blood group
 - A RhD positive

ABO incompatibility

- Rejection of organ
- Acute haemolytic transfusion reactions
- Passenger lymphocyte syndrome

- Anti-A IgG :1/64
- Anti-A IgM :1/8
- Can we avoid possible reaction?
- Red cells and FFP compatible with donor and recipient

- Surgical preparation of the organ (flash)
- Further immunosuppressant
 - Ritoximab
 - IVIG?
 - **Eculizumab**

“passenger lymphocyte syndrome”

- unexpected antibodies of A and B specificity
- 1980 :kidney allografts from ABO minor mismatched donors
- 1991:liver, kidney, pancreas, spleen, heart, lung, and heart-lung
- viable donor B lymphocytes passively transferred with the organ at the time of transplantation

- if they are stimulated shortly after transplant by recipient or transfused red cell antigens, they can start producing antibodies during their life.
- PLS with severe haemolytic anaemia was due to an anti-JK α on day 19 after allogeneic peripheral blood stem cell transplantation

- amount of lymphoid tissue transplanted with the organ
- antibodies to red cell antigens outside the AB system have been reported in association with transplanted
 - kidney, pancreas-kidney, pancreas, liver, and heart-lung

- Donor-derived ABO antibody typically develops 7–14 days after liver transplantation.
 - DAT POSITIVE
 - The serum antibody is predominantly
 - IgG, but it may also be IgM.
- Passenger lymphocyte derived antibodies are short-lived
- persisting for about 2–3 weeks in liver transplant recipients
 - and 5 weeks in kidney transplant recipients

- Haemolysis is usually mild and self-limited
- substantial morbidity such as acute renal failure, DIC, hypotension, and multi organ failure, has been reported

Multi visceral transplantation

- Patients with co-morbidities
- Often coagulopathic
- **Rapid changes** during transplantation
 - assessment
 - Protocols
- Some with very **low body weight** (BMI 15)

Massive Blood Loss in Adults

4 litres in 24 hours 2 litres in 3 hours > 150ml/min

Get help

Contact Transfusion
ext 58405

Contact senior member of clinical team. Contact senior ward nurses
Contact portering services
Contact Transfusion ext 58405

Ask Transfusion to
'Initiate massive
blood loss protocol'

Assess ABC

IV access

2 large cannulae

Send blood samples, cross-match, FBC, coagulation, biochemistry
Consider arterial blood gas measurement

Send FBC and coagulation samples after every 5 units of blood given

Resuscitate

IV warm fluids – crystalloid or colloid
Give Oxygen

Give blood

Blood loss >40% blood volume is **immediately** life-threatening
Give 4 units via fluid warmer. Aim for Hb<8g/dl

Give Group O Rh D negative if immediate need
and/or blood group unknown

Blood Transfusion lab will provide group specific cross-matched
red cells as required

Before Transfusion
• Check Patient ID
• Use wristbands
• FBCARS

Blood loss >40% blood volume
• TPO <20000/mls low
• Pulse >120, RR >30
• Hypertensive
• Urine <20ml/h

Prevent coagulopathy

Anticipate need for platelets and FFP after 4 units blood
replacement and continuing bleeding

Give Primary Massive Blood Loss (MBL) Pack

Order Secondary Massive Blood Loss (MBL) Pack

Correct hypothermia

Correct hypocalcaemia (keep ionized Ca > 1.13mmol/L)

Contact Haematologist

Primary MBL Pack
• Blood 5 units
• FFP 4 units

Secondary MBL Pack
• Blood 5 units
• FFP 4 units
• Platelets
• Cryoprecipitate

Reassess and document

Get help to stop bleeding

Contact surgeons,
gastroenterologists,
obstetricians as
appropriate

Give blood

Before Transfusion

- Check Patient ID
- Use wristbands
- FBARS

Blood loss >40% blood volume is immediately life-threatening

Give 4 units via fluid warmer. Aim for Hb>8g/dl

Give Group O Rh D negative if immediate need and/or blood group unknown

Blood Transfusion lab will provide group specific cross-matched red cells as required

Blood loss >40% Blood volume

- 1500-2000mls loss
- Pulse > 120, RR > 30
- Hypotensive
- Urine < 20ml/h

Prevent coagulopathy

Primary MBL Pack

- Blood 5 units
- FFP 4 units

Anticipate need for platelets and FFP after 4 units blood replacement and continuing bleeding

Give Primary Massive Blood Loss (MBL) Pack

Order Secondary Massive Blood Loss (MBL) Pack

Correct hypothermia

Correct hypocalcaemia (i.e. ionised Ca > 1.13mmol/L)

Contact Haematologist

Secondary MBL Pack

- Blood 5 units
- FFP 4 units
- Platelets
- Cryoprecipitate

Reassess and document

Get help to stop bleeding

Contact surgeons, gastroenterologists, obstetricians as appropriate

Massive blood loss in children

>80 ml/kg 24 hours >40 ml/kg in 3 hours >3 ml/kg/min

*Please see guideline for age/weight blood loss estimates

Contact transfusion

Get help

Contact senior member of clinical team. Contact senior ward nurses.
Contact portering services

Contact transfusion

Ask transfusion to 'initiate children's massive blood loss (C-MBL) protocol'
Give the weight, age and location of the child

Assess ABC

Stop overt bleeding where possible

IV access

2 cannula (largest possible)
Send blood samples – crossmatch, FBC, PT / APTT / Fibrinogen,
Biochemistry (U&E, UPT, Ionized Ca, phosphate)
Arterial / venous blood gas measurement

In trauma or surgical bleeding consider
Tranexamic Acid
Initial bolus 15mg/kg
(max 1g) followed by
maintenance infusion

Resuscitate

IV fluids – crystalloid or colloid – 10–20ml/kg
Give oxygen

Give blood

Blood loss >40% blood volume (ie. >30ml/kg) is immediately life-threatening
Give 20ml/kg red cells (up to four units). Aim for Hb>80g/L
Give Group O RhD negative if immediate need
and/or blood group unknown

Blood transfusion lab will provide group specific
crossmatched red cells as required

Before transfusion
• Check patient ID
• Use wristbands
• Ask parent if present

Prevent coagulopathy

Anticipate need for platelets and FFP after 20–30ml/kg blood
replacement and continuing bleeding
Give Primary Children's Massive Blood Loss (C-MBL) Pack
Order Secondary Children's Massive Blood Loss (C-MBL) Pack
(Secondary pack to be given if bleeding continues)
Correct hypothermia and use fluid warmer
Correct hypocalcaemia (keep Ionized Ca>1 mmol/L)
Contact Haematologist

Primary C-MBL pack
• Blood 30ml/kg
(up to 5 units)
• FFP 20ml/kg FFP
(up to 4 units)

Secondary C-MBL pack
• Blood 30ml/kg
(up to 5 units)
• FFP 20ml/kg
(up to 4 units)
• Platelets 15ml/kg
(up to 1 unit)
• Cryoprecipitate 5ml/kg
(up to 300ml)

Maintain stability

Repeat blood gas (including Hb,
Ionized Ca, Na, K, glucose) every 30 minutes
Repeat FBC, coagulation after every 40ml/kg blood components given
Monitor HR, BP, capillary refill, saturation, temperature, urine output

Re-assess
• Re-assess ABC and
clinical parameters
regularly
• Document status

Get more help to stop bleeding

Contact paediatric surgeons, paediatric gastroenterologists,
PICU, radiology as appropriate

Suspect 40% blood loss if significant source of bleeding suspected and clinical parameters as follows:

Age	Heart rate	Systolic BP
<1 year	>160	<70
1–2 years	>150	<80
3–5 years	>140	<90
6–12 years	>120	<90
>12 years	>100	<100

Urine output <0.5ml/kg/hour

Therapeutic aims

Hb	>80g/L
Platelets	>75 x 10 ⁹ /L
Fibrinogen	>1g/L
APTT	<1.5x midpoint of normal range
Ionized calcium	>1mmol/L
pH	>7.2
Core temperature	>35°C

Prevent coagulopathy

Primary C-MBL pack

- Blood 30mVag (up to 5 units)
- FFP 20mVag FFP (up to 4 units)

Anticipate need for platelets and FFP after 20–30mVag blood replacement and continuing bleeding

Give Primary Children's Massive Blood Loss (C-MBL) Pack

Order Secondary Children's Massive Blood Loss (C-MBL) Pack (Secondary pack to be given if bleeding continues)

Correct hypothermia and use fluid warmer

Correct hypocalcaemia (keep ionized Ca²⁺ >1 mmol/L)

Contact Haematologist

Secondary C-MBL pack

- Blood 30mVag (up to 5 units)
- FFP 20mVag (up to 4 units)
- Platelets 15mVag (up to 1 unit)
- Cryoprecipitate 5mVag (up to 300ml)

Reassess

- Re-assess ABC and clinical parameters regularly
- Document status

Maintain stability

Repeat blood gas (including Hb, ionized Ca, Na, K, glucose) every 30 minutes

Repeat FBC, coagulation after every 40mVag blood components given

Monitor HR, BP, capillary refill, saturation, temperature, urine output

Get more help to stop bleeding

Contact paediatric surgeons, paediatric gastroenterologists, PICU, radiology as appropriate

- Campath-1H
- Need for irradiated products
- Hyperkalaemia/renal failure

RhD positive organs to RhD negative recipients

- Women of child bearing potential
- Although sensitisation is described to be low a number of cases are reported

Transplant related TTP

- ? Role of plasma exchange
 - Raised WVF and fibrinogen
- Platelet transfusion
 - *Guidelines*