Allogeneic Hemopoietic Stem Cell Transplantation: Transfusion issues

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Red cell antigens, NOT part of the HLA system

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Chromosome</th>
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<tbody>
<tr>
<td>HLA</td>
<td>6</td>
</tr>
<tr>
<td>ABO</td>
<td>9</td>
</tr>
<tr>
<td>Rh</td>
<td>1</td>
</tr>
<tr>
<td>Kell</td>
<td>7</td>
</tr>
<tr>
<td>Kidd</td>
<td>18</td>
</tr>
<tr>
<td>Duffy</td>
<td>1</td>
</tr>
<tr>
<td>Lewis</td>
<td>19</td>
</tr>
<tr>
<td>MNS</td>
<td>4</td>
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## Challenges

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
<th>Bidirectional</th>
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</table>
| • Intravascular hemolysis  
  • Continued production of anti-donor iso-agglutinins with delayed engraftment / PRCA | • Intravascular hemolysis  
  • Production of anti A / anti B by donor B lymphocytes  
  • PLS | Both major and minor challenges |

### Adverse effects of transfusions:
- Platelet refractoriness
- Allergic reactions
- BACON
- Red cell alloimmunisation
- TRALI
- DMSO toxicity
Jan 2015-Oct 2016

HSCT 113

- Allo 59
  - MRD 48
  - MUD 11

- Haplo 9

- Auto 45

- HPC – M 11
- HPC – A 102
- HPC – C nil
Immuno-hematologic evaluation

Pre-HSCT
- ABO & Rh
  - Recipient, donor/product
- DAT, Ab screen, auto
  - Donor & recipient
- Cross match
  - major & minor
- Iso-agglutinin titers

Post-HSCT
- Blood group Tube & CAT
- DAT antibody screen
- Iso-agglutinin titers
Transfusion policy for ABOi transplants at Tata Medical Center

<table>
<thead>
<tr>
<th>ABO mismatch</th>
<th>Transfusion policy</th>
</tr>
</thead>
</table>
| Major        | **RBC, granulocytes** – O group/recipient type until recipient isoagglutinins disappear  
**Platelets, FFP** - AB group/donor type until recipient red cells disappear |
| Minor        | **RBC, granulocytes** – O group/donor type until recipient isoagglutinins disappear  
**Platelets, FFP** - AB group/recipient type until recipient red cells disappear |
| Bidirectional| Group O RBC until recipient isoagglutinins are undetectable; group AB plasma until recipient red cells disappear, then switch to donor type products |
Packed red cells
Packed red cells

• RBC transfusions for (auto / allo HSCT) donors should be autologous; if autologous not possible, allogeneic irradiated RBC given

• Recipient RBC requirements - usually after transplant, until engraftment, more in ABOi, MUD transplants, sometimes pre-transplant (chemotherapy)

• RBC - leuco-depleted, irradiated, compatible with both donor and recipient

• We transfuse at hct < 24% or if symptomatic

• Our red cell alloimmunisation in HSCT is only 1.6%

Red cell alloimmunisation in oncology patients: A study from eastern India
Supriya Dhar and Sabita Basu
Transfusion and Apheresis Science 2015;52: 345-349
Platelets

RDP / SDP – leucoreduced, irradiated
SDP preferred

Platelet transfusions are usually prophylactic, group sp preferred

Trigger: < 10\times10^9/l in absence of bleeding, < 20\times10^9/l with signs of bleeding

Split product into two; interchange donors and products amongst patients
**FFP, Cryoprecipitate**

- Transfusion requirements for FFP, CP less than that for RBC and platelets
- Increased demand – APML, GVHD, sepsis, bleeding, DIC coagulopathy, liver disease, cyclosporine induced TTP .......... several CPP units issued
- Plasma containing products should be compatible with both donor and recipient, no need for irradiation
Granulocyte transfusions

**Indications:** Proven infection, refractory to antimicrobials with ANC < 500 /ul

- **Apheresis granulocytes**
  Screened donor- group specific, cross match compatible
  Neupogen 5 ug/kg + 8 mg dexamethasone

- **BC granulocytes**
  Group specific BC bags, cross match compatible
  Usually prepared for 3 consecutive days,
  option when apheresis donor is not available / cost constraints

*Product cross-matched, irradiated, issued 6-8 hours*
*Transfused without a filter, allergic reactions*
Granulocyte apheresis
Donor lymphocyte infusion

• In relapse after HSCT, an option to avoid another transplant

• Lymphocytes from original stem cell donor are infused to induce remission by a process called the graft-versus-tumor (GVT) effect.

• Whole blood from stem cell donor (specific volume) transfused, without irradiation/leuco-filter
Case 1

- 11 years male child, HSCT for Fanconi anemia from HLA matched, ABO matched sibling donor
- Had complete engraftment by day +28, CMV reactivation since day +40, received valganciclovir
- On day +67, presented in emergency with pallor, deep yellow urine, icterus
Request for 2 RBC received.....

Hb 2.9 g/dl  Retic 17.8%  LDH 2915 U/l  
Bilirubin (unconj) 3.3 mg/dl  
Red cell agglutination at room temp

- Type IV blood group discrepancy  
- Resolved with warm saline washing  
- DAT 4+  IgG and C3  
- Autocontrol positive  
- Antibody screen: panagglutination

Immune-hemolytic anemia

Alloadsorption done (R1R1,R2R2,rr cells) : no alloantibodies  
Thermal amplitude test and DTT treatment revealed mixed type AIHA  
Mixed type AIHA due to CMV reactivation
• Phenotype matched RBC (O, DcE/Dce) were transfused, Hb 7.3g/dl post-transfusion
• Rituximab - 4 weeks + steroid

Mixed type AIHA due to CMV reactivation after HSCT:
• 3-6 % incidence
• More in young patients, non-malignant disease transplants
• Infections may be an important trigger for autoimmune events after HSCT
• CMV may contribute to the onset of post-transplant complications

Indian J Hematol Bl Transf 2016; 32: 211-13
Datta SS, Reddy M, Basu S, Krishnan S
Case 2

Pre-transplant blood group A positive

At 16 weeks; Patient was transfusion dependent, Hb ranged from 5.8-8 g/dl
Reticulocytes 0.05%
ANC > 500/UL
Unsupported platelet count > 20000/cmm

Mixed RBC chimerism

At 16 weeks, anti B titer = 2048
**B >> A**
Recipient anti B titer = 2048
Time to disappearance of anti B = 22 weeks

**Red cell engraftment criteria:**
- Independence of RBC transfusion
- Reticulocytes >1%
- 100% donor RBC chimerism
- Coincides with disappearance of recipient anti-donor isoagglutinins

PRCA confirmed on bone marrow biopsy

**Risk factors for PRCA:**
- A >> O transplants, increased time to disappearance of recipient iso-agglutinins, cyclosporine for GVHD prophylaxis
Case 3

• 6 years F child, beta thalassemia major on regular transfusion; every 20-25 days.
• Was receiving phenotype matched RBC, oral iron chelation with S.ferritin monitoring
• Now to undergo allogenic HSCT from her 3 years sister (donor); was complete 6/6 HLA match, both B positive
• Minor cross match was incompatible

Clinically significant, naturally occurring anti M antibody, with both IgG and IgM components in the stem cell donor
• Recipient was M antigen positive
• Stem cells were harvested from marrow, donor required one RBC transfusion

*Group specific, M antigen negative, leucocyte-reduced, irradiated RBC transfused to donor
Harvested product was plasma depleted

**Lessons learnt:**

• Complete pre-HSCT immuno-hematologic evaluation necessary for donor and recipient
• Stem cell harvest may need modification
An analysis of transfusion support in HSCT - report from a centre in India

Datta SS, Basu S and Chandy M
Transfusion and Apheresis science 2015; 53:373-77
First 100 days blood product requirement among different HSCT categories

<table>
<thead>
<tr>
<th>Blood product</th>
<th>Auto (40)</th>
<th>Allo (50)</th>
<th>Haplo-identical (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>1.45 +/- 0.50</td>
<td>6.7 +/- 1.6</td>
<td>7.5 +/- 1.4</td>
</tr>
<tr>
<td>RDP</td>
<td>1.85 +/- 0.82</td>
<td>8.38 +/- 3.2</td>
<td>15.1 +/- 2.8</td>
</tr>
<tr>
<td>SDP</td>
<td>1.87 +/- 0.84</td>
<td>3.26 +/- 1.2</td>
<td>4.3 +/- 1.2</td>
</tr>
<tr>
<td>FFP</td>
<td>0.23 +/- 0.10</td>
<td>5.9 +/- 1.8</td>
<td>7.4 +/- 2.2</td>
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</tbody>
</table>
Mean blood product requirement among the ABO matched groups

<table>
<thead>
<tr>
<th>Blood product</th>
<th>Major + Bidirectional (08)</th>
<th>Minor + same group (52)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>15.8</td>
<td>5.25</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>SDP</td>
<td>5.25</td>
<td>3.52</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>RDP</td>
<td>20.5</td>
<td>6.94</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>FFP</td>
<td>12.75</td>
<td>3.98</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>
Mean blood product requirement among the allo-HSCT categories (MRD vs MUD)

<table>
<thead>
<tr>
<th>Blood product</th>
<th>MRD n=46</th>
<th>MUD n=4</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>6.43</td>
<td>10</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>SDP</td>
<td>2.93</td>
<td>7</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>RDP</td>
<td>6.78</td>
<td>17.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>FFP</td>
<td>4.97</td>
<td>16.5</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>
Factors affecting transfusion requirements

- Type of HSCT: auto / allo / haplo
- Conditioning regimen (myelo-ablative, reduced intensity)
- Graft source: HPC-A, HPC-M, HPC-C
- Dose of CD 34+ cells
- Previous chemotherapy
- Time to engraft
- Complications: GVHD, CMV infection
Transfusion support in allogenic HSCT challenging - immuno-compromised, sepsis, multi-transfused, alloimmunisation, platelet refractoriness

Immuno-hematologic evaluation to include –red cell phenotype, minor cross match and antibody titers

Improved HSCT survival rates - organ damage is rising; ESRD occurs due to prior chemotherapy irradiation, sepsis, nephro-toxic drugs; second transplants

Inappropriate transfusion might compromise transplantation outcome