Autoimmune Haemolytic Anaemia post Bone Marrow Transplant

A Case Study

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ACT Pathology

Patient History

- Master X
  - 22 months old
- Presented to the Paediatric Dept – March 2015
  - Lethargy
  - Upper respiratory tract infection – 1 week
- Clinical History
  - Chronic Granulomatous Disease (CGD)
  - Post BMT
  - Prednisolone commenced 5 days prior due to falling Hb

Chronic Granulomatous Disease

- CGD is a primary immune disorder
  - Results in defective production of NADPH oxidase
    - Critical to the oxidative destruction of phagocytosed pathogens
    - Leading to recurrent infections forming granulomas in the organs
- Treatment consists of antibiotic prophylaxis and interferon therapy
- The only curative treatment is allogeneic bone marrow transplant

Bone Marrow Transplant

- Bone Marrow Transplant – November 2014
  - Sydney Children's Hospital
  - Unrelated matched donor - 10/10
  - Discharged under the care of SCH

AIHA post BMT

- AIHA is a rare complication of BMT
  - Reported incidence of 3-4.4% in paediatrics
- Most patients require medical intervention
  - IVIg, steroid treatment, transfusion
- Median time of onset is 273 days post first BMT
  - 157 days post second BMT
- There is a significant association with AIHA in recipients of mismatched related, matched unrelated and mismatched unrelated donors
  - Compared to matched related donors

AIHA post BMT

- There is a higher incidence in patients undergoing BMT due to non-malignant disorders
  - Possibly due to the patient having a relatively competent immune system prior to BMT
  - No significant association between the incidence of AIHA and HvGD
- Overall survival did not differ significantly among recipients of single BMT with and without AIHA

Case Study

- Haemolytic Screen - May 2015

Hb	55	(ref. 102-132g/L)
Retics	14.25%	(ref. 0.5-2.0%)
Haptoglobin	<0.1	(ref. 0.3-2.0g/L)
Bilirubin	24	(ref. 2-20umol/L)
LDH	481	(ref. 164-286U/L)

Case Study

- Serology – May 2015
  - Blood Group - O RhD positive
  - DAT – positive grade 4
    - Specificity IgG and C3b
    - Insufficient sample for elution
  - Antibody Screen – positive
    - Pan-agglutinating
    - Insufficient sample for full panel investigation

Case Study

- Abtect 3 Cell Screen

	D	C	E	c	e	K	Fya	Fyb	Jka	Jkb	M	N	S	s	IAT
R_1R_1	+	+	0	0	+	+	0	+	0	+	0	+	0	+	3
R_2R_2	+	0	+	+	0	0	+	0	+	0	+	+	+	+	4
rr	0	0	0	0	+	+	+	0	0	+	+	0	+	+	3

- Abbreviated Phenocell B panel

	D	C	E	c	e	K	Fya	Fyb	Jka	Jkb	M	N	S	s	IAT
R_1R_1	+	+	0	0	+	+	+	+	0	+	+	0	+	+	3
R_1R_1	+	+	0	0	+	0	0	+	+	+	+	0	+	0	3
R_2R_2	+	0	+	+	0	0	+	0	+	0	+	+	+	+	4
R_2R_2	+	0	+	+	0	0	0	+	0	+	0	+	0	0	4
Auto															3

Case Study

- A full phenotype – post BMT
  - R_1r K- Jk(a-b+) M+N- S+s-
  - Weak reactions against K, N & s
    - Due to interference from auto-antibody
    - Interpreted as negative

- Strong reacting pan-agglutinating auto-antibody with an underlying allo Anti-E

Case Study

- A rr, CMV-, irradiated and phenotype matched unit was IAT crossmatched and released as “least incompatible”
  - Grade 3 reaction against the unit
  - Grade 4 reaction against the auto control
- IVIg 1g/kg was also given

Case Study

- The transfusion was well tolerated
  - No adverse reactions noted
- Discharge diagnosis
  - AIHA post BMT
  - Steroid therapy to continue

Case Study

- Haemolytic Screen - March 2016

Hb	43	(ref. 107-136g/L)
Retics	>30.0%	(ref. 0.5-2.0%)
Haptoglobin	<0.1	(ref. 0.3-2.0g/L)
Bilirubin	46	(ref. 2-20umol/L)
LDH	983	(ref. 164-286U/L)

Case Study

- Serology unchanged
  - Strong reacting pan-agglutinating auto-antibody with an underlying allo anti-E
- R_1r, CMV-, irradiated and phenotype matched unit **with the exception of Jka** was IAT crossmatched
  - Grade **4** reaction against the **unit**
  - Grade **3** reaction against the **auto control**
- Due to clinical necessity the unit was released with Haematologist approval

Case Study

- The transfusion was well tolerated
  - No adverse reactions noted
- Discharged
  - Steroid therapy re-commenced

Case Study

- X presented again with declining Hb - August 2016
- Finally received adequate samples for full investigations
  - Allo-adsorption
  - Genotyping

Case Study

- Allo-adsorption Panel – 3rd pass

	D	C	E	c	e	K	Fya	Fyb	Jka	Jkb	M	N	S	s	IAT
R_1R_1	+	+	0	0	+	0	0	+	0	+	0	+	0	+	+/-
R_1R_1	+	+	0	0	+	+	+	0	0	+	+	0	+	0	+/-
R_1R_1	+	+	0	0	+	0	+	0	+	0	+	0	+	0	+/-
R_2R_2	+	0	+	+	0	0	0	+	+	0	+	0	+	0	3
R_2R_2	+	0	+	+	0	0	+	0	0	+	+	0	0	+	3
r'r	0	+	0	+	+	0	+	0	+	+	+	0	0	+	+/-
r"r	0	0	+	+	+	0	+	0	+	0	0	+	+	+	2
rr	0	0	0	+	+	+	0	+	0	+	+	+	0	+	0
rr	0	0	0	+	+	0	+	+	0	+	0	+	+	+	0
rr	0	0	0	+	+	0	+	0	+	0	0	+	0	+	0
rr	0	0	0	+	+	0	0	+	0	+	+	0	+	+	0

Case Study

- Allo-adsorption showed an allo Anti-E
  - Also suggestive of an auto Anti-C
    - This may be the reason why the last unit transfused (R_1r) gave stronger reactions than the auto control
- A rr, CMV-, irradiated and phenotype matched unit was IAT crossmatched
- The transfusion was tolerated well
  - No evidence of reaction
- Discharged
  - Steroid therapy to continue

Genotyping Results

- Beadchip predicated phenotype
  - c+C+e+, K-k+ Fy(a+b+) Jk(b+) M+N-S+s-
- Serology phenotype
  - RhE-, Jk(a-)
- Comments
  - As a recipient of a marrow transplant the genotype for this latest sample is showing a mixed chimerism leading to allelic imbalance, for the RHE and JKA

Questions

- The introduction of molecular testing often provides valuable information when dealing with patients with complex transfusion requirements
  - But can also give rise to many questions…
    - Is the detected chimerism an early sign of BMT rejection or did X just not fully engraft?
    - Does chimerism / incomplete engraftment pre-dispose recipients to post BMT AIHA?

Song *et al*. "Chronic granulomatous disease: a review of the infection and inflammatory complications" Clinical and Molecular Allergy 2011, 9:10

Ahmed *et al*. "The incidence of autoimmune haemolytic anaemia in paediatric haematopoietic stem cell recipients post first and second haematopoietic stem cell transplants" Pediatr Transplant 2015, 19(4): 391-398