

Haemolytic transfusion reactions with no cause?

Keep calm and carry on

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Haemolytic transfusion reactions

- Haemolytic transfusion reactions are either acute or delayed
 - Acute reactions
 - intravascular – involve complement binding antibodies
 - occur within 24 hrs of transfusion
 - dyspnoea, chest pain, fever, chills, ↓BP
 - Delayed reactions
 - extravascular
 - occur over 24hrs after transfusion
 - unexplained fall in Hb, dark urine



Haemolytic transfusion reactions

- Confirmed by:
 - fall in Hb or failure of increment
 - rise in bilirubin
 - haemoglobinuria
 - positive direct antiglobulin test (DAT)
 - positive crossmatch which was not detected pre-transfusion
 - spherocytes on blood film



Case 1

- 36 year old Indian lady
- 2 weeks post miscarriage (3rd in 2 yrs)
- 2 units of blood were given at time of miscarriage
- Admitted to A&E with Hb 7.8 complaining of severe headaches and high temperature
- Infection?
- Hb continued to fall to 6.8 with no apparent bleeding
- 2 units of blood requested
- G&S – O Positive, NAD
- 2 units O Pos, K neg issued

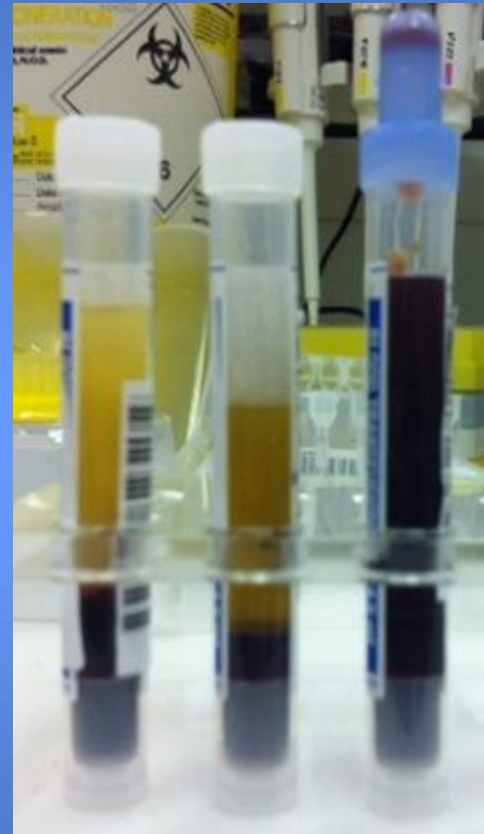


The reaction

- First unit given uneventfully
- 2nd unit - stopped after 1hr
 - Pyrexia
 - temperature had risen to 38.1°C (from 36.6°C)
 - Hypotensive
 - BP fell to 120/65 (from 120/90)
 - Tachycardic
 - Vomiting
 - Went on to develop acute kidney injury and was hospitalised for 12 days



The investigation



Innovation and excellence in health and care



The investigation

- Post transfusion results:
- Septic screen was negative
- Group: O Positive
- DAT: 1+ IgG & C3d positive (not MF)
- Screen: negative
- IAT & enzyme IAT panel, LISS-tube panel: NAD
- Eluate: NAD
- Sample sent to RCI, Colindale



RCI investigation

- No atypical antibodies were detected by:
 - IAT (Diamed & Biovue)
 - LISS-tube IAT
 - Papain IAT
 - Manual polybrene
 - 2 stage LISS-IAT
- Returned units did not grow any microorganisms
- Sample was sent to H&I, Colindale & IBGRL



H&I investigation

- HLA antibodies were detected:
 - HLA-B44, B45, B57 & B58
 - No evidence that these HLA specific antibodies contribute to HTR
- HLA-A2 antibodies were also detected
 - Tentative link between HLA (Bg) antibodies and shortened red cell survival in some patients
 - Takeuchi, C. *et al*, 2005. Delayed and acute hemolytic transfusion reactions resulting from red cell antibodies and red cell-reactive HLA antibodies. *Transfusion*, 45(12):1925-9



HLA/Bg antigens

- Expressed on immature red cells but most disappear as red cells mature
- Some HLA antigens persist and are known as Bg antigens
- HLA-A28 corresponds to Bg^c antigen
- HLA-A28 cross-reacts with HLA-A2
- 49% of the population are HLA-A2 antigen positive
- Generally antibodies to these antigens do not cause HTRs
 - Exception to every rule!



Hyperhemolysis syndrome

- Well described in sickle cell disease sometimes without development of red cell antibodies
- Rarely reported in non-SCD patients (often those with other haemoglobinopathies)

	Normal range	Pre-tx (18.04.12)	Pre-tx (28.04.12)	Post-tx (30.04.12)
Hb	11.5-16g/dl	8.2	6.8	5.9
Bilirubin	0-17umol/l	7	11	252
LDH	81-224U/L	-	184	2248
Retics	20-120x10 ⁹ /l	-	98	35

- Fever, pain, and hemoglobinuria within 10 days of a previous transfusion



Future transfusions

- Transfusion should be/have been avoided
- If transfusions are required, use of IVIg and steroids should be considered as cover
 - IVIg has been associated with renal toxicity, thrombosis and stroke



Case 2

- 45 year old Caucasian male
- 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:

Red cell reactions with:				Plasma reactions with:	
Anti-A	Anti-B	Anti-D	Control	A ₁ cells	B cells
MF	0	4+	0	0	0.5+

- Pre-transfusion results the same



Investigation

- Antibody screen – pre = negative, post = weakly positive
- DAT: 2+ C3d positive (1+ pre-transfusion)
- IAT, Enzyme IAT and Eluate:

Instructions for use can be found at http://www.blood.co.uk/hospitals/diagnostic_services/reagents/index.asp#Pro

	Rh	C	D	E	c	e	C ^w	M	N	S	s	P1	Lu ^a	K	k	Kp ^a	Le ^a	Le ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	Other	IAT	Enzyme IAT	Eluate
1	R ₁ ^w R ₁	+	+	0	0	+	+	0	+	0	+	0	0	0	+	0	0	+	0	+	0	+		0	0	0
2	R ₁ R ₁	+	+	0	0	+	0	+	+	+	0	2	0	+	+	0	+	0	+	0	+	0		0	0	0
3	R ₂ R ₂	0	+	+	+	0	0	0	+	0	+	0	0	0	+	0	+	0	+	0	0	+		0	0	0
4	r'r	+	0	0	+	+	0	+	0	+	0	3	0	0	+	0	+	0	+	0	+	0		0	0	0
5	r''r	0	0	+	+	+	0	+	0	+	0	2	0	0	+	0	0	+	0	+	+	0		0	0	0
6	rr	0	0	0	+	+	0	+	0	0	+	2	0	+	0	0	0	+	0	+	0	+		0	0	0
7	rr	0	0	0	+	+	0	0	+	0	+	0	+	+	+	0	+	0	0	+	0	+		0	0	0
8	rr	0	0	0	+	+	0	0	+	0	+	0	0	0	+	+	0	+	+	0	+	0		0	0	0
9	rr	0	0	0	+	+	0	0	+	+	0	3	0	0	+	0	+	0	+	0	0	+	Cob+	0	0	0
10	rr	0	0	0	+	+	0	+	0	+	0	0	0	0	+	0	0	0	0	+	+	0		0	0	0



2nd reaction

- 10 days later
- 3 units ordered
- Severe reaction at end of 1st unit
 - Temperature rose to 38°C (from 36.6°C)
 - Respiratory rate rose to 20 breaths per min (from 14)
 - Feverish, rigors and chest pain
 - Haemoglobinuria



Investigation

- Anti-E only found by IAT
- Eluate negative
- DAT = C3d 3+ positive
- Another case of hyperhemolysis syndrome?
- Samples sent to RCI, Colindale & IBGRL
- RCI reported additional cold antibody with undetermined specificity detected by polybrene technique
- ? high thermal range
- Recommended that future transfusions should be genotype compatible and given through a blood warmer

