

SHOT

Haemolytic Transfusion Reactions

Interactive Cases Including Clinical Outcomes

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Starter for 10....

Q: How confident are you in getting all of these questions correct?

A:

1. No hope at all
2. It could go either way
3. Fairly
4. Confidence is my middle name
5. I'm willing to bet my Christmas bonus on it!

Case 1: Patient History & Clinical Presentation

- Male, 56 years old
- Admitted to A&E 25/04/18: Epistaxis & “feeling unwell”
- Patient is relapsed and refractory NHL
- Post allogeneic stem cell transplant in 2017
- Admission Hb=70 g/L

Case 1: Laboratory Findings

- Previously known antibodies:
 - Allo Anti-E
 - Auto Anti-D
 - IAT reactive autoantibody (pan-reactive)
- 25/04/18: 2 units RBC requested, XM and transfused
- 26/04/18: 2 further units RBC requested, XM and transfused
- No increment in patient's Hb

Case 1: Question 1

Q: What should be considered next?

A:

1. XM and transfuse a further 2 RBC units
2. XM and transfuse just one RBC unit
3. Give immunoglobulins and steroids
4. Reassess Hb and bilirubin; do not transfuse further red cells
5. Something else

Case 1: Further Clinical Information

30/04/18: Medical staff reported patient becoming jaundiced and noted falling Hb

01/05/18: 2 units RBC requested, XM and transfused

03-08/05/18: 3 further units RBC requested, XM and transfused
Bilirubin continued to rise, Hb continued to fall
(Reticulocyte count also low)

Case 1: Question 2

Q: What possible diagnosis should be considered in light of this information?

A:

1. TACO
2. Delayed haemolytic transfusion reaction
3. Hyperhaemolysis
4. Bacterial infection
5. TRALI

Case 1: Question 3

Q: What is the likely mechanism of hyperhaemolysis?

A:

1. Activation of the coagulation cascade
2. Activated macrophages leading to destruction of both patient & donor red cells
3. I have no idea
4. Activation of the complement cascade
5. Antibodies causing intravascular haemolysis

Case 1: Question 4

Q: What is the most effective treatment for hyperhaemolysis?

A:

1. Transfusion of additional RBC units
2. Avoidance of further transfusion but supportive immunoglobulins and steroids
3. I have no idea
4. Transfusion of additional RBC units with immunoglobulins and steroids
5. Administration of colloids instead

Case 1: Patient Outcome

- Patient developed impaired renal function
- Confirmed diagnosis of hyperhaemolysis
- Patient died 3 days later with Hb of 36g/L

NB: The Patient's final Hb was significant lower than initial Hb despite being transfused 9 RBC units over 13 days



Case 1: Learning Points

Hyperhaemolysis remains a cause of transfusion-related mortality and major morbidity

Hyperhaemolysis is NOT only associated with Sickle Cell Disease patients

Key message from SHOT report: Important that ALL clinicians involved in the transfusion process have an awareness of the SIGNS and SYMPTOMS of HYPERHAEMOLYSIS so that ANY suspected cases are investigated thoroughly.

Case 2: Patient History & Clinical Presentation

- Female, 19 years old
- Admitted with Ulcerative colitis
- Transfused one unit RBC on 15/09/18
- No previous transfusions

Case 2: Laboratory Findings

- 18/09/18: Initial investigation = negative Ab screen
- Eligible for Electronic Issue crossmatch (EI XM)
- Patient reviewed by Haem. Reg, Consultant and Transfusion Practitioner
- Increased temperature $>2^{\circ}\text{C}$, 24 hrs post transfusion

Case 2: Question 1

Q: What is a likely cause of fever following a transfusion?

A:

1. Febrile non-haemolytic transfusion reaction
2. Acute/delayed haemolytic reaction
3. Bacterial contamination
4. Underlying condition
5. Any of the above

Case 2: Laboratory Findings

- Investigated for HTR = All negative serology (DAT+)
- Repeat investigation (4 days later) = Possible anti-Jk^a
- Confirmed by NHSBT

	Rh	M	N	S	s	P1	Lu ^a	K	k	Kp ^a	Le ^a	Le ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	Other	Cell
1	R ₁ *R ₁	0	+	0	+	4	+	0	+	0	0	+	+	0	0	+		3
2	R ₁ R ₁	+	0	+	0	1	0	+	+	0	0	+	0	+	+	0		3
3	R ₂ R ₂	+	0	0	+	3	0	0	+	0	0	0	0	+	+	0		3
4	r'r	+	0	0	+	0	0	0	+	0	0	+	0	+	+	0		3
5	r''r	0	+	+	0	0	0	0	+	0	0	+	0	+	+	0		3
6	rr	+	+	0	+	2	0	+	0	0	0	0	+	0	0	+		3
7	rr	0	+	0	+	0	0	+	+	0	0	+	0	+	0	+		3
8	rr	0	+	0	+	2	0	0	+	+	0	0	+	+	+	0		3
9	rr	+	0	+	0	1	0	0	+	0	0	0	+	0	+	0		3
10	rr	+	0	+	0	1	+	0	+	0	+	0	+	0	+	0		3
Auto																		3
																	Cell 2 LI (OK) K	3
Antibody Titre																	Group	Pheno
Dilution																	Cell Id	
Anti-																	Conclusion	
Archive																	Anti-Jk ^a	
Anti																		
Archive																		
DAT Batch No																	Self from 1508	
PS																	4	
IgG																	0	
IgA																	0	
IgM																	0	
C3c																	0	
C3d																	2	
Ctl																	0	
Reagent																	Reporting BMS:..... Check	
Batch No's																		
Pipette batch No's																	11/20260	

- Unknown if the patient had been transfused elsewhere-Patient was from Australia-Limited historical information

Case 2: Question 2

Q: What additional test could you perform on the patient's red cells?

A:

1. Antigen typing
2. Neutralisation
3. Elution
4. Titration
5. I'm not sure

Case 2: Question 3

Q: When does haemolysis occur for a DHTR?

A:

1. <24 hours post transfusion
2. >28 days post transfusion
3. >24 hours <28 days post transfusion
4. >24 hours <7 days post transfusion
5. >14 days post transfusion

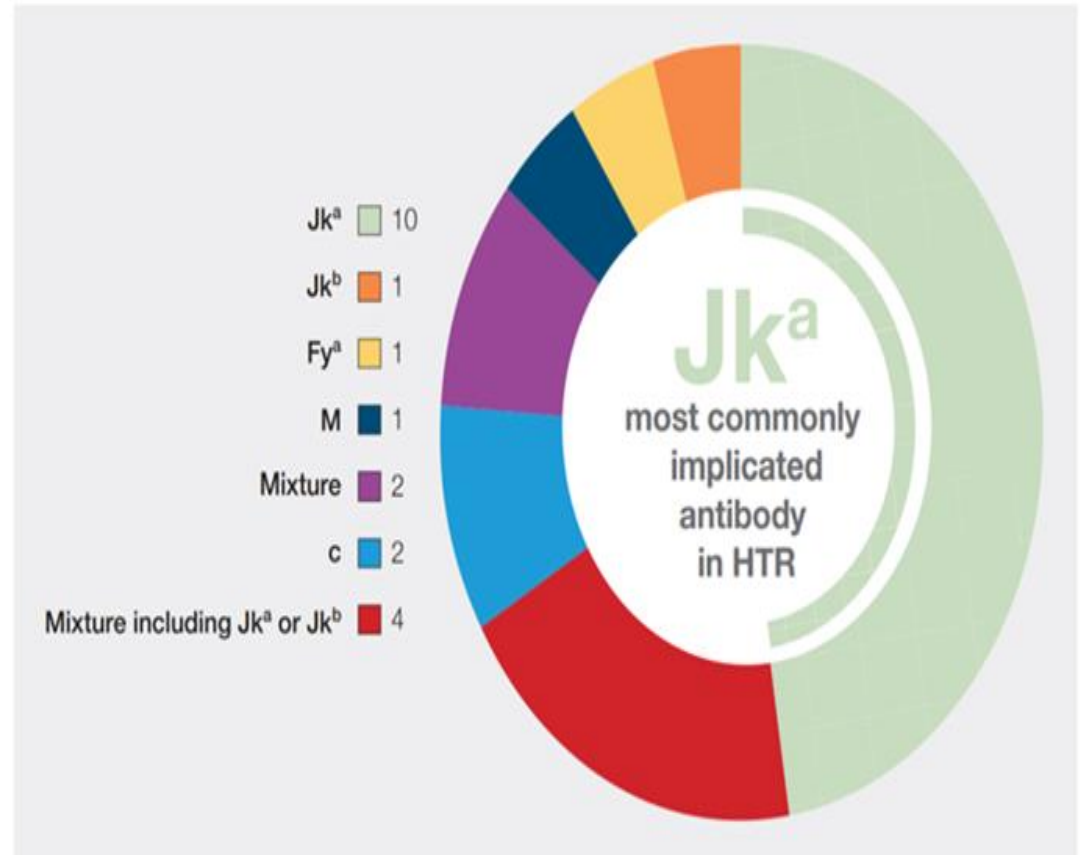
Case 2: Patient Outcome

- Patient recovered and survived
- No treatment was necessary
- Diagnosis was complicated by sepsis

Case 2: Learning Points

Key message:
Sharing information
benefits patient care
(SpICE)

**Key message: Be
wary of anti-Jka:
Most commonly
encountered
antibody in DHTR**



Case 3: Patient History and Clinical Presentation

- Female, 25 years old
- Known Sickle Cell Disease (SCD) patient with multiple historical alloantibodies:

Anti-A1, Anti-S, Anti-M, Anti-Jk^a, Anti-Le^a, Anti-Le^b

- Admitted with sickle cell crisis during pregnancy (1st pregnancy)
- Multi-transfused due to SCD

Case 3: Laboratory Findings

- At time of transfusion serology only Anti-Le^a, Anti-Le^b and Anti-A1 were identified
- Historical Anti-S, Anti-M, Anti-Jk^a were currently not detected by IAT

Case 3: Question 1

Q: Should we worry about clinically insignificant antibodies?

A:

1. No, they are clinically insignificant
2. Yes, all antibodies have a potential to cause harm
3. Unsure
4. Maybe
5. BSH Guidelines state which antibodies are clinically significant

Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories*

British Committee for Standards in Haematology

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Table A3. Likely clinical significance of red cell alloantibodies, and recommendations for the selection of blood for patients with their presence

System	Specificity	Likely clinical significance in transfusion	Recommendation for selection of red cells for transfusion ¹
ABO	Anti-A ₁	No	IAT crossmatch compatible at 37 °C
Rh	Anti-D, -C, -c, -E, -e	Yes	Antigen negative
Rh	Anti-C ^w	No	IAT crossmatch compatible ²
Kell	Anti-K, -k	Yes	Antigen negative
Kell	Anti-Kp ^a	No	IAT crossmatch compatible ²
Kidd	Anti-Jk ^a , -Jk ^b	Yes	Antigen negative
MNS	Anti-M (active 37 °C)	Yes	Antigen negative
MNS	Anti-M (not active 37 °C)	No	IAT crossmatch compatible at 37 °C
MNS	Anti-N	No	IAT crossmatch compatible at 37 °C
MNS	Anti-S, -s, -U	Yes	Antigen negative
Duffy	Anti-Fy ^a , -Fy ^b	Yes	Antigen negative
P	Anti-P ₁	No	IAT crossmatch compatible at 37 °C
Lewis	Anti-Le ^a , -Le ^b , -Le ^{a+b}	No	IAT crossmatch compatible at 37 °C
Lu	Anti-Lu ^a	No	IAT crossmatch compatible at 37 °C
Diego	Anti-Wr ^a (anti-Di3)	Yes	IAT crossmatch compatible ²
H	Anti-HI (in A ₁ and A ₁ B patients)	No	IAT crossmatch compatible at 37 °C
All	Others active by IAT at 37 °C	Yes	Seek advice from Blood Centre

¹Where antigen negative red cells are recommended these should also be compatible in an IAT crossmatch.

²These recommendations apply when the antibody is present as a sole specificity. If present in combination, antigen negative blood may be provided by the blood centre, to prevent wastage of phenotyped units. This guidance is also suitable for patients undergoing hypothermia during surgery (Klein and Anstee, 2005b).

Case 3: Laboratory Findings & Clinical Information

- Anti-Le^a and Anti-Le^b were classed by RCI as “not clinically significant” in accordance with BSH Guidelines
- 2 RBC units were transfused over a two day period:
Group O rr, S-, M-, Jka-, Fya-, K-, HbS-
- Units transfused: 1 unit Le(a-b+) and 1 unit Le(a+b-)
- Intravascular haemolysis noted with both units
- Transfusion stopped:
 - Raised bilirubin
 - Falling Hb
 - Haemoglobinuria
 - Positive DAT

Case 3: Question 2

Q: What is the most likely type of transfusion reaction?

A:

1. TACO
2. TRALI
3. Bacterial infection
4. Hyperhaemolysis
5. Delayed haemolytic transfusion reaction

Case 3: Question 3

Q: What additional tests are useful when delayed HTR is suspected?

A:

1. Hgb/HCT
2. LDH
3. Bilirubin
4. Serum haptoglobins
5. All of the above

Case 3: Patient Outcome

- Outcome: Patient survived and recovered
- Successful pregnancy
- Subsequent Le(a-b-) units have been transfused during further sickle crisis

Case 3: Learning Points

- Multi transfused patients carry additional risk of immunisation & extra risk of HTR
- Intravascular haemolysis of transfused cells due to Anti-Le^a and Anti-Le^b is **very rare**
- A reaction reported due to Lewis antibodies which according to the text books “don’t cause reactions”
- **Key message: Occasionally “clinically INSIGNIFICANT” antibodies cause haemolytic transfusion reactions too**

Case 4: Patient History & Clinical Presentation

- Male, 51 years old
- Routine surgical case (day surgery)
- Proximal Left Anterior Descending (LAD) Coronary Artery Occlusion (high mortality risk)
- Patient had no apparent prior transfusion history
- Negative antibody screen (Pre-op)

- 16/03/18: XM and transfused 3 units ABO & RhD matched RBC during surgery

Case 4: Laboratory Findings

- 23/03/18: Anti-Fy^a, Anti-E and Anti-c were identified in antibody identification panel with +DAT
- 26/03/18: Patient had raised bilirubin level (suspecting haemolytic transfusion reaction)
Full investigation & blood films requested
- 28/03/18: Sample referred to NHSBT who confirmed Anti-Fy^a, Anti-E and Anti-c + additional Anti-K in patient plasma and Anti-Fy^a in patient eluate

Case 4: Question 1

Q: What was observed on the patient's blood film?

A:

1. Elliptocytes
2. Normocytic RBC
3. Spherocytes
4. Fragments
5. Spherocytes, reticulocytes and fragments

Case 4: Question 2

Q: What are the most commonly responsible antibodies in DHTRs?

A:

1. Anti-Ch1
2. Anti-A1
3. Anti-K, Anti-Fy^a and Anti-Jk^a
4. Anti-S, Anti-M and Anti-s
5. I don't know

Case 4: Question 3

Q: What is the frequency of a DHTR?

A:

1. 1:500 – 1:1,000 transfusions
2. 1:2,500- 1:11,000 transfusions
3. 1:50,000 – 1:100,000 transfusions
4. 1:5,000,000 – 1:10,000,000 transfusions
5. I wouldn't like to hazard a guess

Case 4: Patient Outcome

- Patient transferred to ICU
- Treatment involved steroids and immunoglobulins
- Survived and recovered fully
- Was discharged 8 days later

Case 4: Learning Points

- **Key message: Not all DHTRs are due to pre-formed antibodies**
- Need for vigilance even in presence of negative antibody screen
- This case was initial antibody screen negative BUT had multiple antibodies in the post transfusion samples
- **Key message: COMMUNICATION is essential**
- Use of electronic data sharing (SpICE) improves patient outcomes

Case 5: Patient History & Clinical Presentation

- Female, 33 years old
- Admitted 05/09/18 with PPH (Post Partum Haemorrhage)
- Actively bleeding
- Patient received two units of Emergency O- RBC on 05/09/18 at 02:20hrs
- The patient had a known (allo) Anti-Jk^a

Case 5: Laboratory Findings

- The patient had an acute transfusion reaction to these units
- The patient required ventilation and admission onto ICU due to renal impairment
- NHSBT was contacted to determine the Jka status of these units: confirmed verbally that both emergency O RhD- units were Jka +

Donation Serology

Data retrieved using multiple donation numbers

Page 1 of 1

Donation No	ABO/Rh/Fct	D	C	E	c	e	Cw	M	N	S	s	P1	Lua	Lub	K	k	Kpa	Kpb	Lea	Leb	Fya	Fyb	Jka	Jkb	A1	Sickle	Proc.	Ethnicity
[REDACTED]	O- rr	-	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	N	-	[REDACTED]	[REDACTED]
[REDACTED]	O- rr	-	N	N	P	P	-	+	-	+	-	-	-	-	N	-	-	-	-	-	P	-	+	+	-	-	[REDACTED]	[REDACTED]

End of Report

Case 5: Question 1

Q: How many cases within the latest SHOT report were due to the use of emergency O- blood?

A:

1. 10
2. 2
3. 4
4. 6
5. 1

Case 5: Question 2

Q: When is the most severe reaction likely?

A:

1. 15 mins
2. 30 mins
3. 60 mins
4. 90 mins
5. 120 mins

Case 5: Question 3

Q: Will the DAT always be positive?

A:

1. Yes
2. Yes, unless all of the donor cells have been destroyed
3. No
4. I'm not sure
5. Sometimes

Case 5: Clinical Outcome

- Patient was transferred to ICU where vital parameters (blood pressure, heart rate, respiration) and urine production were be monitored continuously
- Patient survived and recovered
- Major morbidity associated with this case

Case 5: Learning Points

Key message: Emergency units save lives

- No patient should die from lack of blood
- There is a balance between not withholding transfusion when clinically urgent and waiting to provide compatible units

Key message: Close monitoring of the patient is essential

- Reaction in a patient given antigen + blood due to clinical urgency

Thank you for listening

Dr Shruthi Narayan & Nicci Wilkes

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