

Intravascular haemolytic transfusion reaction without detectable antibody: Use of extended phenotyping and red cell survival studies

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Clinical case

64 year old lady

No previous transfusions

Two previous successful pregnancies

- No neonatal jaundice or transfusion

Lymphoplasmacytic lymphoma

- 'Watch and wait'

Newly diagnosed ovarian clear-cell cancer

- Surgery
- Adjuvant chemotherapy (carboplatin and paclitaxel)

Transfusion reaction

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 - Bilirubin 40umol/l
 - Creatinine 77umol/l

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 - Hb 77g/l
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 - Creatinine 77umol/l
- 17/4/17 – Transfused 2 units red cells
 - Felt unwell following 2nd unit blood
 - Rigor
 - Developed ‘red urine’ lasting 2 days
 - Sample sent for ‘transfusion reaction testing’
 - Antibody screen and eluate negative, DAT negative
 - Following day creatinine 288umol/L, Hb 67g/L, bilirubin 106umol/L

Transfusion reaction

Transfusion reaction

- 19/4/17 – 2 units red cells transfused
 - Felt generally unwell following 2nd unit
 - No rigors
 - Haemodynamically stable
 - 'Red urine'
 - Creatinine 411umol/L post transfusion, Hb 83g/L, bilirubin 60 umol/L
 - 'Transfusion reaction' bloods sent

Urine sample



FBC sample - centrifuged



Investigations

Haptoglobins undetectable

Haemoglobinuria confirmed in laboratory

Urine positive for haemosiderin

Blood film showed occasional spherocytes only

Donath-Lansteiner test negative

Serological investigations

On pre and post transfusion samples

- DAT (IgG, IgM, C3d, C3c, IgA) negative
- Eluate negative against panel

- Serum and plasma antibody panels
 - IAT Negative
 - Enzyme IAT Negative
 - IAT –NHSBT Negative
 - IAT anti IgA Negative
 - LISS tube Negative
 - Polyethylene glycol Negative

Red cell phenotype

Red cell phenotype

Pt/Donations	D	C	E	c	e	f	Cw	K	k	Kpa	Kpb	Jsa	Jsb	Fya	Fyb	Jka	Jkb	Lea	Leb	S	s	M	N	P1	Lua	Lub	Wra
Patient	4	0	4	4	4			0						0	3	4	0	0	1	3	3	4	0	4			0
10/04/17																											
Unit 1	4	4	4	4	4			0																			
Unit 2	4	4	0	4	4			0																			
17/04/17																											
Unit 3	4	4	0	0	4			0																			
Unit 4	4	4	0	4	4		0	0						3	0	3	0	0	3	3	0	3	3	4			
19/04/17																											
Unit 5	4	0	4	4	4		0	0								0	4										
Unit 6	4	4	0	0	4			0						3	0	3	0	4	0	0	3	2	4	4			0

Nuclear medicine investigations

Nuclear medicine investigations

Red cell survival scan was performed using Tc99m labelled C negative and C positive donor red cells

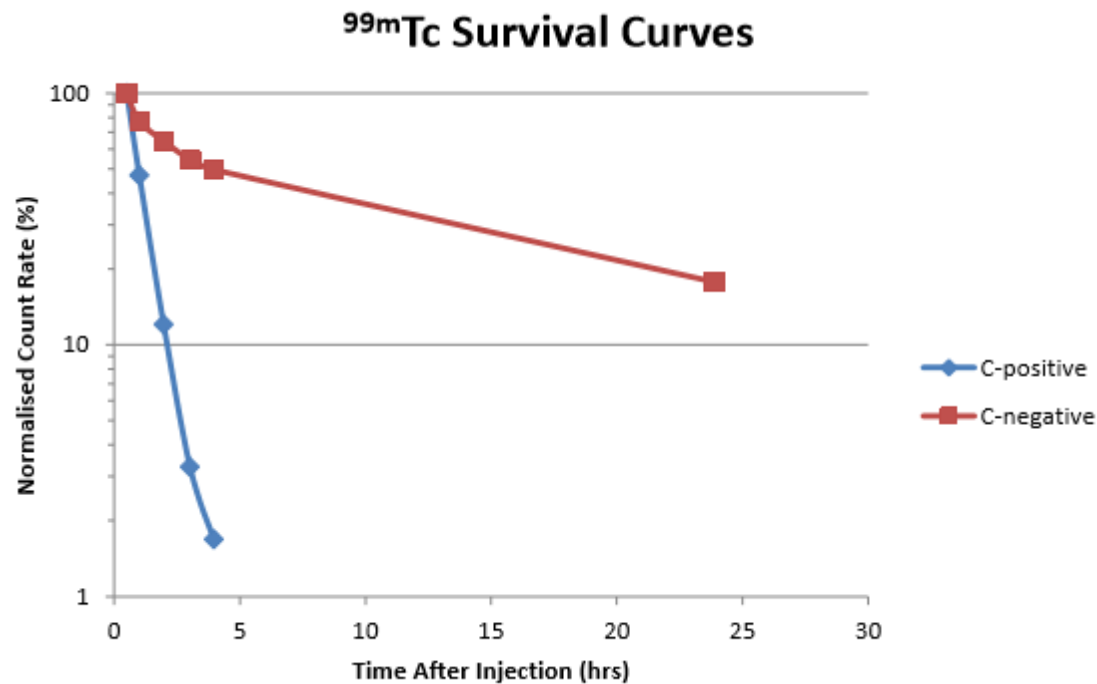
6mls of red cells were administered for each test

Levels taken at 1,2,3,4 and 24 hours

Gamma camera images taken at 1,2 and 4 hours

Units used in red cell survival study:																											
	D	C	E	c	e	f	<u>Cw</u>	K	k	<u>Kpa</u>	<u>Kpb</u>	<u>Jsa</u>	<u>Jsb</u>	<u>Fya</u>	<u>Fyb</u>	<u>Jka</u>	<u>Jkb</u>	Lea	<u>Leb</u>	S	s	M	N	P1	<u>Lua</u>	<u>Lub</u>	<u>Wra</u>
Patient	4	0	4	4	4			0						0	3	4	0	0	1	3	3	4	0	4			0
cells 1	4	0	4	4	4			0						0	0	3	0	0	0	4	0	4	4				
cells 2	4	4	0	4	4		0	0						0	3	3	0	0	3	3	3	3	4				

Red Cell Survival Studies



Red Cell Survival Studies

1 Hour

2 Hours

4 Hours

C negative red cells

C positive red cells

Clinical course

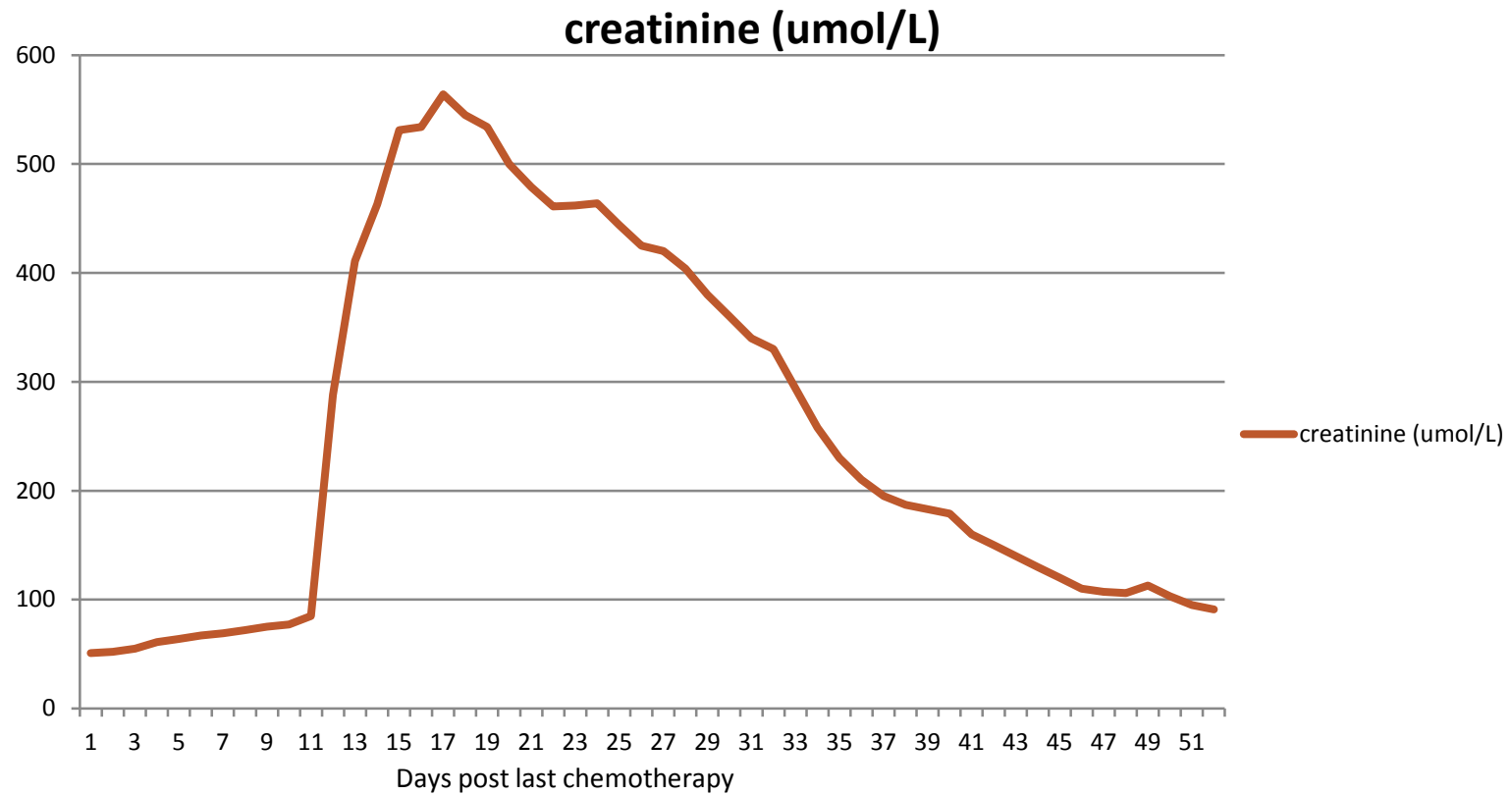
Transfused further unit C negative red cells

- No clinical sequelae

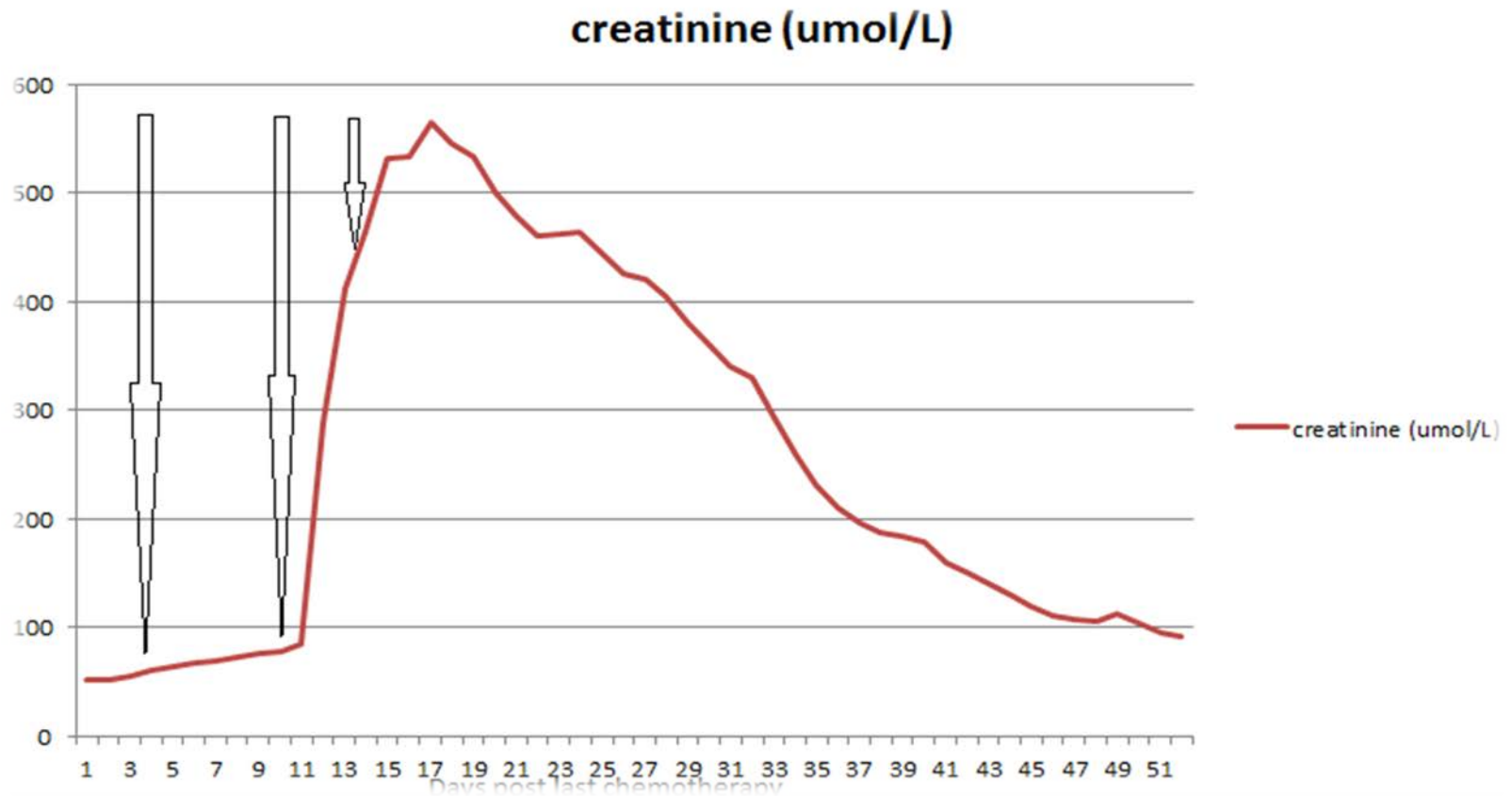
05/05/17																											
	D	C	E	c	e	f	<u>Cw</u>	K	k	<u>Kpa</u>	<u>Kpb</u>	<u>Jsa</u>	<u>Jsb</u>	<u>Fya</u>	<u>Fyb</u>	<u>Jka</u>	<u>Jkb</u>	Lea	<u>Leb</u>	S	s	M	N	P1	<u>Lua</u>	<u>Lub</u>	<u>Wra</u>
Patient	4	0	4	4	4			0						0	3	4	0	0	1	3	3	4	0	4			0
Unit 7	p	0	0	4	4		0	0						0	3	3	0	4	0	0	3	3	0				

- Further phenotypically matched red cells transfused over subsequent days
- Creatinine improved nearly to baseline
- Patient discharged

Creatinine Trend



Creatinine Trend



Discussion and literature review

Intravascular haemolytic transfusion reaction with undetectable antibodies likely due to anti-C

Intravascular haemolytic transfusion reactions rarely reported with undetectable antibodies. ^{1,2}

Cause:

? Potent antibodies at too low a level for in-vitro detection

? Antibody mediated lymphocytotoxic activity

1. Intravascular haemolytic transfusion reaction without detectable antibodies: a case report and literature review. C.R. Harrison et al 1986 Vox Sang. 51:96-101
2. Haemolytic transfusion reaction due to Rh antibodies detectable only by manual polybrene and polyethylene glycol technique. Lin CK et al Am J Clin Pathol 1995; 104:660-662

Conclusion

This case highlights the need for further investigation if initial investigations appear negative, but clinical suspicion of a transfusion reaction remains high

Demonstrates the value to extended red cell phenotyping of patient and donor cells

Red cell survival studies can offer reassurance in this setting, especially if further transfusions required

Thank you

Any questions?