A clinical and transfusion conundrum

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Background

- 25 year old, severe sickle cell disease
- Started hydroxycarbamide 2016, considerable improvement including increased weight (previous BMI 16.5)
- Presented 09/08/2017 at 5 weeks pregnant
- Multiple red cell antibodies from previous transfusions, none clinically significant at time of presentation with pregnancy

Background

- Hydroxycarbamide (and iron chelation) stopped
- Counselled and wanted to continue with pregnancy
- Painful crisis 3 weeks after stopping hydroxycarbamide (8/40)
- Further painful crisis treated on delivery suite at 21+4/40, treated with analgesia and fluids

Background

- Readmitted at 22+6/40
- Pain; blurred vision; Hb52
- Subsequently found to have pyelonephritis
- Transferred to ITU for exchange transfusion
- Hb rose appropriately but by D5 of ITU admission had drifted back to baseline.

Differential diagnosis

- Sickle cell crisis causing haemolysis
- Bleeding in a pregnant patient
- Hyperhaemolysis
- Haemolytic transfusion reaction

Treatment

- Further transfusion, no Hb increment
- Long clinical discussions – what's going on?

- Given IVIg
- **We asked for help**

Laboratory aspects

- Previous Serology:-
- Well known patient
- Multiple atypical antibodies :-Anti-M, Anti-S, Anti-Jka , Anti-Lea, Anti-Leb and Anti-A1.
- Which ones are not clinically significant in pregnancy?

Laboratory aspects

- 28 weeks bloods Antibody screen was **negative**
- Molecular genotype known.
- Antigen negative blood ordered for crossmatch including Hbs neg, CMV neg blood pre-ordered.
- Normally crossmatch compatible at IAT 37 ^{o}C

Current Serology

- During current crisis
- IAT Antibody Screen Positive, DAT negative, then positive

			Rh-hr								KELL						DUFFY		KIDD			LEWIS		MNS				P			Special AntigenTyping		IAT
Cell #	Rh-hr	Donor Number	D	C	E	c	e	f	C^w	V	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xg^a	Le^a	Le^b	S	s	M	N	P_1	Lu^a	Lu^b		Cell #	
1	R1wR1	320703	+	+	0	0	+	0	+	0	0	+	0	+	/	+	0	+	+	+	0	+	0	+	0	+	+	0	0	+		1	0.5
2	R2R2	309445	+	0	+	+	0	0	0	0	+	+	0	+	0	+	+	0	+	0	0	+	0	0	+	+	+	+	0	+		2	0.5
3	rr	320521	0	0	0	+	+	+	0	0	0	+	+	+	/	+	0	+	0	+	+	0	+	0	+	+	0	+	0	+		3	0

Antibody ID

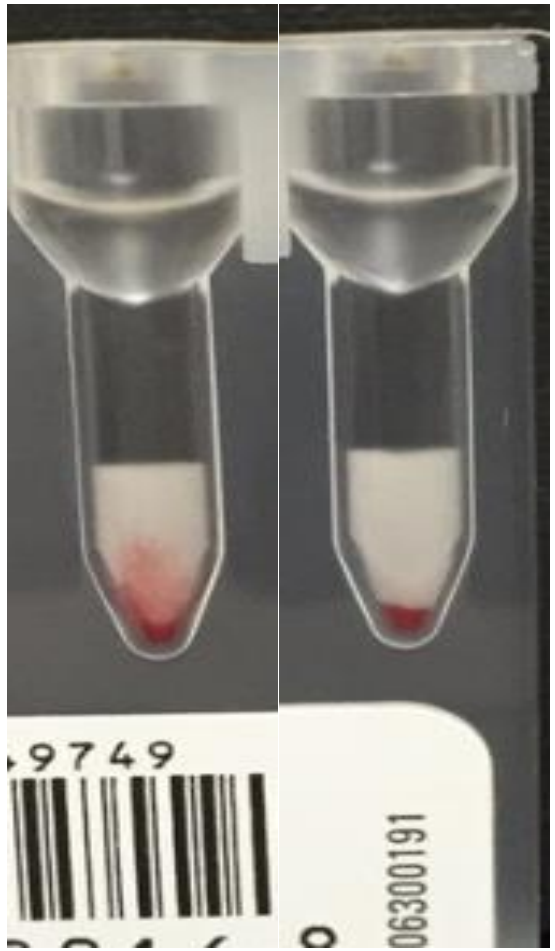
Cell #	Rh-hr	Donor Number	D	C	E	c	e	f	C^w	V	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xg^a	Le^a	Le^b	S	s	M	N	P_1	Lu^a	Lu^b	Special Antigen Typing
1	R1wR1	101267	+	+	0	0	+	0	+	/	0	+	0	+	/	+	+	+	+	0	0	+	0	+	+	+	0	+	0	+	
2	R1R1	101268	+	+	0	0	+	0	0	/	0	+	+	+	/	+	+	+	+	+	+	0	+	+	+	+	0	+	0	+	
3	R2R2	101269	+	0	+	+	0	0	0	/	0	+	0	+	/	+	0	+	+	0	+	0	0	+	+	+	+	+	0	+	
4	Ror	101057	+	0	0	+	+	+	0	/	0	+	0	+	/	+	+	0	0	+	+	0	+	0	+	+	+	0	0	+	
5	r'r	100593	0	+	0	+	+	+	0	/	0	+	0	+	/	+	+	0	0	+	+	0	+	0	+	+	+	0	0	+	@
6	r''r	101271	0	0	+	+	+	+	0	/	0	+	0	+	/	+	0	+	+	0	0	0	+	+	0	+	0	+	0	+	@
7	rr	101272	0	0	0	+	+	+	0	/	+	+	0	+	/	+	+	0	+	0	0	0	+	+	+	+	0	+	+	+	@
8	rr	101030	0	0	0	+	+	+	0	/	0	+	0	+	/	+	+	0	+	+	+	+	0	0	+	0	+	+	0	+	@
9	rr	101273	0	0	0	+	+	+	0	/	0	+	0	+	/	+	+	0	0	+	+	0	0	+	0	+	0	+	0	+	
10	rr	101274	0	0	0	+	+	+	0	/	+	+	0	+	/	+	0	+	+	+	+	0	+	0	+	+	0	0	0	+	
11	R1R1	101275	+	+	0	0	+	0	0	/	+	+	0	+	/	+	0	+	+	+	+	0	+	+	+	0	+	+	0	+	HLA+
	Patient Cells																														

Cell #	Test Results
1	IAT 0.5
2	1
3	0
4	0.5
5	0.5
6	0.5
7	0.5
8	1
9	0
10	0.5
11	0.5
	A O

- Most likely Anti-Lea and Anti-Leb (Lewis System)
- Referred NHSBT to rule out underlying antibodies:- Confirmed Lewis Antibodies , Anti-Lea and Anti-Leb.
- Lewis:-Not clinically significant in Pregnancy and rarely implicated in Haemolytic transfusion reaction (HTR)

Positive IAT Crossmatch!

- 0.5 and 1+ reactions seen in IAT crossmatch.
- NHSBT only detecting anti-Lea at 37^{o}C(by their technique)
- ? sensitive Lab automated method most likely due to Lea or Leb positive antigens on donor units.
- NHSBT crossmatch compatible



Differential diagnosis

- Sickle cell crisis causing haemolysis – would expect HbS to fall relative to HbA
- Bleeding in a pregnant patient – always possible
- Hyperhaemolysis – would expect HbS to fall

- Haemolytic transfusion reaction – but no significant antibodies???

Haematologist : Scientist discussion

- Clinicians not happy with clinical picture……?Haemolysis but why???
- BMS not happy as positive reaction in crossmatch ?but why
- Could Lewis antibodies be reacting *in vivo*?
- Phenotyping of the positive crossmatch units were either Le^a + **or Le^b +** .
- Look at HbS and HbA levels post transfusion of such units

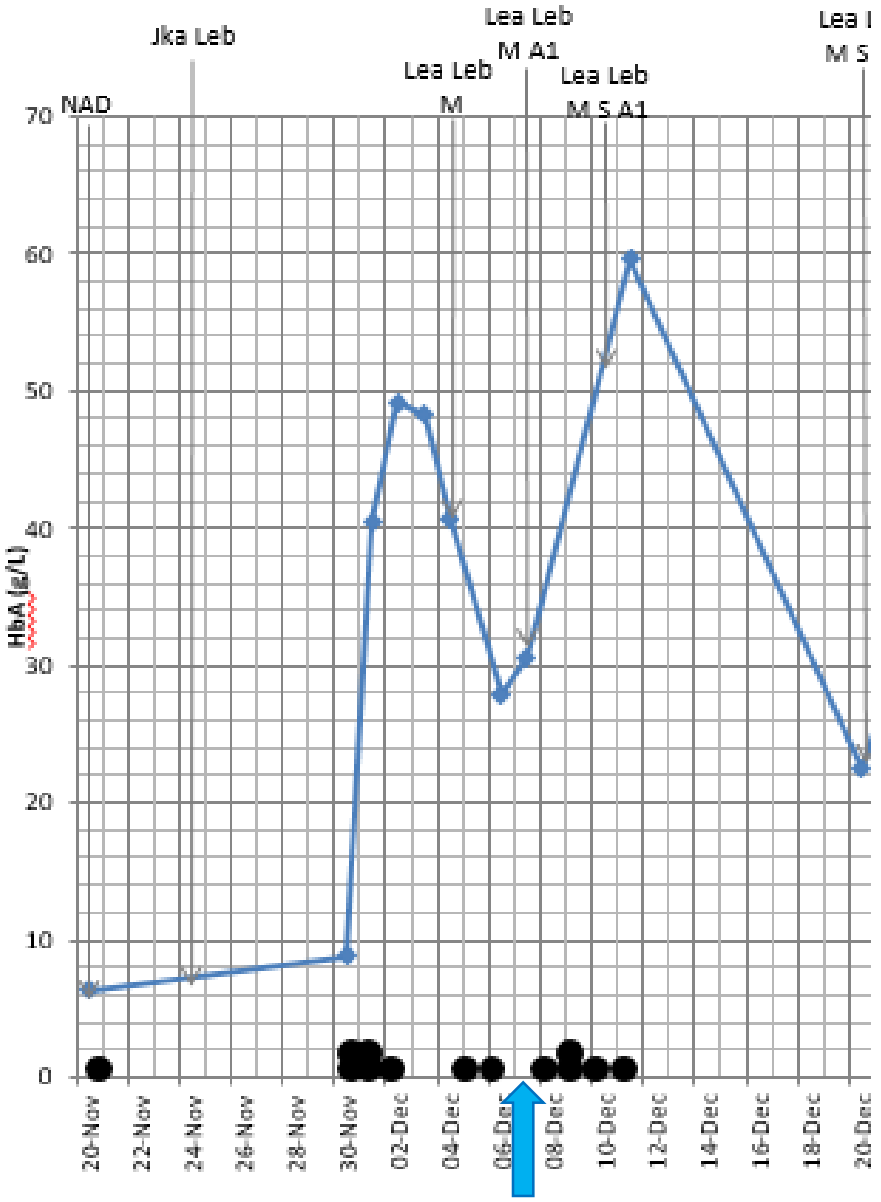


Image Courtesy of Stephanie Teasdale BMS NUTH

Response to Transfusion; Hb and HbS % over time
RBC transfusions and Lewis phenotype if known noted

N.B Haemoglobin shown is post transfusion result

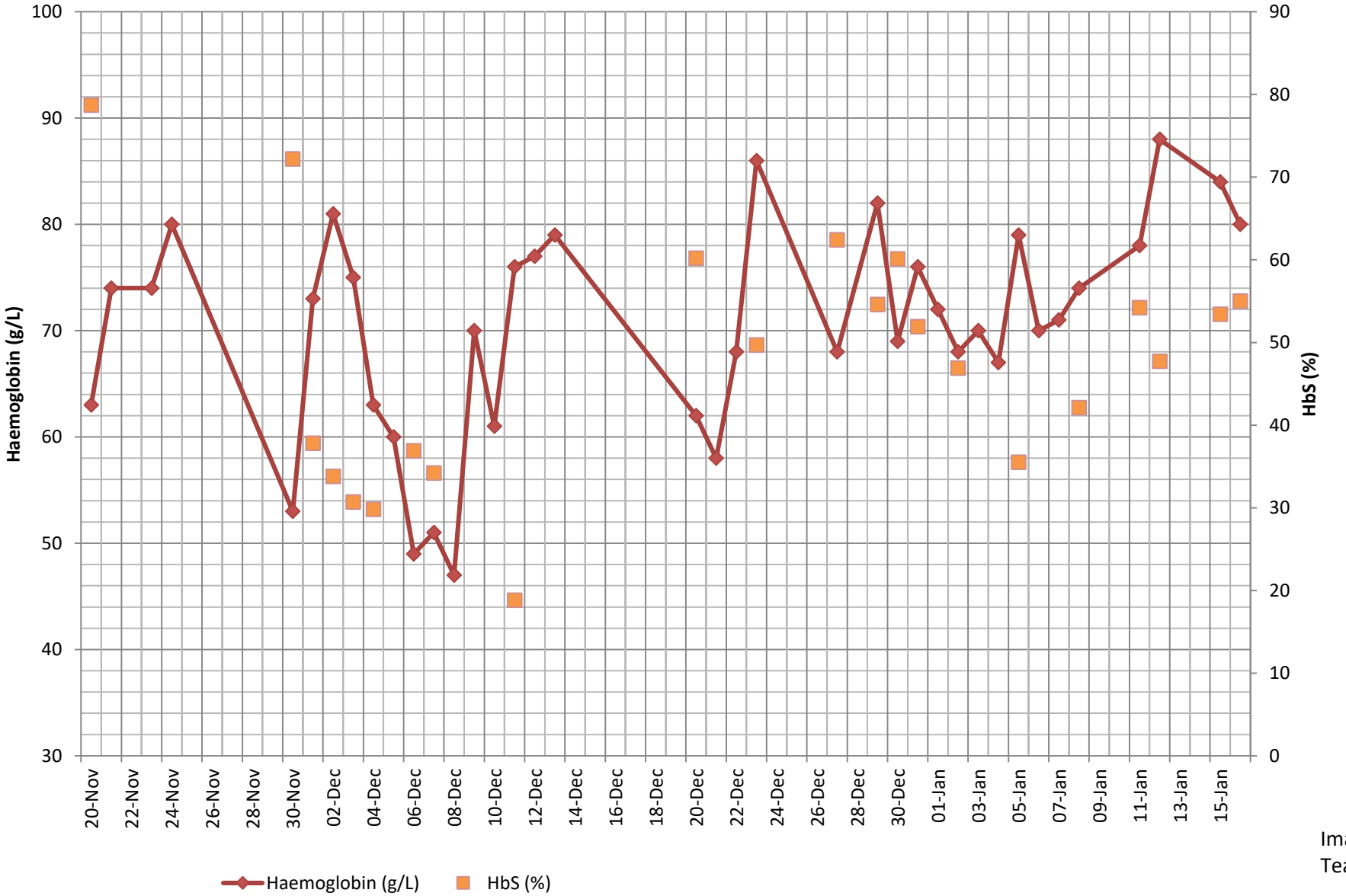


Image Courtesy of Stephanie Teasdale BMS NUTH

Differential diagnosis

- Sickle cell crisis causing haemolysis – would expect HbS to fall relative to HbA – It didn’t
- Bleeding in a pregnant patient – always possible, but no evidence, and HbS should fall in step with HbA – it didn’t
- Hyperhaemolysis – would expect HbS to fall - no

- Haemolytic transfusion reaction – BINGO

Action

- Consultant Haematologist approved switch to group Le(a-b-) donations.
- Negative IAT and Crossmatch compatible
- Rare donor phenotype required to meet all antigen negative requirements.
- Sourcing blood suddenly became extremely difficult
  - Multiple NHSBT centres involvement
  - Delays due to logistics of getting blood
  - Reduced amount available due to scarcity.

Antenatal and Delivery Plan

- Weekly communications
  - NHSBT >Haematologist>clinical team >transfusion manager>TP>laboratory senior> Lab staff
- Sample timings, Blood for top up , blood for cover
- Specific Donors arranged to provide Le (a-b-) units consistently
- Negate Leb- Fya –,M -, CMV neg requirements if emergency.
- 4 units on standby at all times for remainder of pregnancy and up to 8 held at NHSBT for expected delivery induction.

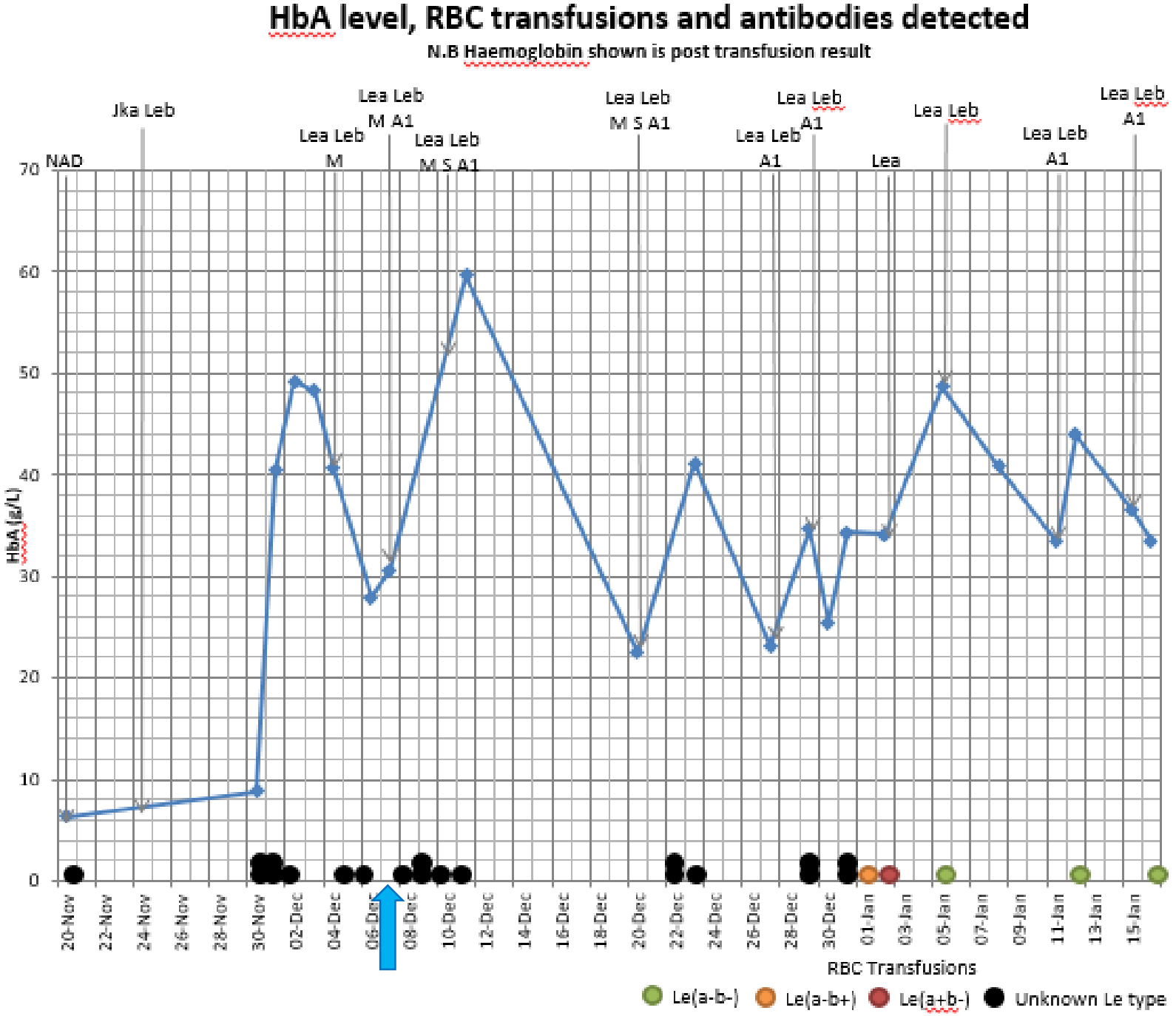


Image Courtesy of Stephanie Teasdale BMS NUTH

Follow up

- Weekly top up transfusions (as unable to obtain blood for regular exchange)
- Several further painful crises, but more easily controlled
- Delivered a healthy boy by elective CS at 36+5 weeks
- Re-established on hydroxycarbamide

Thank you
Any questions?