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
- Counselling 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
• 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 °C
Current Serology

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

- 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°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
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.
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?