NHS Blood and Transplant

# Case Details

- May 2016, sample sent on 37 year old female
- Diagnosis: pregnant (18 weeks) PV bleed, EDD of Oct 2016.
- Ethnicity: Black African
- Patient has Sickle Cell Trait and Thalassaemia.
- Group O RhD Negative
- ?allo anti-D and allo anti-C +?pan reactive
- Hospital want to know if they should give anti-D prophylaxis

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# Initial investigation

- Patient was known to RCI with history dating back to 2007

| Date | Diagnosis | Findings |
|---|---|---|
| Dec 2007 | Pregnant | Allo anti-D (0.57 IU/L) and allo anti-C |
| Jan -Feb 2008 | Pregnant | 3 samples in period all allo anti-D (peaked at 0.64 IU/L) and allo anti-C |
| Apr – July 2010 | Pregnant | 4 samples in period. All allo anti-D (peaked at 1.44IU/L) and allo anti-C (titre peaked at 2) |
| July-Aug 2010 | Pregnant | 2 samples in period. Allo anti-D (peaked at 1.2IU/L), allo anti-C (titre peaked at 2) + UNID (Enz) |
| Dec 2013 | Unknown | Panreactive in IAT and Enzyme – insufficient sample to complete investigation. Further samples requested |
| May 2016 | Pregnant | Current case study. |

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## Does the patient require anti-D prophylaxis?

1. Yes
2. No
3. Unsure

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# Results of panel 1

| | 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 | IAT | ENZ IAT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $R1^wR1$ | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | Yka- | 3 | 5 |
| 2 | R1R1 | 0 | + | 0 | + | 4 | 0 | + | + | 0 | 0 | + | + | 0 | + | 0 | | 3 | 5 |
| 3 | R2R2 | 0 | + | 0 | + | 3 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | + | | 4 | 5 |
| 4 | r'r | + | 0 | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | | 3 | 5 |
| 5 | r''r | + | 0 | + | 0 | 1 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | | 3 | 5 |
| 6 | Rr | + | + | + | 0 | 3 | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | + | | 3 | 5 |
| 7 | rr | + | 0 | + | 0 | 3 | 0 | 0 | + | 0 | 0 | + | + | 0 | + | 0 | | 3 | 5 |
| 8 | rr | + | 0 | 0 | + | 3 | 0 | 0 | + | + | 0 | + | 0 | + | + | 0 | HLA+ | 3 | 5 |
| 9 | rr | 0 | + | 0 | + | 2 | + | 0 | + | 0 | + | 0 | + | 0 | 0 | + | Cob+ | 3 | 5 |
| 10 | rr | 0 | + | + | 0 | 0 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | HLA+ | 3 | 5 |
| Auto | | | | | | | | | | | | | | | | | | 0 | / |
| Ctrl | | | | | | | | | | | | | | | | | | 3 | / |

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## WHAT TESTING WOULD YOU UNDERTAKE NEXT?

1. Eluate
2. Adsorbtion
3. Titration
4. Genotype
5. Phenotype

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# Results of Absorbtions and Tube IAT

| | Rh | M | N | S | s | P1 | $Lu^a$ | K | k | $Kp^a$ | $Le^a$ | $Le^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | rr x 2 IAT | R1R1 X2 IAT | Tube IAT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $R1^wR1$ | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 2 | 0 | 4 |
| 2 | R1R1 | 0 | + | 0 | + | 4 | 0 | + | + | 0 | 0 | + | + | 0 | + | 0 | 2 | 0 | 4 |
| 3 | R2R2 | 0 | + | 0 | + | 3 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | + | 2 | 0 | 4 |
| 4 | r'r | + | 0 | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | 1 | 0 | 4 |
| 5 | r''r | + | 0 | + | 0 | 1 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | 0 | 4 |
| 6 | Rr | + | + | + | 0 | 3 | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | + | 0 | 0 | 4 |
| 7 | rr | + | 0 | + | 0 | 3 | 0 | 0 | + | 0 | 0 | + | + | 0 | + | 0 | 0 | 0 | 4 |
| 8 | rr | + | 0 | 0 | + | 3 | 0 | 0 | + | + | 0 | + | 0 | + | + | 0 | 0 | 0 | 4 |
| 9 | rr | 0 | + | 0 | + | 2 | + | 0 | + | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | 4 |
| 10 | rr | 0 | + | + | 0 | 0 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | 0 | 4 |
| Auto | | | | | | | | | | | | | | | | | / | / | 0 |
| Ctrl | | | | | | | | | | | | | | | | | 3 | 3 | 3 |

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# What do you think is present?

1. Allo anti-D, allo anti-C
2. Allo anti-D, allo anti-C, pan reactive auto antibody
3. Allo anti-D, allo anti-C, other undetermined allo antibodies
4. Allo anti-D, allo anti-C, allo antibody to high frequency antigen
5. Inconclusive

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# Results of Absorbtions and Tube IAT

| | Rh | M | N | S | s | P1 | $Lu^a$ | K | k | $Kp^a$ | $Le^a$ | $Le^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | rr x 2 IAT | R1R1 X2 IAT | Tube IAT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $R1^wR1$ | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 2 | 0 | 4 |
| 2 | R1R1 | 0 | + | 0 | + | 4 | 0 | + | + | 0 | 0 | + | + | 0 | + | 0 | 2 | 0 | 4 |
| 3 | R2R2 | 0 | + | 0 | + | 3 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | + | 2 | 0 | 4 |
| 4 | r'r | + | 0 | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | 1 | 0 | 4 |
| 5 | r''r | + | 0 | + | 0 | 1 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | 0 | 4 |
| 6 | Rr | + | + | + | 0 | 3 | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | + | 0 | 0 | 4 |
| 7 | rr | + | 0 | + | 0 | 3 | 0 | 0 | + | 0 | 0 | + | + | 0 | + | 0 | 0 | 0 | 4 |
| 8 | rr | + | 0 | 0 | + | 3 | 0 | 0 | + | + | 0 | + | 0 | + | + | 0 | 0 | 0 | 4 |
| 9 | rr | 0 | + | 0 | + | 2 | + | 0 | + | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | 4 |
| 10 | rr | 0 | + | + | 0 | 0 | 0 | 0 | + | 0 | + | 0 | 0 | + | + | 0 | 0 | 0 | 4 |
| Auto | | | | | | | | | | | | | | | | | / | / | 0 |
| Ctrl | | | | | | | | | | | | | | | | | 3 | 3 | 3 |

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# Further testing results

- DAT

| PS | IgG | IgA | IgM | C3c | C3d | Ctrl |
|---|---|---|---|---|---|---|
| / | 0 | 0 | 0 | 0 | 0 | 0 |

- Titration of anti-C - TWTT
- Quantification of anti-D 0.59IU/L
- Phenotype

| M | N | S | s | P1 | $Lu^a$ | $Lu^b$ | K | k | $Kp^a$ | $Kp^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | - | + | + | + | - | + | - | + | - | + | - | - | + | - |

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# Rare cell panel

| Cell | Rarity 1 | Rarity2 | Rarity3 | Result |
|---|---|---|---|---|
| O r’’r | Ch- | Lan+,Vel+ | | 2 |
| O rr | Lub- | | | 2 |
| O rr | Rg- | | | 3 |
| O rr | Yta- | Coa+ | | 3 |
| O rr | Kna- | Yka- | | 3 |
| Ctrl (c) | | | | 3 |

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# What else could we do?

1. R2R2 panel
2. Alternative panels (e.g. BioRad)
3. Refer sample to IBGRL for investigation
4. Feto-maternal protein testing to genotype baby

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# Results from IBGRL

- Patient found to have rare At(a-) phenotype with anti-At$^{a}$ detectable by LISS IAT in the plasma
- Anti-K and anti-Jk$^{b}$ were excluded but anti-E, anti-Fy$^{a}$ could not be excluded due to insufficient sample.
- Allo anti-D and allo anti-C found in the absorbed plasma
- Due to the rarity of D-, C-, At(a-) there are no known donors on the International Rare Donor Panel and no frozen units available worldwide
- Fetal protein testing sample was sent for fetal genotyping but a genotype could not be obtained.

# At$^{a}$ (Augustine)

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- First described by Applewhaite *et al* in 1967.
- >99.9% frequency in Caucasians
- Mostly IgG but an IgM case has been recorded.
- Not known to cause HDN (one case – mild) – so baby should not need blood; just monitor bilirubin & Hb and give phototherapy +/- IVIg (as per NICE guidelines) if needed.
- 1 known case caused HTR
- Recommendation for crossmatching is serologically least incompatible red cells, but antigen negative for strong examples of the antibody.

# Challenges

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- The patient is due to deliver in Oct 2016
- No matched blood cover available
- Sickle trait & Thalassaemia – needs clarification as is this could be sickle-B Thal (which is effectively Thal major) or sickle trait & perhaps alpha-Thal (lower risk)
- What options exist (for discussion)?
  - Vaginal delivery – avoid anaesthesia
  - CS delivery - planned date.
  - Optimise pre delivery Hb (SCD and Thalassaemia)
  - Cell Salvage
  - Best matched blood with steroid cover?
    rr, K- Fya-, Jkb-? What about Fyb? GATA mutation?
  - Other options? Specialist Obstetric unit?

# Learning points

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- Antibodies to rare antigens will not always have suitable red cell units available for use even in frozen stocks.
- Serology and molecular testing may be able to identify antibodies present, and the patients antigenic expression, but this information may not present an easy solution for patient management.
- Discussions on patient management (for both mother and baby) should involve multiple teams with clear communication of the plan to all concerned.
- Even with robust patient management plans there is still a need to cross fingers
- When a follow up sample is requested to resolve a case it is a good idea to ensure the sample(s) are sent.