Transfusion case studies in haemoglobinopathy

Midlands National Education day
22nd November 2023

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West Midlands STN

WMSTN
West Midlands Sickle Cell and Thalassaemia Network

Sickle Cell: West Midlands region
Thalassaemia and Rare Inherited Anaemias: Midlands region

CASE 1 (DR S NICOLLE)

Mrs R

- HbSS sickle cell disease, very mild phenotype in terms of crises
- Jamaican origin, lived in Rugby most of her life
- Worked for sexual assault charity up to her death aged 73 (in 2022)
- First formally seen in a haemoglobinopathy specialist clinic aged 69!!
- Previously under a combination of general/ thrombosis haematologists, orthopaedic surgeons and renal physicians

Medical history/complications

- Protein S deficiency with multiple venous thromboembolic events, on long term warfarin therapy
- Baseline Hb ~88g/l
- Osteoathritis in multiple joints, said to be too complex for surgery for decades (due to her haematology problems)
- Dyspnoea, no underlying respiratory condition found ?related to previous clots ?fibrosis
- Multiple intracerebral haemorrhages 2008 with tonic-clonic seizures. No abnormal vessels. No long term neurological disability
- Aneurysmal ascending aorta noted on echo

SLE?

- Vasculitis screen done to investigate haemorrhages, positive ENA with raised anti-Ro titres
- Could explain VTE and cerebral haemorrhages and arthritis and…
- Deteriorating renal function, started with proteinuria in 2011, with rising creatinine (although this could be sickle and a biopsy was never done)

Transfusion history (1)

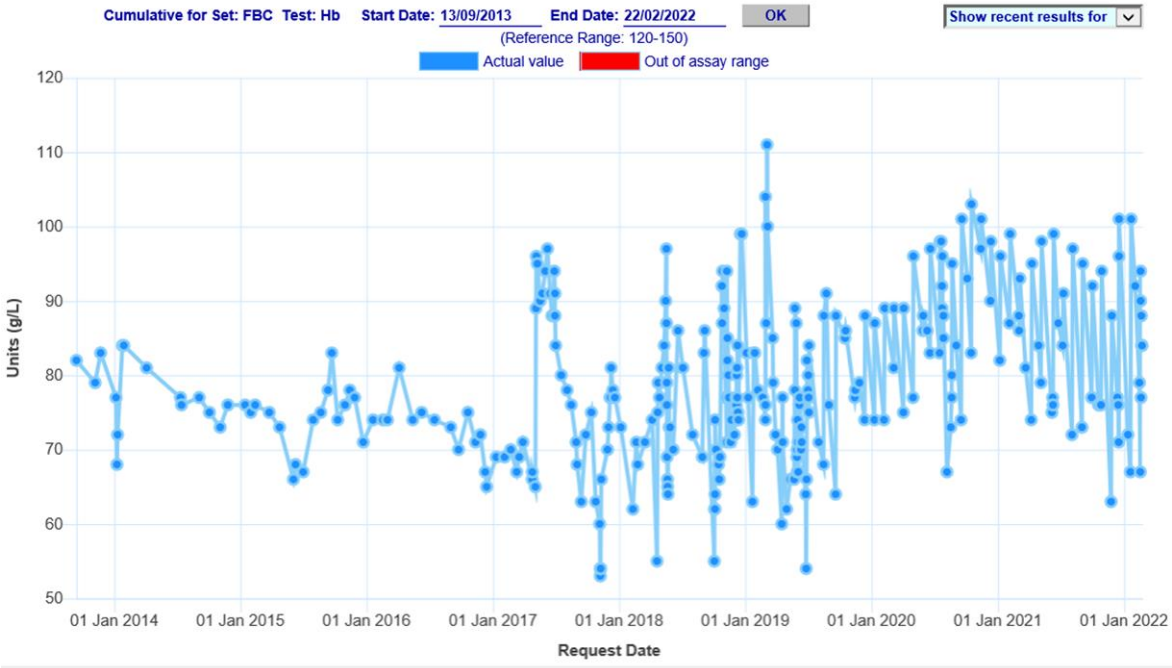
- Mrs R had had intermittent transfusions for anaemia and shoulder washouts in 2008- on second sample she had anti-K, Fya and NS antibodies identified
- Decision made to go for right THR for avascular necrosis in 2011:
- Group and antibody screen sent to Birmingham- no antibodies present
- Planned for blood transfusion (top up) 1 week prior to operation, with further top up if Hb <80 on day of op, CXM 3 for peri-operatively

Transfusion history (2)

- Deteriorating renal function led to the decision to go for peritoneal dialysis in 2016
- Transfused prior to PD catheter insertion which was timed to be done with hip injection
- Transfused prior to removal of PD catheter in 2017- no antibodies present
- Went onto haemodialysis and EPO was introduced to support Hb
- 2018- plans made for a new PD catheter and Total knee replacement and Shoulder decompression- I had persuaded her into red cell clinic by then, so exchange transfusion was done prior to surgery (all procedures done in one theatre session)

Transfusion history (3)

- Further planned exchange transfusions pre-procedure (Mrs R was becoming the bionic woman)-PD catheter changes, second knee replacement, inguinal hernia repair…
- In between, however…



Ad hoc transfusions

- Usually admitted from Rugby dialysis unit with very low Hb, symptomatic
- Usually renal led, very rarely haematology input
- Used in addition to variable EPO and also intermittent IV iron given in the dialysis unit (!)
- So…

Rising ferritin and risks of iron overload

- Plus return of Fya antibody
- Then positive DCT

How to reduce risks?

1. Plan
   - Reduces the risk of admission with very low Hb
   - Reduces the risk of giving just group specific because “it’s an emergency” and haematology not contacted
   - Reduces the risk of additional iron being given
2. Exchange rather than top up
   - Vascath already in situ
   - Reduces huge swings in Hb and symptoms which go with this
   - Reduced the degree of iron loading
   - Allows for planning of any additional procedures
   - Allows time for CXM to go to NHSBT and best blood to be given

Improvements?

- Hbs relatively steady, mid 80s-high 90s
- No more emergency admissions for severe anaemia, less symptomatic in terms of breathing
- Ferritin stabilised
- T2* MRI showed no cardiac loading, mild liver loading
- Excellent parameters when emergency surgery was needed for incarcerated inguinal hernia
- When Mrs R went back on PD, we continued to use the Vascath without problems

But?

- Increasing numbers of antibodies despite careful crossmatches/ extended match:
  - Fya, Kpa, auto-e, NS, K (intermittent), C
- Difficulties getting blood of an appropriate age due to antibodies (although does this matter?)

- Difficult to get blood in an emergency

Last admission

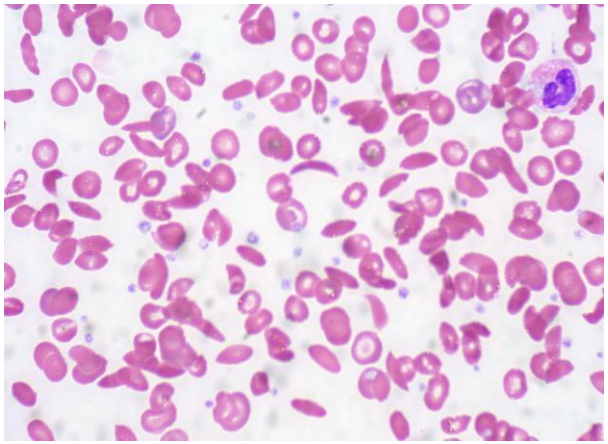
- Fall with #neck of femur
- Needed urgent operation
- PD needed prior to operation
- Timing of transfusion around PD was difficult
- Delays in operation

- Fixation of fracture done, with ITU admission
- Sudden death- at PM found to be ruptured aortic aneurysm

CASE 2

History

- 20 yr old Hb SS Hb F 11.8% Transitioned age 16
- Recurrent Splenic Sequestration
  - Hypersplenism and significant anaemia
  - Poor growth and delayed puberty
  - Started transfusion programme age 11 for 10 months
  - Splenectomy age 12
- Other complications
  - Enuresis – failed DDAVP.
  - Gallstones age 13 – declined cholecystecomy
  - Septic Arthritis (Lt elbow) age 16.
- Declined Hydroxycarbamide



Transfusion history

- Hyperhaemolysis –March 2014 age 12
  - IV methylprednisolone
  - IVIg
  - PEX x 6
  - Erythropoietin (PICU admission).
- Subsequent transfusion age 15 for parvovirus infection/red cell aplasia
  - Top up transfusion with IVIg and Methylprednisolone cover.

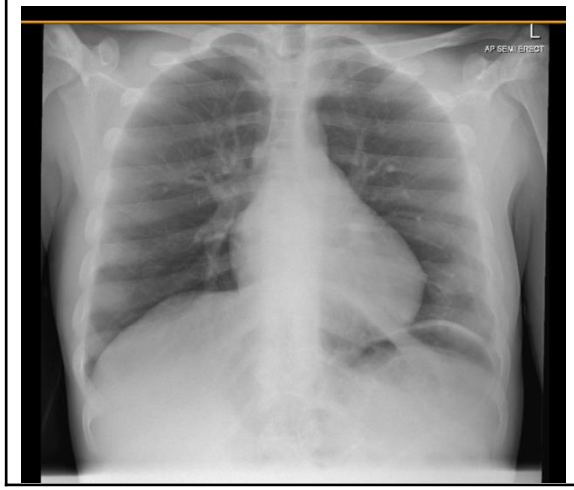
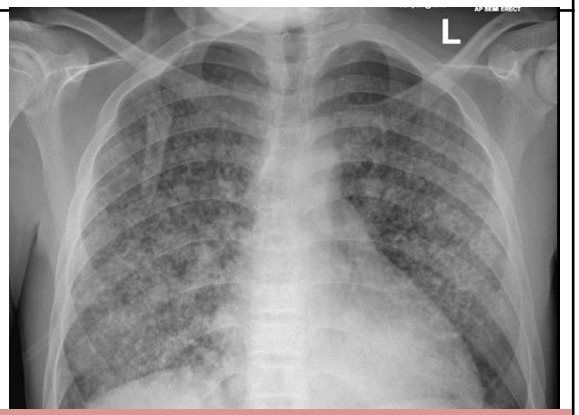
What is hyperhaemolysis?

- A severe form of delayed haemolytic transfusion reaction most commonly described in patients with sickle cell disease
- Involves destruction of both donor and recipient red blood cells (RBCs).
- Worse Hb than pretransfusion
- May not have detectable Allo-Ab
- High LDH, Haemoglobinuria

Post transition admission

- Blood bank notified of transfusion history (day of transition MDT 2019)
- 1-2 admissions per year
- Septic arthritis right elbow 2020, left tibia 2022
- In date annual review
- Continues to decline hydroxycarbamide
- Planning for University

Index admission Oct 22

Day I	Day 2	Day 5
VOC pain temperature spike 38.8 HR 133- Sepsis 6 started – IV antibiotics Covid negative	drop in Hb 42g/L (baseline 80-90) 2 unit top up transfusion (Hb 58g/L) **Discussed with patient and mother**	sats 72% air, HR 140, temp 39
		 **Automated RCE**

At no point was his previous transfusion history noted

Progress post RCE

- Recovered and discharged 5 days later
- Review 1 week post discharge in the MDT
  - What are the obstacles to disease modifying therapy?
  - CNS mentions history of Hyperhaemolysis
- Urgent review

No evidence of haemolysis

Key checks for HH

Clear handover of information at transition	
Enter of information on transfusion laboratory information systems	Done. LIMS upgrade 6 months prior. Validated, change control. His transfusion history not transitioned to new system **X**
Transfusion history with patient and parent	Done. Previous transfusion issues not mentioned **X**
Documentation	**X**
Team collective memory of difficult to transfuse patients	**XX**

Changes since

1. Review of all historical LIMS records (+ network)
2. Modifications to annual review proforma
3. Reiterate with patients with history of HH

SHOT 2022

Key SHOT messages

- Alloimmunisation and HTR are a significant risk of transfusion in SCD and may not be appreciated by medical teams
- This year saw the highest number of reports of HTR in SCD accounting for 22/49 (44.9%) of all HTR reported
- Hyperhaemolysis is a unique and potentially fatal complication of transfusion and contributed to major morbidity in 7 patients. All were in patients with SCD

Recommendations

- Haematology teams must be involved in the care of haemoglobinopathy patients presenting to secondary care and provide advice regarding transfusion. Specialist haematology advice should be taken regarding transfusion decisions
- For ad-hoc transfusion decisions it is important to seek transfusion history from the patient, transfusion laboratory and the national database (Sp-ICE or equivalent)
- All haemoglobinopathy patients should have a baseline extended red cell phenotype or genotype prior to transfusion (BSH Trompeter et al. 2020)

Action: Hospital transfusion teams, clinical teams looking after patients with haemoglobin disorders, laboratory management

SHOT Bite No. 15:
Hyperhaemolysis

SHOT Serious Hazards of Transfusion
January 2021

Hyperhaemolysis (HH) is a severe and potentially life-threatening complication of transfusions. Whilst it is predominantly seen in patients with sickle cell disease there are several reports of this complication in patients with other haemoglobinopathies as well as patients with a range of other haematological diagnoses who have blood transfusions as part of their management. HH is a complex syndrome characterised by destruction of transfused and autologous red blood cells following transfusion resulting in haemoglobin drop to below pre-transfusion level, reticulocytopenia with significant decrease to below baseline level and absence of new detectable alloantibodies in acute HH in contrast to delayed events. Prompt recognition and appropriate management of all hyperhaemolytic transfusion reactions is vital. Reporting to SHOT helps optimise learning from these events.

Hyperhaemolysis cases reported to SHOT 2010-2019 n=50

92% of HH cases were in sickle cell patients (46/50), with 10% reported in paediatric patients (5/50)

We are aware that hyperhaemolysis is under-reported to SHOT. Improved reporting helps optimise learning from these events.

HH can be seen in non-haemoglobinopathy patients as well so all clinicians handling transfusions need to be aware of this complication.

Patients need to be educated to seek help promptly in cases of delayed events.

NHS England

Clinical Commissioning Policy; Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies [URN 1821] [200602P]

Commissioning position

Summary

Rituximab and eculizumab is recommended to be available as a treatment option through routine commissioning for delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies within the criteria set out in this document.

Treatment and prevention of DHTR/HH

Figure 1: Pathway for management of DHTR/HH in patients with haemoglobinopathies

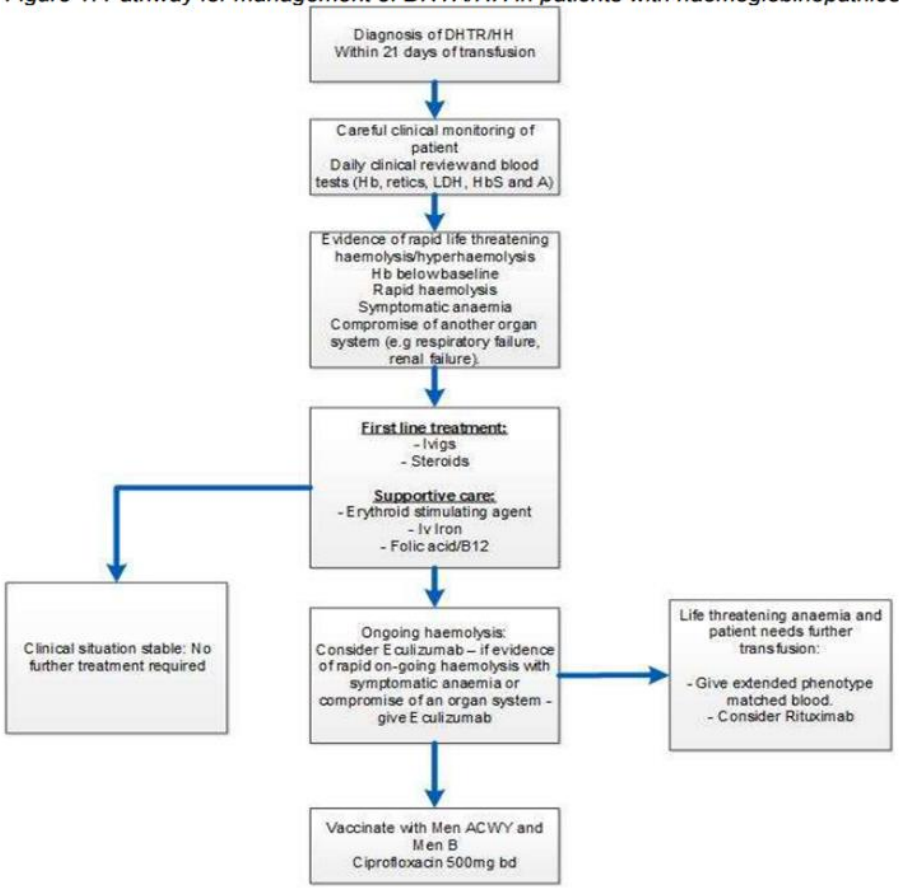
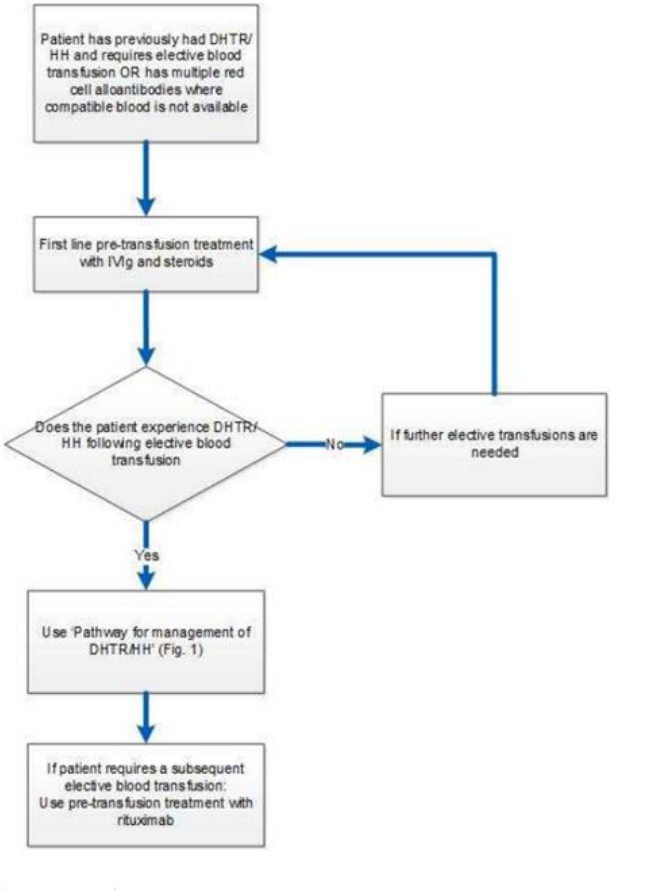


Figure 2: Pathway for prevention of DHTR/HH in patients with haemoglobinopathies



Clinical comissioning policy: rituximab and eculizumab for DHTR/HH Oct 2020

- ***How would knowledge of past transfusion history impacted on management***
  - Patient needed RBCs
  - Given IvIg and steroids pre transfusion
  - May have given top up rather than RCE

BSH guideline: Red cell transfusion in SCD

Indications where primary goal of transfusion is to correct acute anaemia	**GRADE evaluation**	**Type of transfusion**
Aplastic crisis	1B	Simple top up
Acute splenic sequestration	1B	Simple top up
Acute hepatic sequestration	1B	Simple top up
Delayed haemolytic transfusion reaction (transfusion should be avoided unless the anaemia is severe or life-threatening)	1C	Simple top up

BSH guideline: Red cell transfusion in SCD

Indications where primary goal of transfusion is to reduce HbS concentration in relation to HbA	**GRADE evaluation**	**Type of transfusion**
Acute sickle chest crisis	1B	Simple or exchange
Acute stroke or other neurological deficit (e.g. TIA)	1B	Exchange
Acute multi-organ failure	1C	Exchange
Mesenteric/girdle syndrome	1C	Exchange
Severe sepsis	2C	Exchange
Acute intrahepatic cholestasis	1C	Exchange
Primary stroke prevention	1A	Simple or Exchange
Prevention of silent cerebral infarct recurrence	1A	Simple or Exchange
Secondary stroke prevention	1B	Simple or Exchange

BSH guideline: Red cell transfusion in SCD

Surgery		
SS patients – elective low or medium risk surgery	1A	Simple or exchange
SC patients – elective low or medium risk surgery	1C	Exchange
All sickle genotypes – elective high risk surgery	1C	Exchange
Emergency surgery	1D	Individual considerations
Pregnancy		
Sickle complications (e.g. painful crises, ACS, stroke)	1B	Simple or exchange
Severe anaemia	1C	Simple
High obstetric, medical or fetal risk	1C	Simple or exchange
Recurrent ACS	2C	Simple or exchange
Recurrent painful crises	2C	Simple or exchange

CASE 3 TRANSFUSION IN THALASSAEMIA

Case history

- 39 yr old
- Hb E/B thal (non transfusion dependent thalassaemia)
- Splenectomy as a child
- Baseline Hb 60-70g/L
- Had first transfusion in first pregnancy 2012
  - 2 units RBCs
  - Allo E, Jra, Cw

- Intrauterine death 2018 31 weeks
  - No cause identified
- Now in third pregnancy, 11 weeks complaining of tiredness Hb 61g/l
- What would you advise?

Indications for transfusion for non transfusion dependent thalassaemia

- Transfusion may be required short term during acute infection, pregnancy and following surgery
- After transfusion for an episode of acute anaemia, the patient should be observed carefully for several months to determine steady-state symptoms and haemoglobin level.
- The decision for regular transfusions should be made in collaboration with the thalassaemia specialist team.
- Indications for long-term transfusions include symptomatic anaemia, falling growth velocity, delayed puberty, bone problems (facial deformities, recurrent fractures, premature epiphyseal fusion), pulmonary hypertension, symptomatic extramedullary haematopoietic masses, chronic ankle ulceration. Regular transfusions result in lower rates of these complications and improved survival but these benefits must be balanced with the risk of iron overload.
- Red cell units transfused must be matched for ABO, Rhesus antigens (C/c,D,E/e) and Kell.

Considerations for this patient

- Haemolytic disease of the fetus/ newborn
- Minimise requirement for transfusion
- Multidisciplinary management – haematologists, obstetric team, NHSBT

THANK FOR YOUR ATTENTION