

Haemolytic Transfusion Reactions (HTR) Case Studies

2016-2022

You are free to use these examples in your teaching material or other presentations, but please do not alter the details as the copyright to this material belongs to SHOT

Diagnosis of delayed haemolytic transfusion reaction delayed due to supply of incorrect transfusion history

- *A patient presented at the emergency department feeling unwell and experiencing thigh pain and pyrexia*
- *The patient reported receiving a recent transfusion but when the previous hospital was contacted, they stated that the patient had only received plasma products*
- *Laboratory results were suggestive of haemolysis with a high bilirubin, raised lactate dehydrogenase, positive direct antiglobulin test and haemoglobinuria*
- *An anti-E antibody was detected in the group and screen sample*
- *The patient's Hb dropped to 60g/L overnight*
- *The transfusion practitioner at the previous hospital later confirmed that the patient had received four units of red cells in her last transfusion episode at the hospital of which at least one was confirmed as positive for the E antigen*

Clinical notes stated patient history not available on a haemoglobinopathy patient

- *Anti-S was detected in an initial sample and three units of S-negative red cells were issued by indirect antiglobulin test (IAT) crossmatch*
- *The patient was being monitored as having a high risk for hyperhaemolysis when classical symptoms indicative of a delayed haemolytic transfusion reaction were reported, including a falling Hb, high bilirubin, raised lactate dehydrogenase, positive direct antiglobulin test (DAT) and haemoglobinuria*
- *The post-transfusion sample was DAT-positive and anti-Jk^b plus another possible IAT-reactive antibody were detected in addition to the anti-S*
- *Samples were referred to the reference laboratory who confirmed they had previously investigated this patient in 2015 when they confirmed the presence of anti-Jk^b*
- *This result was available on Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE)*
- *Investigation into the reaction by the hospital found that the patient had a clinical note on record stating that the ward had attempted to obtain the patients previous history, but this had not been available*

Reaction due to anti-B in platelet unit

- *An infant with blood group AB was transfused with group A platelets*
- *The platelets were labelled 'not for neonatal transfusion' and were not high-titre (HT)-negative*
- *The patient also received a group AB red cell top up*
- *A reaction was reported 8 hours following transfusion with an increase in the patient's bilirubin, and no haemoglobin (Hb) increment was observed following the red cell transfusion*
- *Following investigation, it was identified that the issuing biomedical scientist (BMS) in the laboratory had been focused on whether the 'not for neonatal transfusion' label was applicable to a patient >1 year of age and failed to consider the need for a HT-negative unit*
- *Information regarding the anti-B titre in the transfused component was not available*

Investigations post transfusion identifying delayed haemolytic transfusion reaction (DHTR) and prompting patient follow up

- *An anaemic patient was transfused two units of red cells as an outpatient*
- *Two weeks later the patient attended for a routine check-up*
- *Direct antiglobulin test (DAT) was positive, a new anti-Jk^a was identified and eluted from her red cells*
- *In addition, her haemoglobin (Hb) had dropped to 64g/L from a pre-transfusion level of 78g/L with a rise in bilirubin and lactate dehydrogenase (LDH)*
- *The transfusion laboratory recommended that the patient was monitored for a delayed transfusion reaction*
- *A letter was sent to the patient asking her to attend the general practitioner (GP) surgery for further blood tests at which point the patient reported that she had been feeling unwell following the transfusion and her Hb had dropped further to 49g/L*

Haemolytic transfusion reaction (HTR) investigation prompted by a failure in haemoglobin (Hb) increment post transfusion

- *A patient with B cell lymphoma was transfused to treat chronic anaemia*
- *A non-specific antibody was reported in the pre-transfusion antibody investigation and two units of crossmatch-compatible red cells were issued*
- *The patient did not show any clinical symptoms of HTR except that they failed to show the expected increment in Hb post transfusion*
- *Repeat samples were sent to the transfusion laboratory. The post-transfusion direct antiglobulin test (DAT) was positive and anti-Jk^a was identified in the plasma*
- *The pre-transfusion serology was reviewed, and it was concluded that the pre-transfusion sample also showed evidence of anti-Jk^a*

Failure to issue extended rhesus (Rh) matched units

- *A young patient with sickle cell anaemia received an exchange transfusion in 2014 without being tested for an extended phenotype*
- *In 2020 the patient was given another exchange transfusion. The patient had the Ro (D+C-c+E-e+) phenotype however the units transfused were only matched for ABO and K type*
- *Following transfusion, the patient showed signs of haemoglobinuria, jaundice and a falling haemoglobin (Hb) and anti-C and anti-E were detected in the post-transfusion sample*

Hyperhaemolysis in a patient with myelodysplastic syndrome and cold agglutinin disease

- *A haematology patient with a provisional diagnosis of myelodysplastic syndrome was transfused one unit of red cells due to a haemoglobin (Hb) 64g/L*
- *The patient immediately experienced symptoms of a transfusion reaction including fever, hypotension, nausea and dyspnoea*
- *The transfusion was stopped and the post-transfusion Hb dropped to 54g/L*
- *The patient was transfused another four times over the following 7 days, each time with hydrocortisone cover*
- *However, each transfusion resulted in similar reactions, although the symptoms were less severe*
- *At this point a decision was made to stop transfusion and to treat the patient with intravenous immunoglobulin (IVIg) and erythropoietin*
- *The patient improved and the Hb began to rise over the following 3 weeks with the Hb stabilising at 86g/L 7 weeks after the initial reaction*

Anti-Jk^b detected in eluate post transfusion

- *The patient reported feeling unwell 30 minutes into the transfusion of the second unit*
- *The transfusion was stopped, and a transfusion reaction investigation performed*
- *Both pre- and post-transfusion samples demonstrated a non-specific pan reactive antibody detectable in Biovue[®] and low ionic strength saline (LISS) tube indirect antiglobulin test (IAT)*
- *No underlying antibodies were detected in either sample however an eluate on the post-transfusion sample demonstrated the presence of anti-Jk^b*

Patient visiting from abroad with multiple antibodies

- *A Ghanaian national visiting the UK was admitted to hospital in sickle crisis*
- *The initial antibody screen was positive, and samples were sent to the Blood Service for investigation*
- *The Red Cell Immunohaematology (RCI) laboratory was unable to identify the antibody and samples were sent to the International Blood Group Reference Laboratory (IBGRL) for further investigation*
- *Two units of crossmatch-compatible blood were issued by the Blood Service and transfused prior to the IBGRL investigation being completed*
- *Following transfusion, the patient required urgent treatment for bleeding in the brain and had evidence of haematuria however this was initially attributed to the sickle crisis*
- *IBGRL subsequently reported anti-D, anti-E and anti-Js^b*
- *The units which had been transfused were negative for the D and E antigens but were both Js^b positive*
- *The patient had stated that she had an antibody, but she did not know which one*

Patient with anti-E, -C^w, -S, -Jk^a and -k

- *A patient required urgent transfusion for chronic anaemia after presenting at hospital with haemoglobin (Hb) 31g/L*
- *The patient had a known history of anti-E, -C^w, -S, -Jk^a and -k, however no red cells units of this specification were available at the Blood Service or the frozen blood bank*
- *The anti-Jk^a was not detectable in the sample therefore following discussion between the consultant haematologists at the hospital and Blood Service it was decided to transfuse units which were Jk^a-positive but negative for all detectable red cell antibodies*
- *The patient's Hb initially rose post transfusion however 6 days later the Hb had dropped by 18g/L, the direct antiglobulin test (DAT) had become positive and anti-Jk^a was detectable in the post-transfusion sample*

Delayed haemolytic transfusion reaction (DHTR) in an O D-negative female transfused with D- positive blood

- *A female patient in her 70s presented in the emergency department (ED) with an abdominal aortic aneurysm*
- *The major haemorrhage protocol was activated*
- *The patient's antibody screen was negative, and the patient was transfused with emergency D-positive blood*
- *Six days later the patient experienced symptoms of a transfusion reaction including raised bilirubin, raised lactate dehydrogenase (LDH), falling haemoglobin (Hb), positive direct antiglobulin test (DAT) and impaired renal function*
- *Anti-D was detected in the post-transfusion sample and was also eluted from the patient's red cells*
- *Following investigation, the patient informed the clinical area that she had developed an antibody in a previous pregnancy*

Acute haemolytic transfusion reaction (AHTR) reported with a direct antiglobulin test (DAT)-positive unit

- *A cancer patient transfused two units for anaemia became unwell during the transfusion of the second unit, exhibiting symptoms of a HTR*
- *The transfusion was stopped, and the unit was sent to the transfusion laboratory for investigation*
- *The pre- and post-transfusion samples both gave a negative antibody screen and negative DAT*
- *A DAT performed on the unit found that it was positive for C3d*
- *There have been no previous reports of adverse events in patients due to the transfusion of a DAT-positive component, however no alternative cause of the reaction could be found*

Delayed haemolytic transfusion reaction (DHTR) in a patient with anti-HI

- *A patient with sickle cell anaemia and a negative antibody screen was treated by exchange transfusion*
- *Eleven days later they were readmitted with a suspected delayed transfusion reaction*
- *The patient had a rising bilirubin and falling haemoglobin (Hb) and the post-transfusion sample was found to be direct antiglobulin test (DAT) positive, with a non-specific pan-reactive autoantibody detected*
- *Further samples sent to the Blood Service were found to contain anti-HI*

Hyperhaemolysis post allogeneic stem cell transplant

- *A haematology patient with T-cell lymphoma post stem cell transplant developed symptoms consistent with hyperhaemolysis following a four-unit red cell transfusion*
- *The patient was transfused a further five red cell units, but the bilirubin continued to rise and the haemoglobin (Hb) to fall*
- *The patient developed impaired renal function and died 9 days later*

Hyperhaemolysis in a patient with Rosai-Dorfman Syndrome

- *A patient with known Rosai-Dorfman syndrome was admitted with symptomatic anaemia, and a haemoglobin (Hb) of 24g/L*
- *The patient had previously confirmed autoimmune haemolytic anaemia*
- *The patient was treated with steroids, erythropoietin and rituximab in addition to red cell transfusion*
- *Within 7 hours of transfusion the patient experienced fever, back and chest pain, dyspnoea and haemoglobinuria*
- *The patient's Hb dropped from 81g/L immediately post transfusion to 20g/L, the bilirubin and lactate dehydrogenase (LDH) became raised and spherocytes were detected on the blood film*
- *The patient developed impaired renal function and died 6 days later*

Antibody detectable pre transfusion in eluate

- *The patient was admitted for laparotomy for a small bowel obstruction*
- *Fully automated pre-transfusion testing was performed, and a negative antibody screen result obtained using the Ortho AutoVue Innova*
- *Blood was crossmatched by electronic issue*
- *During the transfusion the patient's heart rate increased and their temperature rose by 2°C*
- *The transfusion was stopped, and a transfusion reaction investigation requested*
- *As part of the investigation the antibody screen on the pre-transfusion sample was repeated as negative, however a direct antiglobulin test (DAT) was also performed on this sample*
- *The DAT was positive and anti-Jk^a was detected in the eluate. Anti-Jk^a was also detected in the post-transfusion sample and in an eluate performed from this sample*
- *One of the units transfused was confirmed as Jk^a-positive*

Discrepant pre-transfusion results obtained using automated analysers

- *Blood was issued by electronic crossmatch following a negative antibody screen result using the Ortho AutoVue analyser*
- *Ninety minutes post transfusion the patient experienced rigor, back pain and fever*
- *Samples were sent to the laboratory for investigation of a transfusion reaction*
- *Pre- and post-transfusion samples were tested on a second Ortho AutoVue analyser*
- *They both gave positive reactions and anti-Jk^a was subsequently identified*
- *This was reported to the analyser manufacturer for investigation*
- *Following testing of the antibody titre it was concluded that the antibody was at a level that was below the minimum level for detection*

Death following emergency transfusion of a patient in sickle crisis

- *A pregnant patient in her 40s with SCD in sickle crisis and symptoms of acute chest syndrome received an urgent red cell exchange transfusion prior to emergency caesarean section*
- *During the transfusion the patient developed symptoms of a transfusion reaction and the transfusion was stopped*
- *The patient had a history of anti-U and possible anti-Jk^a, however due to the emergency nature of the transfusion and the rarity of U-negative, Jk^a-negative red cells, Jk^a-negative units were not selected and units negative to the U antigen only were transfused*
- *The justification given for this was that the presence of anti-Jk^a had not been positively confirmed*
- *The patient developed disseminated intravascular coagulation (DIC) and possible hyperhaemolysis syndrome*
- *At post mortem the death was attributed to acute chest syndrome related to SCD*

Hyperhaemolysis in patient with variant Rh phenotype and known alloantibodies (1)

- *A patient with SCD received an elective ten-unit exchange transfusion prior to surgery*
- *The patient was known to have allo anti-Ce, anti-s, anti-K and anti-Jk^b*
- *The patient also had a previously reported auto anti-e*
- *The patient was genotyped as part of the Blood Service genotyping project for haemoglobinopathy patients and found to have a variant D- and e-genotype*
- *The previously reported auto anti-e was therefore recharacterised as allo anti-e*
- *Due to the unavailability of D- C- E+ c+ e- s-K-Jk^b- red cells the decision was made not to provide e-negative units*

(continued)

Hyperhaemolysis in patient with variant Rh phenotype and known alloantibodies (2)

- *The rationale for excluding the anti-e for the purposes of blood selection was that the patient had been transfused e-positive units prior to the identification of the variant e-genotype without symptoms of haemolysis and also that data collected by National Health Service Blood and Transplant (NHSBT) for transfusion of antigen-positive units to patients with variant phenotypes had no reports of haemolysis in e-variant patients with anti-e*
- *Five days post transfusion the patient developed haemoglobinuria and was readmitted to hospital and required ventilation*
- *The Hb fell from 83g/L to 48g/L and the bilirubin and LDH were raised The patient was transfused three units of D+ C- E+ c+ e- s- K- Jk^b- red cells*
- *However, monitoring of HbS levels demonstrated that these transfused cells were also haemolysed*
- *No new antibodies were detected on serological investigation and the DAT was positive pre and post transfusion with no change seen in the reaction strength*

DHTR due to anti-c

- *A patient receiving chemotherapy was transfused two units of red cells issued by electronic crossmatch following a negative antibody screen using a fully automated system*
- *The following week the patient returned to hospital with discoloured urine and anaemia*
- *The patient's bilirubin had risen from 10 to 40micromol/L and her Hb had dropped from 102g/L to 88g/L*
- *The antibody screen on the new samples was positive and anti-c was identified*
- *The transfused units were confirmed as c-antigen positive*

DHTR due to anti-Fy^a

- *A renal patient with history of a negative antibody screen was transfused two units of red cells*
- *Eleven days later the patient returned for their next routine appointment*
- *Investigation of the samples taken during this admission found that anti-Fy^a was now detectable in the plasma*
- *Anti-Fy^a was also eluted from the patient's red cells*
- *The patient had reported no clinical symptoms but laboratory tests indicated the Hb had not incremented following the transfusion and she had now developed a positive DAT*

Failure to identify previous antibody history available in a patient treated across multiple hospitals (1)

- *Anti-C and anti-S were confirmed in a patient in 2000 by the Blood Service and a report and antibody warning card for the patient issued to the referring hospital (Hospital 1)*
- *In 2015 the same patient was seen in Hospital 2 and samples referred to the International Blood Group Reference Laboratory (IBGRL) for red cell genotyping*
- *In February 2017 the patient was seen in Hospital 3 and another sample was sent to the IBGRL for genotyping*
- *At this time both the report from 2000 and the genotype report from 2015 were available on Sp-ICE*
- *In May 2017 the patient was seen at a 4th hospital (Hospital 4)*

(continued)

Failure to identify previous antibody history available in a patient treated across multiple hospitals (2)

- *Samples were again referred to the Blood Service reference laboratory and this time anti-Lu^a and anti-Fy^a were detected*
- *A report was issued to Hospital 4 stating the new antibodies and also the previously detected anti-C and anti-S*
- *A new antibody card for the patient, listing all four antibody specificities was sent with the report*
- *This new report was also uploaded to Sp-ICE*
- *In July 2017 the patient presented again to Hospital 1*
- *An antibody screen was performed and found negative and ABO, Rh and K group-matched blood was issued*
- *Approximately 5 days later, the patient was admitted to a 5th hospital (Hospital 5) with symptoms of a HTR including an acute drop in Hb and positive DAT*

Transfusion of emergency O D-negative red cells later found to be incompatible

- *A patient suffered a major gastrointestinal arterial bleed and required immediate transfusion*
- *The two emergency O D-negative units were taken from the hospital transfusion laboratory refrigerator and a further three uncrossmatched group O units were provided*
- *Subsequent testing of the pre-transfusion sample identified anti-Jk^b in the patient's plasma*
- *Three of the units issued were confirmed to be positive for the Jk^b antigen*
- *The patient developed fever and jaundice and laboratory tests confirmed haemoglobinuria, raised bilirubin, raised LDH, a rapid drop in Hb and positive DAT*
- *The patient recovered and survived*

Issue of 'best match' in major haemorrhage

- *A major haemorrhage alert was called on a bleeding patient with cholecystitis and the emergency O D-negative units were collected*
- *Part of the first unit was transfused before the transfusion laboratory staff were able to inform the clinical area that the patient had a history of anti-E, anti-Fy^a and anti-Jk^a*
- *On discussion with the consultant haematologist it was agreed to crossmatch two E-negative Fy^a-negative, Jk^a-untyped units as no suitable Jk^a-negative units were available in the hospital transfusion laboratory*
- *These units were subsequently confirmed as Jk^a-positive*
- *The patient did not suffer any clinical symptoms of a HTR but laboratory tests showed a positive DAT and rapid fall in Hb*
- *The patient recovered and survived*

Death probably related to hyperhaemolysis

- *A young male patient with sickle cell anaemia received a red cell transfusion in ITU in view of hepatic sequestration*
- *Seven days later he had a sudden reduction in his Hb from 85g/L to 45g/L and then a further drop to 31g/L. He had haemoglobinuria, chest pain and had a tachycardia*
- *He was treated with methylprednisolone and intravenous immunoglobulin (IVIg) and further red cell transfusion*
- *While he was being transfused with his first unit he deteriorated, developed chest infiltrates and acidosis*
- *He died of circulatory collapse and respiratory failure some 12 hours later despite maximum support*
- *The coroner's report is awaited*

Severe reaction possibly due to exacerbation of autoimmune haemolytic anaemia (AIHA) (imputability 2)

- *A patient suffered dyspnoea, hypotension, rigors, lower back pain, a feeling of impending doom and loss of consciousness, 5-10 minutes after commencing a second unit of red cells, and was subsequently transferred to ITU*
- *The Hb fell post transfusion and there was a rise in bilirubin*
- *Pretransfusion testing showed panagglutinins detected by low ionic strength saline (LISS) indirect antiglobulin test (IAT), and a strongly positive DAT (IgG, IgM and C3d coating), but no underlying alloantibodies*
- *The serological picture did not change post reaction and this is possibly a case of exacerbation of AIHA*

Life-threatening fall in Hb in a paediatric patient with sickle cell disease (imputability 3)

- *A child with sickle cell disease was admitted to ITU with acute chest crisis and received a six unit red cell exchange transfusion*
- *Thirteen days later the patient was readmitted with jaundice, limb pain, dark urine and Hb of 32g/L, which fell further to 22g/L*
- *Anti-M and anti-S were identified in both the plasma and eluate*
- *The patient suffered a stroke prior to transfusion of compatible red cells, but recovered quickly following transfusion*

Kidd antibodies identified but relation to the reaction is unclear (Case 1)

- *A 19-year-old female patient with apparently no previous transfusions suffered chills, rigors and nausea during the third unit of red cells, which was stopped*
- *She had a weak pan-reactive antibody and a strong positive DAT (IgG and C3d) pre transfusion, but anti-Jk^a was identified in addition to the panreactivity in the post-transfusion plasma sample, and the DAT was more strongly positive*
- *There was no evidence of alloantibody in the eluate and the units were Jk(a-)*
- *It was thought that the haemolytic episode may have been caused by cold agglutinins following transfusion of cold red cells*

Kidd antibodies identified but relation to the reaction is unclear (Case 2)

- *A regularly transfused patient with anti-E and anti-Ch/Rg, received two E-negative red cell units uneventfully*
- *Twenty four days later she was admitted with acute bleeding, Hb 52g/L and a positive DAT (1+), and anti-C^w was also identified*
- *Transfusion was stopped after one unit when the patient became febrile, dyspnoeic and hypotensive; the LDH was raised, and spherocytes were noted on the blood film*
- *A new sample demonstrated the same antibodies as before in the plasma but also a stronger positive DAT (3+) and anti-Jka in the eluate*
- *The Jk^a status of the units transfused 24 days earlier was unknown but the one transfused during the current transfusion was Jk(a-)*
- *The next day, a new sample was sent to the Blood Centre reference laboratory but on this occasion the eluate was negative*

Anti-E possibly present in the pre-transfusion sample

- *Towards completion of a second unit of red cells, a patient developed fever, rigors and passed red urine*
- *He had a rise in bilirubin and no Hb increment*
- *The DAT was negative, but anti-E was identified in the post-transfusion plasma and at least one of the red cell units was confirmed as E-positive*
- *Retrospective testing of the pre-transfusion sample showed some weak reactions by enzyme technique that were suggestive of anti-E*
- *The patient had also been transfused 17 days earlier, and it is probable that the anti-E was developing in response to this earlier transfusion*

Passive ABO antibodies

- *Passive anti-A in a unit of group O apheresis platelets caused an acute reaction and haemolysis in a paediatric patient (weight 22.5kg)*
- *The unit was high-titre (HT) negative*
- *The patient had a fall in Hb (of 22g/L) and a rise in bilirubin, with spherocytes noted on the blood film; anti-A was confirmed in the plasma and eluate*
- *It is not known whether the HT testing was repeated*

Probable autohaemolysis following haemopoietic stem cell transplant (HSCT) (imputability 2)

- *Five months prior to this transfusion a group O D-positive child with acute lymphoblastic leukaemia (ALL) received a HSCT from a group A D-negative donor, and had developed weak anti-D*
- *Two hours into a group O D-negative red cell transfusion, the patient developed a rash all over her abdomen, torso, face and hands; she had an increased heart rate, developed back pain and passed dark red urine*
- *Haemolysis was confirmed by a fall in Hb and a sharp rise in bilirubin (21 to 117micromol/L)*
- *The DAT became positive post transfusion and although the eluate was positive by IAT, no specificity was determined*
- *The patient had similar reactions during subsequent transfusions with phenotyped matched red cells, but following treatment with IVIg tolerated further transfusions well*

Avoidable DHTR following transfusion of inappropriate antigen-positive red cells

- *The patient with SCD received an eight unit red cell exchange transfusion at hospital A (prior to surgery at hospital B) with red cells matched only for Rh and K*
- *She was admitted to hospital B six days later, very unwell, with fever, jaundice, black urine and a falling Hb*
- *Hospital B had a historical record of anti-E+S+Fy^a+Fy^b+Fy³ for this patient and confirmed that several of the units used in the exchange were antigen positive; anti-Fy^a+Fy³ were identified in the plasma and eluate*