11a Delayed Transfusions n=129

Definition:

Where a transfusion of blood or blood component was clinically indicated but was not undertaken or was significantly delayed or non-availability of blood components led to a delay with impact on patient care (not restricted to emergency transfusion).

Key SHOT messages

- Patients are put at risk when staff do not act appropriately in the event of major haemorrhage
- Isolated prolongation of the activated partial thromboplastin time (normal prothrombin time, thrombin time and fibrinogen) in a male infant indicates factor VIII or IX deficiency and warrants urgent investigation. Laboratory standard operating procedures (SOP) should reflect this and all biomedical scientists who work 'on call' should be appropriately trained to recognise this

Recommendations

- All hospitals should regularly review their major haemorrhage procedures to ensure communication lines and practice this with drills (NPSA 2010)
- Laboratory tests of haemostasis must be interpreted in the context of clinical findings as well as other laboratory test results. Appropriate timely actions will help to avoid unnecessary delays in diagnosis and enable potentially lifesaving treatment for patients with unexplained bleeding

Action: Hospital transfusion teams, consultant haematologists, laboratory managers

Introduction

The number of reported delayed transfusions has increased from 106 in 2018 to 129 in 2019. There were 83/129 (64.3%) reports where the primary error occurred in the clinical setting, 45/129 (34.9%) in the laboratory and 1/129 (0.8%) was caused by a delayed flight. In 63/129 (48.8%) reports the need for the transfusion was emergency/urgent, 36/129 (27.9%) were elective transfusions and in 30/129 (23.3%), this was not recorded. Poor communication between the clinical and laboratory settings and staff shortages were the main contributory factors in these cases. In addition, there were 11 delays in administration of PCC, and these are counted and considered in that section. Please see Chapter 11d, Incidents Related to Prothrombin Complex Concentrate (PCC) for further information.

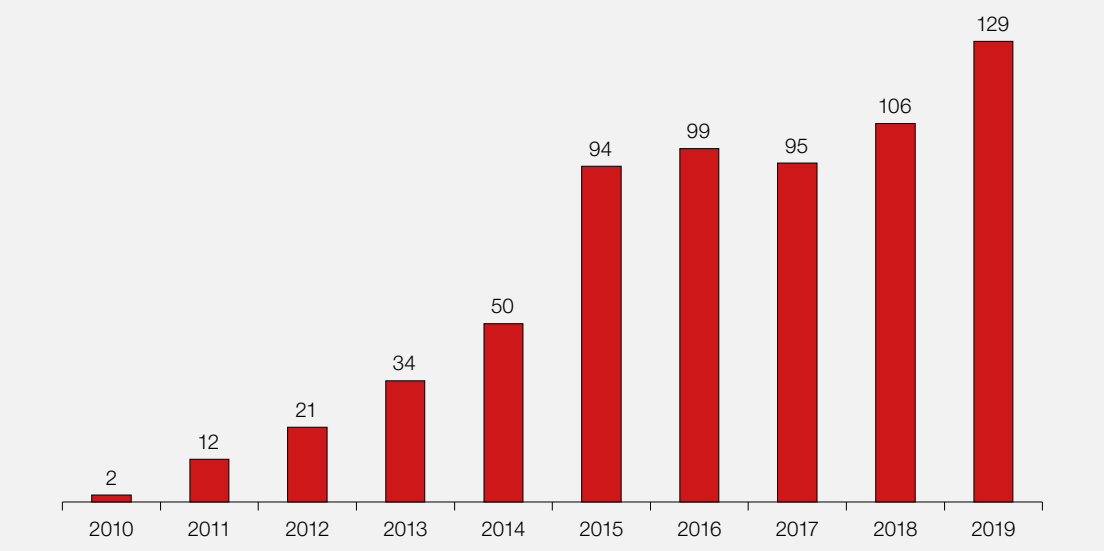

Figure 11a.1: Delayed transfusion reports by year 2010 to 2019

Death n=2

The delay was 'possibly' contributory to the patient's death in 2 cases.

A young man with bone marrow infiltration due to cancer (leucoerythroblastic blood picture) had a reported haemoglobin (Hb) 47g/L and was scheduled for a four-unit transfusion. He died two days later, not having received the planned transfusion. His Hb, prior to his death, was recorded on a point-of-care machine as 26g/L. The investigation noted that his life-expectancy was very poor, and it was unlikely that the transfusion would have made a difference.

A case that was not recognised by the reporter as a death related to delayed transfusion involved an elderly man with gastrointestinal bleeding with delayed diagnosis of a large duodenal ulcer. Clinical reviews and transfusions were repeatedly delayed with poor recognition of ongoing bleeding and transfers between departments. His Hb remained less than 60g/L over a prolonged period (17 hours) resulting in a cardiac arrest. At the inquest the coroner concluded that the recorded cause of death at 1b on the death certificate was 'haemorrhagic cardiac arrest'.

Learning point

- Gastrointestinal bleeding can be difficult to assess. Prompt recognition and timely management is imperative. Delays can contribute to patient death. Every second counts

A male infant in whom a diagnosis of haemophilia was delayed died from intracranial haemorrhage. This was due to an arteriovenous (AV) malformation and the clinicians did not think that an earlier diagnosis would have made a difference.

In a further case of delay, a woman in her 90s had delayed administration of PCC in relation to an intracranial bleed (this case is counted and described in Chapter 11d, Incidents Related to Prothrombin Complex Concentrate (PCC)).

Major morbidity n=4

Three cases were reported in relation to major haemorrhage.

A young man was admitted with major haemorrhage caused by a stabbing injury to his carotid artery. Red cells were rapidly available but the provision of fresh frozen plasma (FFP) was delayed (slow thaw) and platelets were not ordered urgently. The biomedical scientist (BMS) was lone working covering two departments leading to communication problems. The patient suffered a stroke which was attributed in part to delay in receiving plasma and platelets. A complete overhaul of the major haemorrhage policy and education of medical staff were undertaken.

An elderly man had severe gastrointestinal bleeding. There was delay in provision of blood components due to constraints in contacting the porter because of industrial action. Delay in correction of his coagulopathy resulted in admission to the intensive care unit (ICU).

A man in middle age was admitted as an emergency with serious gastrointestinal bleeding. There was delay in obtaining blood components for 1.5 hours after the major haemorrhage call due to lack of porters. This delay contributed to his deterioration requiring admission to the ICU with renal failure.

Case 11a.1: Inappropriate interhospital transfer in a patient with a falling Hb

An elderly woman was admitted after a fall (no fracture) 2 weeks from discharge following hip surgery (Hb 90g/L). She was found to have a popliteal vein thrombosis and was anticoagulated. Eight days later she was considered fit for transfer. However, her Hb had been falling and on the day of transfer was 58g/L. She was transferred at 12:00 before the blood results were reviewed. The hospital was experiencing winter pressure and the need to free up beds. Her condition deteriorated during transfer (National Early Warning Score (NEWS), 10), despite five hours at the second hospital, where electronic issue blood was available for the patient, she was returned to the emergency department at the first hospital for transfusion. After a delay of 45 minutes in the ambulance she was admitted at 18:00 (Hb now 46g/L). At this point the patient was showing signs of hypovolaemic shock. The first request form for crossmatched blood was sent to the laboratory without the required sample which further delayed the transfusion. When a second request for crossmatched blood was sent the laboratory staff were not informed of the urgency of the situation. The patient was transferred to a ward at 19:00; a blood transfusion had not been administered up to this point. The patient had a cardiac arrest at 22:00 and it was not until this point that she received a unit of emergency group O D-negative blood. Three additional crossmatched units were later made available and transfused. The patient survived and was eventually discharged home.

The internal review noted that 'the root cause of the incident was the most recent blood results for the patient were not reviewed prior to the patient transfer. A breakdown in communication, undefined control and command by the various teams involved in the patient's care led to fragmented management of the patient's clinical care'. A review of the transfer criteria/checklist for patients who are to be transferred between hospital sites was carried out to ensure patients are clinically fit and now includes a review of a patient's most recent bloods. At the time of the incident not all staff were aware of the major haemorrhage protocol, this highlighted learning and training needs. Staff are now aware of the major haemorrhage protocol and how it should be triggered. Staff training has been carried out for the administration of electronic issue blood. Provision of a 24/7 patient safety team including operational bed manager and critical care outreach team now provides organisational wide command and control for such unpredictable patient deterioration. The pressure on bed availability was a systems issue which contributed to the need for transfer.

Delayed transfusion associated with major haemorrhage n=16

Sixteen cases of major haemorrhage were associated with delay. One was not associated with activation of the major haemorrhage protocol (MHP), but 15 were. Six cases reported delay due to porter access, 2 due to pager failure. Overall, 6 reports cited issues with logistics and provision of components and 6 cited communication issues between the clinical area and the laboratory, but review of the cases showed several problems with communications affecting 15/16 cases. These are the same issues as identified in 2018. Eleven were emergency transfusions, 3 urgent and in 2 cases not specified. Six cases were in the emergency department or medical admissions unit, 4 in wards, 5 in theatre, recovery or ICU and 1 in obstetrics.

There was poor understanding of MHP; staff had not been trained and did not know what number to call. In 8 cases FFP provision was delayed. Further education about the time required to thaw FFP is required for clinical teams.

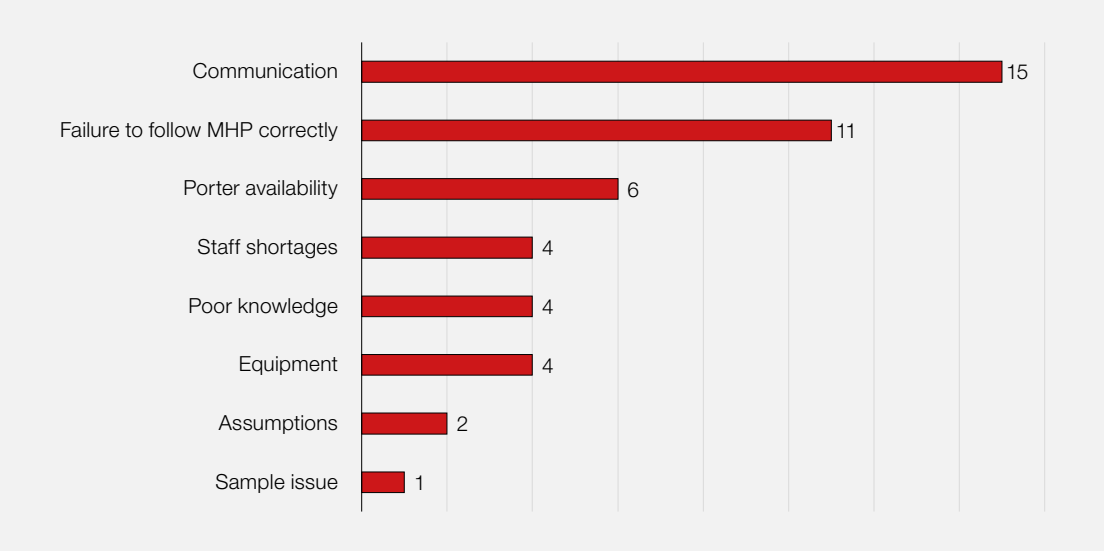

Figure 11a.2: Factors contributing to delayed transfusion in 16 cases

MHP=major haemorrhage protocol

There were delays in transportation of components between a hub with a transfusion laboratory and a specialist hospital with a surgical unit. A young man bled during elective surgery for malignant disease requiring platelets and plasma which took 1.5 hours to arrive (a distance of about 2 miles, usual transport time less than 10 minutes). The courier was delayed and could not be contacted. This patient received eight units of red cells, eight of FFP and two of platelets.

Illustrative cases

It is important that there are clear lines of investigation and accountability where multifactorial errors occur. One elective transfusion was delayed by several hours following a need for samples to be taken four times. After the first sample was sent the ward was told no request for blood had been made by the doctor. The second and third samples were rejected by the laboratory staff as the sample forms were not completed correctly. A fourth sample was sent, tested and blood was made available. The original request form was eventually found in the laboratory, meaning the first sample could have been tested after all. This caused a delay of 9 hours. There was no case review and no transfusion team input as the hospital had contracted out to a private laboratory provider. The fundamental reason for the delay in this case was the misplaced blood request form in the laboratory. A junior doctor involved with the inaccurate request form completions received training due to the subsequent sample errors.

Treatment with solvent-detergent treated FFP was delayed for a woman with acute myeloid leukaemia because the BMS did not know how to issue it – this case is discussed in Chapter 14, Laboratory Errors, Case 14.2.

Case 11a.2: Delayed treatment of gastrointestinal haemorrhage

A man in his 60s was admitted with chest symptoms and possible gastrointestinal bleeding. His Hb fell over 2 days from 115g/L to 96g/L on day 2, and 50g/L early the following morning when he had a cardiac arrest. Although the laboratory staff provided all components promptly there were misunderstandings with the medical staff who had not received adequate training, and communication was confused. The review considered that transfusion could have occurred earlier as the Hb was clearly falling.

Case 11a.3: Delayed treatment of severe anaemia

An elderly woman was admitted with anaemia, possibly due to bleeding. Her Hb was 45g/L and she was not adequately transfused over the next 6 hours and had a cardiac arrest. The patient was located in a busy and overflowing department and was moved several times during her stay which contributed to the delay. As a result of this incident changes to clinical practice have been implemented regarding the group-check sample rule (i.e. that in an emergency, O D-negative units can be obtained).

Case 11a.4: Missed diagnosis and delay in treatment of a child with haemophilia and intracranial bleeding

A male infant <6 months of age presented to hospital A with a history of falling down the stairs while in his mother's arms. The child was seen by a consultant and was noted to be unharmed, and there were no safeguarding concerns.

Six days later the infant re-presented at hospital A with an acute collapse. The computerised tomography (CT) scan showed an extensive intracranial bleed with mid-line shift. Two coagulation screens showed an un-clottable activated partial thromboplastin time (APTT) with normal prothrombin time (PT). No further investigations such as coagulation factor assays were performed. The infant had vitamin K administered before transfer to a tertiary centre, hospital B. He was transferred as a time critical transfer, details of the discharge summary and communication between hospitals was not available.

At hospital B the infant was electively intubated. Coagulation samples were sent to the laboratory ~8 hours following admission. His APTT was 101 seconds with normal PT and thrombin time. The BMS noted in the report that these were abnormal and requested a repeat, but the abnormal results were not discussed with a haematologist by either the laboratory or clinical teams. Solvent-detergent fresh frozen plasma (SD-FFP) was requested, and 3 units of SD-FFP were issued and transfused. This resulted in partial improvement in APTT to 47s but not full correction. After the third plasma transfusion, the results were discussed with a haematologist over 24 hours after admission to hospital B. A diagnosis of haemophilia A was made following specific blood tests for clotting factors (factor VIII found to be 7IU/dL). Factor VIII concentrate was administered 48 hours after admission, and 36 hours post APTT of 101s. The child also had a pulmonary haemorrhage and subsequently died from the intracerebral bleed. The case review noted that an intracranial arteriovenous malformation was the cause of bleeding. RCA identified lone BMS working overnight covering haematology/ blood transfusion with unclear SOP combined with lack of recognition of importance of isolated prolongation of APTT by clinical and laboratory staff as key factors and corrective and preventive action to address these were instituted.

There are several learning points from the case to help improve patient safety and care given in similar situations in the future with learning applicable to both clinical and laboratory teams. Essentially the diagnosis of haemophilia was delayed resulting in delayed institution of the right treatment.

An isolated prolonged APTT in a male infant (with normal PT and TT) is characteristic of severe haemophilia A (factor VIII) or B (factor IX deficiency). This requires urgent investigation, even outside core hours, as the correct replacement therapy can be lifesaving. This was missed in both the hospitals involved. At each hospital, no contact was made by either the clinical or the laboratory staff to immediately alert the haematology medical staff to seek advice or arrange factor assays. Intracranial haemorrhage is a recognised presentation of severe haemophilia at this age and although this child had an AV malformation, the previous history of a fall down the stairs 6 days prior has added significance. If the haemophilia had been known the child would have received prophylactic factor cover. Vitamin K is not indicated for treatment of an isolated prolonged APTT.

The BMS in the second hospital was under pressure, lone working on night shift covering haematology, coagulation and blood transfusion. Whilst coagulation results are often abnormal in patients in ICU, medical staff also failed to recognise the significance of isolated prolongation of APTT in a male infant with intracranial bleeding. The standard operating procedures (SOP) have been revised appropriately to clarify laboratory action when there is an isolated prolonged APTT and procedures for authorising FFP. Laboratory staffing has been reviewed with a plan to ensure that there are two qualified BMS at night with clear policy for escalation. The UK Transfusion Laboratory Collaborative standards (2014, being updated currently) set out the minimum standards for staff qualifications, training, competency and the use of information technology in hospital transfusion laboratories and compliance with these are accepted by both the United Kingdom Accreditation Service (UKAS)/Clinical Pathology Accreditation (UK) Ltd (CPA) and the Medicines and Healthcare products Regulatory Agency (MHRA) as evidence to support their inspection programmes for laboratories.

This case also demonstrates the importance of a comprehensive, full handover of complex patients between hospitals to ensure no relevant history or test results are overlooked. Education of clinical staff as well to be able to recognise red flags in interpreting basic haemostatic tests and the importance of timely management is vital.

Delay in requesting appropriate tests was a significant factor in this case. Clinical teams need to ensure that appropriate samples are sent based on clinical profile with correct tests requested, results followed up and actioned. Safe patient care is only possible when all staff involved work collaboratively with a shared responsibility. Coagulation screening is frequently performed in unwell patients, often inappropriately, and results are often misunderstood (Amukele et al. 2011, Samkova et al. 2012). Consultant and trainee haematologists will be able to assist in interpreting the results and taking appropriate actions. Figures 11a.3 and 11a.4 summarise the basic coagulation tests and their interpretation.

Learning points

- Severe abnormalities of coagulation in a bleeding patient require urgent discussion with a haematologist
- Severe bleeding disorders can present in neonates and early childhood in the absence of family history
- In the neonatal period and up to 6 months of life the interpretation of coagulation results can be complex and normal ranges appropriate for age and gestation should be used, thus underlining the need for early specialist input
- Laboratory coagulation standard operating procedures should state what action to take when there is an unexpected isolated prolonged APTT. There should be urgent discussion with a haematologist. Factor VIII and IX assays should be performed as an emergency so that the missing factor can be replaced. Fresh frozen plasma does not contain a sufficient concentration of the missing factor to correct haemophilia A or B and treat bleeding in this setting
- Communication between hospitals during patient transfer must be comprehensive and include all laboratory information including any pending results
- Clinicians must provide laboratory staff with relevant clinical information so that they provide appropriate interpretation of results and be open to challenge by laboratory staff
- A holistic systems approach to incident investigation, reviewing timelines and mapping events throughout the patient journey would help to identify missed learning opportunities

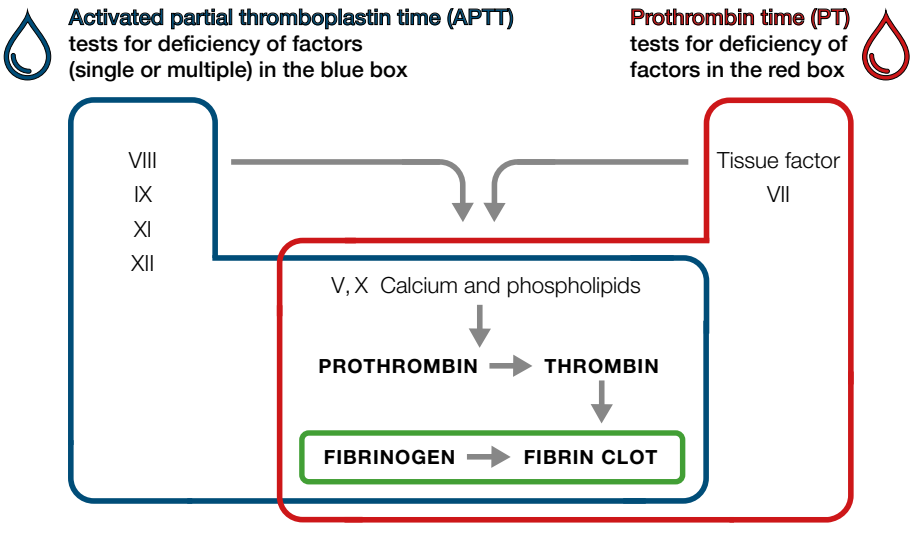

Figure 11a.3: Mechanisms of the coagulation screen to show which coagulation factors affect the standard tests

Figure 11a.4: Interpretation of the coagulation screen

Prothrombin time	Activated partial thromboplastin time	Thrombin time	Interpretation
Abnormal	Normal	Normal	Factor VII deficiency
Normal	**Abnormal**	Normal	Deficiency of FXII, XI, **IX, VIII** (single or multiple)
Abnormal	Abnormal	Normal	Deficiency in the common pathway, isolated V or X deficiency. Multiple factors e.g. liver disease, warfarin therapy

Notes: *many sick patients have disturbances of coagulation tests that* ***do not predict bleeding (and in some cases are associated with a thrombotic risk)****. These tests were introduced in the 1960s to screen for congenital factor deficiencies. The PT is very sensitive to FVII deficiency and is used for warfarin monitoring but note that the APTT will also be prolonged (because FIX is reduced) but to a lesser extent. The sample must be taken carefully (good venepuncture, free flow) to avoid activation and in the correct volume (as it is taken into a specific volume of anticoagulant citrate) to avoid erroneous and misleading results.*

Isolated prolongation of the APTT can be due to haemophilia A (FVIII deficiency) or B (FIX deficiency,) where the need for diagnosis and treatment is urgent. It is also prolonged in FXII deficiency (common but of no clinical significance) and factor XI deficiency (uncommon and usually not associated with serious bleeding). The thrombin time does not depend on other coagulation factors as thrombin is added to the test system. Many laboratories measure the amount of fibrinogen rather than the thrombin time. (Prolongation of standard coagulation tests can also be caused by inhibitors).

Vitamin K results in increased synthesis of factors II, VII, IX and X so will correct the PT but not FVIII, FXI, V or X deficiency. Normal ranges are different in childhood and any hospital with paediatric patients must use an age-appropriate normal range to avoid unnecessary investigation and treatment.

Near miss delays n=1

A major haemorrhage call was initiated for a patient with an obstetric bleed. Emergency group O D-negative red cells were not available from the two satellite refrigerators due to the need for temperature calibration but were rapidly released from the main laboratory. Laboratory staff had not informed clinical staff that no emergency units would be available from the satellite refrigerators.

Conclusion

The cases reported and described above are of extreme concern and demonstrate systemic shortcomings that should be urgently addressed. These include review of the porter services and emergency back-up arrangements. Where the use of refrigerators has to be suspended temporarily (or longer) for maintenance there must be clear communication of alternative procedures for emergencies.

The management of major haemorrhage continues to require improvement in many hospitals with attention to streamlining communication, training and drills.

References

Amukele TK, Baird GS and Chandler WL. (2011) Reducing the use of coagulation test panels. *Blood Coagul Fibrinolysis* 2011;**22(8)**:688-695.

NPSA (2010) NPSA Rapid Response Report: The transfusion of blood and blood components in an emergency' 21 October 2010. https://www.transfusionguidelines.org/document-library/documents/npsa-rapid-response-report-the-transfusion-of-blood-and-blood-components-in-an-emergency-21-october-2010-pdf-100kb [accessed 08 June 2020].

Samkova A, Blatny J, Fiamoli V, et al. (2012) Significance and causes of abnormal preoperative coagulation test results in children. *Haemophilia* 2012;**18(3)**:e297-301.