8 Delayed Transfusion Reactions

Definition

Delayed transfusion reactions are defined as those occurring more than 24 hours following a transfusion of blood or blood components. In practice, these are usually delayed haemolytic reactions due to the development of red cell alloantibodies. Simple serological reactions (antibody development without a positive DAT or evidence of haemolysis) are excluded.

Forty-four questionnaires were received, one of which was transferred to the Incorrect Blood Component Transfused section.

This section describes the main findings from 43 completed questionnaires.

Patients

17 males and 26 females.
Ages ranged from 30 to 88.

Outcomes and imputability

Number of reports: 43
Haemolytic: 42
Non-haemolytic: 1

Five patients died, none thought to be related to the transfusion (Imputability 0).

Fourteen patients were asymptomatic with a positive DAT only.

Twenty-three patients had evidence of increased red cell destruction without renal impairment:

- In 9 cases the only sign was a fall in haemoglobin (spherocytes were noted in one case).
- In 14 cases there was a fall in haemoglobin and a raised plasma bilirubin (spherocytes were noted in 2 cases). Haemoglobinuria was also noted in two of these cases. In one (case 11), an autoantibody had also developed, and it is therefore unclear whether the signs of haemolysis were due to allo or autoantibody, or both.

Five patients had increased red cell destruction and renal impairment; one died unrelated to the transfusion, whilst the other 4 did not suffer any long term morbidity:

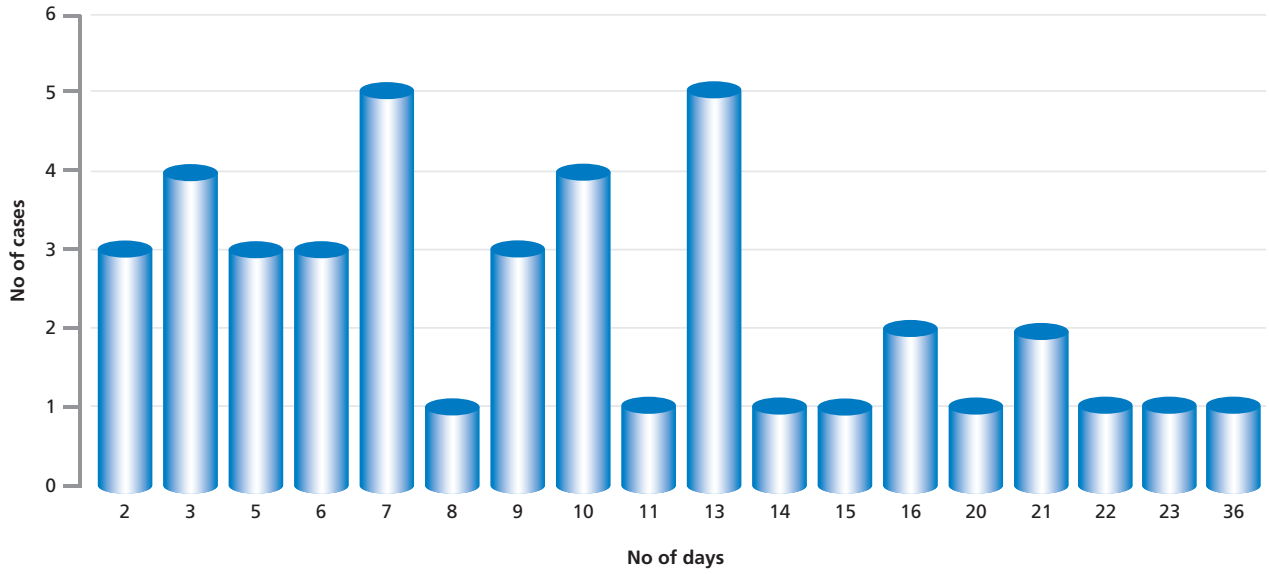
- Case 4 had a raised bilirubin and signs of deteriorating renal function 11 days post transfusion; however, it is not clear that the latter was related to the transfusion. This patient was already on the intensive therapy unit (ITU) following re-do coronary artery bypass grafting and mitral valve replacement.
- Case 7 had haemoglobinuria, raised plasma bilirubin and deteriorating renal function 13 days post transfusion, and required re-admission to hospital.
- Case 10 was re-admitted 9 days post transfusion with abdominal pain and frequency. On day 10, there was laboratory evidence of deteriorating renal function and disseminated intravascular coagulation (DIC), and the patient had jaundice and dark urine.
- Case 20 required ITU admission with falling Hb, raised plasma bilirubin and deteriorating renal function 13 days post transfusion.
- Case 36 had vomiting and tachycardia, 13 days post transfusion. The plasma bilirubin was raised and there was evidence of deteriorating renal function. However, the imputability is low, with the reaction only possibly related to the transfusion. The patient subsequently but co-incidentally suffered a cardiac arrest and died.

Non-haemolytic reactions

There was a single case report of a non-haemolytic delayed reaction.
See vignette for details (case 12, page 39).

Figure 6

Time relationship to transfusion



Median = 9 days

Range = 2 to 36 days

Figure 6 shows the interval in days between the implicated transfusion and signs or symptoms of a DHTR. The intervals given are necessarily those when the signs or symptoms were first noted. However, it is likely that some extravascular haemolysis was ongoing during or shortly after the transfusion in those cases where the causative antibody was retrospectively detectable in the pre-transfusion sample, or when the reaction was clinically noted within 48 hours of the transfusion.

Serological findings

25 (60%) of cases developed Kidd antibodies, either singly or in conjunction with other specificities. One patient with sickle cell disease and sepsis had a severe haemolytic episode two days post transfusion, but had no detectable antibodies. Table 11 shows the specificity of new antibodies detected post-transfusion, by blood group system.

Table 11

New specificities by blood group system

Antibody specificity by blood group system	Number of cases	Sole *new* antibody
Kidd		
Jk^a	19	14
Jk^b	6	1
Rh		
C^w	1	0
E	9	3
c	4	1 (with anti-E)
D	2	0
C	3	0
ce	1	1
Kell		
k	1	1
Duffy		
Fy^a	7	4
Fy^b	1	1
MNSs		
S	1	0
M (37°C)	1	0
Other		
Lu^a	1	0

Techniques Used

Table 12 shows the technology used for antibody screening by IAT.

Table 12

IAT technology used for antibody screening

IAT screening technology	Number of cases	By automation
BioVue	14	14 (100%)
DiaMed	24	16 (67%)
Solid phase	3	3 (100%)
DiaMed/Solid phase	1	no answer

Retrospective testing findings

Retrospective testing was undertaken in 21 (50%) cases; the same result was obtained in 19 of these. In the other 2 cases, anti-Jk^a was retrospectively detected in the pre-transfusion sample. In the first of these, the antibody was detected using additional techniques (PEG and enzyme IAT); in the second, the antibody was detected in the full panel, but not the screen, despite the presence of a Jk(a+b-) cell on the 3-cell screening panel. In both cases the anti-Jk^a was detected by IAT, 3 days post transfusion.

Clinical management and review

21 (50%) of cases were referred to the NBS and 38 (90%) to the HTC. One case was reported to neither.

Vignettes

Case 12

A 48 year old female patient was transfused with 4 units of red cells for menorrhagia. Two days later she suffered from joint swelling and pain, particularly in the knees, and was treated with antihistamines. The presence of anti-IgA antibodies in the patient's serum was confirmed by the reference centre and was the presumed cause of this unusual reaction.

Case 11

A 30 year old, transfusion dependent male patient with ß-thalassaemia major received a regular 2 unit red cell transfusion. The patient had known anti-C^w and anti-Kp^a, but the anti-C^w was no longer detectable and, following blood service policy (and national guidelines), crossmatch compatible blood was given. Twenty-one days later, the patient's Hb was lower than expected, although no investigation was undertaken at that time. Forty-one days post transfusion, retesting demonstrated a strongly detectable anti-C^w and a weak auto anti-e, with both specificities present in an eluate made from the patient's red cells. There was further evidence of haemolysis demonstrated by a raised plasma bilirubin.

Although it is not clear whether the allo anti-C^w or the auto anti-e was responsible for the haemolysis, this case raises an interesting point about policies for not selecting antigen negative red cells for patients with antibodies to low incidence antigens, when the antibody is no longer detectable. This is especially pertinent in patients requiring chronic transfusions.

COMMENTS AND RECOMMENDATIONS

No new recommendations are made this year. The recommendations made in last year's report remain pertinent and are restated here.

- Investigation of a suspected DHTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. This may involve referral to a reference centre.

  Action: Hospital blood transfusion laboratories

- Automated systems or changes to IAT technology should be validated using a range of weak antibodies to ensure appropriate sensitivity.

  Action: Hospital blood transfusion laboratories

- Consideration should be given to issuing antibody cards or similar information to all patients with clinically significant red cell antibodies. These should be accompanied by patient information leaflets, explaining the significance of the antibody and impressing that the card should be shown in the event of a hospital admission or being crossmatched for surgery. Laboratories should be informed when patients carrying antibody cards are admitted.

  Action: The CMO's NBTC and its counterparts in Scotland, Wales, and Northern Ireland

- There is a need for a review, co-ordinated by a professional national body, of how long specimens should be kept post-transfusion. The review needs to consider the relative risks and benefits of storing specimens beyond the time that they are suitable for use in further crossmatching tests.

  Action: BBTS and BCSH