12. Transfusion-Transmitted Infections

Definition

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection;

  and, either

- at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

  or

- at least one component received by the infected recipient was shown to contain the agent of infection.

Reports of suspected transfusion-transmitted infections

During 2006, 28 reports of suspected transfusion-transmitted infections were made from blood centres throughout the UK to the NBS/HPA Centre for Infections Surveillance. All UK blood centres contributed to the scheme. One additional report was also received from a hospital to MHRA (via SABRE) that had not been reported through routine blood service surveillance (see commentary below); this case has been included in the numbers below (29 cases in total).

Two reports (bacteria) were determined to be TTIs according to the above definition. Twenty-five cases were concluded as not transfusion-transmitted infections (5 hepatitis B [HBV], 2 hepatitis C [HCV], 1 hepatitis A [HAV], 1 HIV, 2 CMV and 14 bacteria). One (hepatitis C) involved a multi-transfused patient (dates of transfusion between 1997 and 2005) that could neither be confirmed nor refuted as a TTI, as 3 donors could not be traced. One case (HBV) is pending complete investigation.

A further report was received from the Health Protection Agency of a clinical diagnosis of vCJD in a blood transfusion recipient.

Case report of transfusion-transmitted Klebsiella pneumoniae

One recipient (54-year-old male) with AML received 1 unit of pooled platelets (3 days old). Within 5 minutes of starting the transfusion he became acutely unwell and the transfusion was terminated. The patient was given hydrocortisone and piriton, but died 24 hours post transfusion. The findings confirmed death due to overwhelming septic shock subsequent to either live Gram negative bacteraemia, or as a result of a lethal exposure to Gram negative bacterial endotoxin. *Klebsiella pneumoniae* was isolated from the platelet pack, but not from a sample taken from the patient at the time of transfusion. The platelet pack had been screened as part of a field trial of the BacT/ALERT* system prior to issue and was negative after 24 hours' culture. Four associated red cell units and 3 associated FFP units were investigated and were negative. Skin and throat swabs were taken from all 4 donors and were also negative. Archived plasma donations from all donors were investigated by PCR for *Klebsiella*-specific DNA but none was detected. Extensive investigation of the blood centres at which the component was manufactured, tested and issued did not reveal the presence of *Klebsiella* spp. on or in any of the equipment involved. The investigation concluded that this was bacterial contamination of a pooled platelet unit with *Klebsiella pneumoniae*; no source of the contamination was found.

* BacT/ALERT is a fully automated blood culture system for detecting bacteraemia and fungaemia based on detection of CO_2 production by any organisms present. As well as its clinical application in the diagnosis of bacteraemia, it is validated 'CE marked' and FDA approved for quality control testing of apheresis and platelet concentrates [35,36].

Case report of transfusion-transmitted Streptococcus bovis

A 90-year-old female recipient was found to have low platelet count and bleeding symptoms during an outpatient visit and received pack two of a three part apheresis platelet donation (3 days old). One hour later the patient collapsed on her journey home. She was admitted to A&E where she was resuscitated. On readmission to hospital she was febrile, tachycardic, hypotensive and hypoxic. Cultures were taken and broad spectrum antibiotics and fluids were started. In the initial 48 hours after transfusion she developed signs of mild cardiac failure and renal impairment. *Streptococcus bovis* (biotype II) was cultured from the patient's blood cultures and from the apheresis platelet pack. Pulsed field gel electrophoresis (PFGE) on the isolates from the patient's blood and platelet pack revealed them to be indistinguishable. The patient made a full recovery.

Because of the strong association between *S. bovis* bacteraemia and gut pathology, the donor was referred to the local hospital for colonoscopy and ongoing management. This revealed diverticular disease, together with two small dysplastic tubular villous adenomas, which were removed. It is suspected the donor's diverticular disease was the cause of the *S. bovis* contamination of the platelet donation. The donor was removed from the donor panel and thanked for many previous platelet donations.

Pack 1 of the apheresis donation was transfused to another patient, also on day 3 of the shelf-life, with no adverse reaction. The recipient's blood cultures were negative and the remnants of the implicated pack were investigated but no organisms were isolated. Pack 3 had also been transfused successfully on day 3 of the platelet shelf-life, but the empty pack was not available for investigation. This recipient was on high-dose antibiotics at the time of the transfusion.

This case was concluded to be a proven case of bacterial contamination of an apheresis platelet unit with *Streptococcus bovis*, the source of which was asymptomatic bacteraemia in a donor with undiagnosed asymptomatic diverticular disease.

Reports of further incidents

vCJD

In early 2007, the Health Protection Agency gave notification of a fourth case of vCJD infection associated with blood transfusion. In late 1997, a recipient received transfusion of a number of blood components. The donor of one of the units of non-leucodepleted red cells developed symptoms of vCJD about 17 months after this donation. The recipient developed symptoms of vCJD 8.5 years after receiving the transfusion. The donor is the same as that of Case 3, reported in the SHOT 2005 report. The recipient has since died.

(For more information on variant CJD see http://www.cjd.ed.ac.uk.)

Reports from previous years

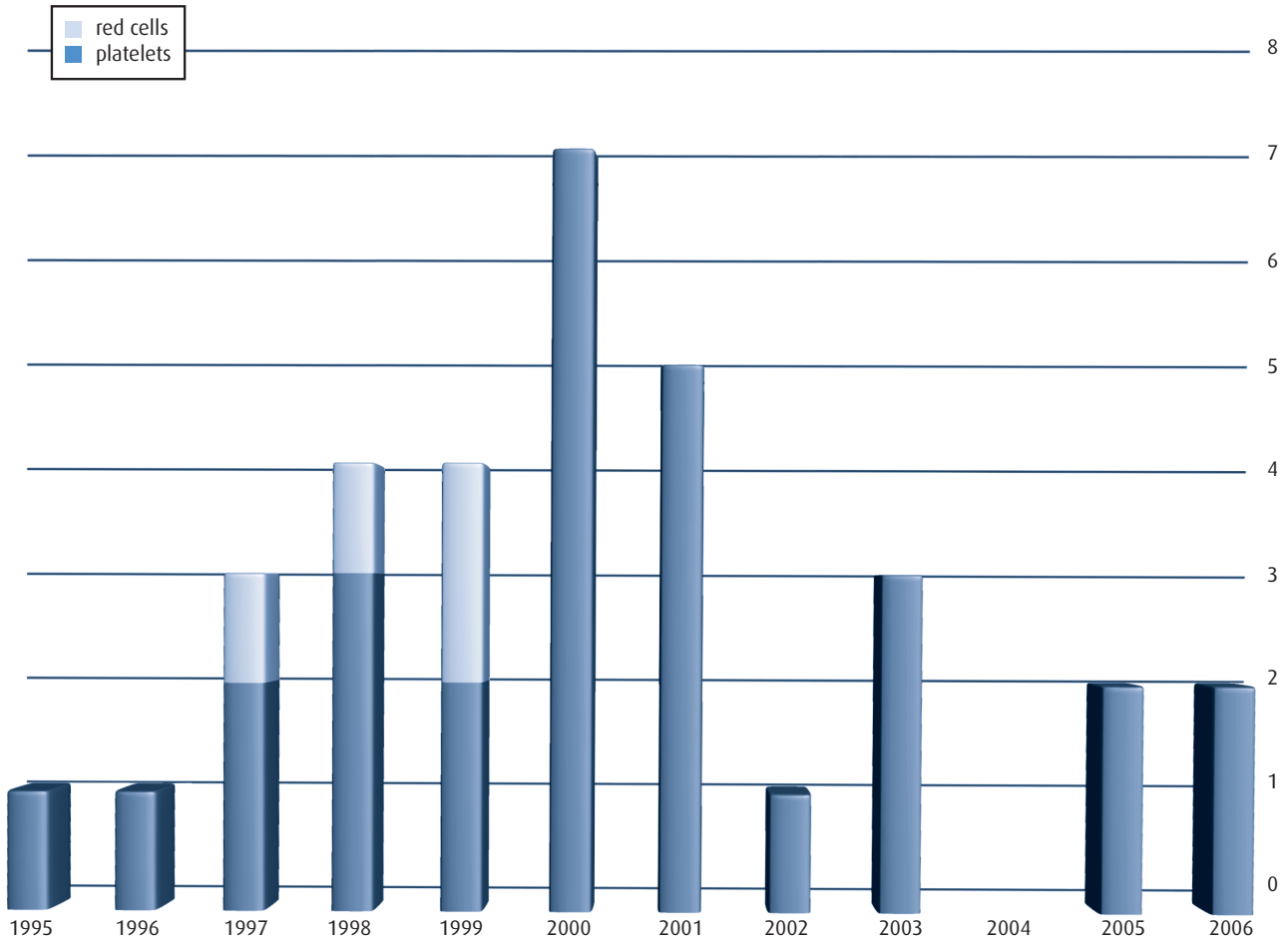
The case reported as pending in 2004 (HHV-8) is now nearing completion; all donors have been recalled and have provided blood samples for HHV-8 testing. Results will be reported when available. The pending HCV case from the 2005 report has been confirmed as not transfusion-transmitted.

Cumulative bacterial data

Since 1995, 33 cases of transfusion-transmitted bacterial infection have been reported (figure 16), of which 9 recipients died (8 due to the transfusion and 1 due to their underlying disease). The majority of these cases (n=29) relate to platelet units (10 apheresis and 19 pooled). In 2004 there was a further incident involving contamination of a pooled platelet pack with *Staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely (not included in figure 16).

Further cumulative data[37] are available at http://www.hpa.org.uk/infections/topics_az/BIBD/menu.htm.

Figure 16
Confirmed bacterial transfusion-transmitted infections, by year of transfusion and type of unit transfused (Scotland included from 10/1998)



COMMENTARY

- The number of cases reported to the scheme is small and fluctuations are to be expected. Infectious complications following transfusion differ from non-infectious complications in several ways that may affect their identification and investigation. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of incidents in a particular year can therefore accrue over subsequent years, and the number ascertained by the end of any period may not necessarily represent the number of infections transmitted. The reporting of incidents involving acute infections that tend to be clinically apparent and diagnosed within days after receipt of the infectious transfusion, such as bacteraemia, may be relatively complete, but incidents involving chronic viral infections may not. This year there were no confirmed viral transmissions, which is consistent with the current very low estimated risk of HIV, HCV, HBV and HTLV infectious donations entering the UK blood supply. The estimated risk in the UK is broadly similar to that in other northern European countries and lower than southern European countries[37].

For current UK risks see http://www.hpa.org.uk/infections/topics_az/BIBD/est_freq_uk.htm).

- One case was initially reported via MHRA as transfusion-transmitted bacteria, which had not been reported via routine NBS/HPA surveillance. This case had been notified to the local blood centre by the HTT and the pack was reported to have been sent to the blood centre. However, it was not received by the blood centre and was therefore not tested. Upon further investigation, the case was determined to be not caused by transfusion, as the isolate identified in the patients blood culture was different to that identified in the pack by the hospital microbiology laboratory. Hospital transfusion teams should ensure that all samples sent for bacterial investigation to their hospital laboratory should record that the sample is part of an investigation into a suspected bacterial transfusion transmission and that all results are collated by the hospital team, prior to making the confirmatory report to MHRA. Additionally, correct sampling of the pack is important to avoid external contamination or the introduction of environmental contaminants. Advice can be obtained from the blood services. Guidance for hospitals can be found

on the NBS hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer.

- The report of a fourth case of vCJD infection increases the concern about the risk of vCJD transmission by blood transfusion. The patient is one of a small group of recipients of blood from donors who later developed vCJD. These recipients have been notified of their possible exposure to vCJD and are under surveillance: this represents active case finding. All 4 cases to date relate to the transfusion of blood components prior to the introduction of leucodepletion; none relate to plasma products. Since 1997 the blood services have introduced a number of precautionary measures against the risk of vCJD. This includes leucodepletion of all blood components (since 1999), the use of methylene blue virally inactivated FFP obtained outside the UK for children under 16, importation of plasma for fractionation, imported solvent detergent (SD) treated FFP for adult patients with thrombotic thrombocytopenic purpura (TTP) and the exclusion of donors who have received a blood transfusion in the UK since 1980.
- The Standing Advisory Committees (SAC) of the Joint UKBTS/NIBSC Executive Liaison Committee (JPAC) make recommendations to the Guidelines for the Blood Transfusion Services in UK in relation to the prevention of transfusion-transmitted infections. For example, SAC Transfusion-Transmitted Infection (SACTTI) regularly reviews the residual risk of transfusion-transmitted HCV, HIV, HBV and HTLV infections to assess any need for additional testing methods, such as HIV RNA testing, HBV DNA or anti-HBc. SAC Care and Selection of Donors ensures donor deferral criteria are optimal in terms of exclusion of donors with behaviour that may put them at increased risk of contracting transfusion transmissible infections. Major decisions are considered by the DH Microbiological Safety of Blood, Tissues and Organs committee.

RECOMMENDATIONS

- Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately, both to MHRA and the blood services. Guidance for hospitals can be found on the NBS hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer. Other services need to be discussed with the supply blood centre.

  Action: HTTs

- Despite good donor selection guidelines, some donors with infections might go on to donate, as in the donor above with undiagnosed diverticular disease. This is rare. Surveillance of testing blood donors for viral infections shows that a tiny proportion of donors have viral infections[38]. It is important for UK Blood Service collection teams to remain vigilant for signs or symptoms of disease and risk factors for infection in potential donors and ensure that guidelines are adhered to, in order to reduce the risk of transmission of blood-borne infections.

  Action: UK Transfusion services

- Hospitals should consult the blood services about the investigation of transfusion reactions suspected to be due to bacteria. Attention should be paid to the sampling and storage of implicated units or their residues and packs returned to blood services for testing. The case reported via MHRA that did not reach the blood service highlighted the need for laboratory reports within each hospital to be clearly marked as part of a suspected transfusion reaction and copied to the HTT. (See above weblink or http://www.transfusionguidelines.org.uk/index.asp?Publication=REGS&Section=23&pageid=789 for more information.)

  Action: HTTs