TRANSFUSION MEDICINE
Official Journal of the British Blood Transfusion Society
British Blood Transfusion Society
Transfusion Medicine | LETTER TO THE EDITOR

Thrombocytopenia secondary to passive transfer of anti-HPA 1a antibodies from male donor plasma

Thrombocytopenia is a rare complication of transfusion. The passive transfer of anti-human platelet antigen (anti-HPA) antibodies from plasma-containing blood components can cause thrombocytopenia in recipients with cognate platelet antigens. This is predominantly seen with female donors who have been previously sensitised through pregnancy. It can, however, occur with donors of either gender who have been sensitised through prior transfusion. We describe a rare example of passive anti-HPA antibody transfer from the plasma of a male blood donor causing acute thrombocytopenia.

A 58-year-old renal transplant recipient was admitted to hospital for investigation and management of acute kidney injury. She had received a deceased donor kidney transplant 13 years before for end-stage renal failure attributed to glomerulonephritis. Prior to her transplant, she had been maintained on haemodialysis for 11 years. Past medical history was significant for ischaemic heart disease, parathyroidectomy and ileal conduit (and reversal). A renal biopsy was consistent with antibody-mediated rejection. She was commenced on plasma exchange, intravenous immunoglobulin (IVIG) and Bactrim (trimethoprim/sulfamethoxazole). A new thrombocytopenia was observed on routine blood tests 24 h after the third day of plasma exchange, with a platelet count of 7×10^9/L (previously normal). This was confirmed on repeat testing. Clinically, she had a large haematoma over the site of a subcutaneous heparin injection but, fortunately, did not have any other bleeding sites. Her platelet count improved over 10 days without requiring transfusion support (see Fig. 1). Plasma exchange was continued during this period.

Heparin was initially withheld; testing for heparin-induced thrombocytopenia (HIT) did not proceed given a low pre-test probability (4 T score of 3: low risk). The time frame did not match the commencement of Bactrim, and the thrombocytopenia improved without discontinuation of this drug. Samples were sent to the Platelet and Granulocyte Reference Laboratory at the Australian Red Cross Blood Service (the Blood Service) for further investigation.

Testing of the fresh frozen plasma (FFP) donors with a monoclonal antibody-specific immobilisation of platelet antigens (MAIPA) assay demonstrated that one of the five donors had anti-HPA-1a antibodies. The donor was subsequently genotyped and found to have a HPA-1bb genotype. The recipient also had a genotype performed and was found to be HPA-1aa. Anti-HPA-1a antibodies were not detected in the patient's serum.

On review, the donor was noted to have provided plasma for 17 other patients. Treating clinicians were notified of the adverse transfusion reaction. Five clinicians reported post-transfusion falls in platelet count. Four were attributed to alternate causes, and one was considered a possible unrecognised adverse transfusion reaction.

Follow up of the implicated donor revealed a distant history of likely red cell transfusion following a motor vehicle accident 18 years prior. The donor was permanently deferred from providing blood components for clinical use. He was also advised to notify treating physicians of his HPA genotype. HPA1bb is an uncommon genotype, and transfusion of HPA-1a platelets would be predicted to result in poor post-platelet transfusion increments and increase the risk of post-transfusion purpura (PTP).

Thrombocytopenia is a rare complication of blood transfusion. Pregnancy, transfusions and transplantation can lead to formation of platelet alloantibodies. These can be clinically significant in a number of settings, including PTP, fetal–neonatal alloimmune thrombocytopenia (FNAIT) and passive alloimmune thrombocytopenia. Passive alloimmune thrombocytopenia secondary to the transfer of platelet antibodies occurs immediately after or during the transfusion of plasma-containing blood products. It is more likely to occur in the context of female blood product donations due to potential sensitisation during pregnancy (Pavenski *et al.,* 2008). Due to the higher incidence of alloantibodies in female donors [which is also a risk factor for transfusion-related acute lung injury (TRALI)], the Blood Service introduced a policy of male-only clinical plasma in 2007 and male-only apheresis platelets in 2013.

Passive alloimmune thrombocytopenia was first reported in 1987 (Ballem *et al.,* 1987), and the first fatal case was reported in 1999 (Solenthalar *et al.,* 1999). A literature review performed by Pavenski *et al.* (2008) identified 19 reports of passive alloimmune thrombocytopenia; all of these cases were associated with female blood donors with a history of pregnancy (Pavenski *et al.* 2008). Subsequent to this review, another case involving a female donor has been published (Collins *et al.,* 2013). Lookback processes (including in our case) have identified additional patients developing severe thrombocytopenia post-transfusion of blood components from the same donor – suggesting that this diagnosis may be under-recognised (Solenthalar *et al.,* 1999). There has been one suspected case where the implicated donor was of male gender (Drakaki & Blanchard, 2013); however, donor antibody detection and recipient genotyping was either not performed or not reported.

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First published online 6 June 2018
doi: 10.1111/tme.12542

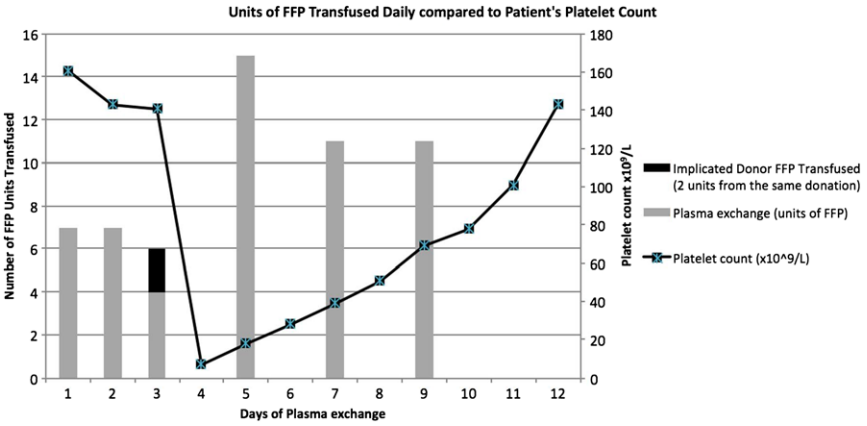

Fig. 1. Trajectory of patient platelet count in the context of FFP transfusion.

The detection of anti-HPA-1a antibodies in the donor in conjunction with HPA-1aa recipient genotyping and a precipitous drop in the platelet count following transfusion is considered diagnostic in this case. Anti-HPA-1a antibodies were not detected in patient serum; this has been recognised previously and attributed to the clearance of the passively transfused antibodies attached to the patient's platelets via the reticuloendothelial system (Brunner-Bolliger *et al.,* 1997). Alloimmune thrombocytopenia related to secretion of anti-platelet antibodies by donor-derived passenger lymphocytes (West *et al.,* 1999) was considered clinically improbable given the significant passage of time since kidney transplantation (13 years).

Passive transfer of anti-platelet antibodies is a rare but serious complication of blood transfusion. This is the first confirmed case from a male donor. The case highlights that this complication can still occur (despite the use of male-only clinical plasma and apheresis platelets) and should remain in the differential diagnosis for acute thrombocytopenia in the context of recent transfusion of plasma-containing blood components.

ACKNOWLEDGMENTS

The Australian government funds the Australian Red Cross Blood Service for the provision of blood, blood products and services to the Australian community. F. S. reviewed the case and literature and wrote the paper. J. C. and R. F. evaluated the patient and results and liaised with the Blood Service regarding further investigations. S. B. evaluated the patient's results and guided Blood Service investigations. M. B., P. H., K. H., G. J., D. M., G. P. and R. H. performed the additional investigations and analysed the data. All authors revised the paper and approved the final version.

CONFLICT OF INTEREST

The authors have no competing interests.

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