Case Report

Passive transfusion of anti-D: a case report to enhance awareness of donor screening and clinical significance

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Background: Blood components collected from volunteer donors remain a cornerstone of modern healthcare, yet there are risks with any transfusion of foreign blood products. These products may contain clinically relevant alloantibodies due to alloimmunization of volunteer blood donors. The process of donor screening, the utilization of blood products containing alloantibodies, and the clinical implications of these products being transfused is rarely discussed in literature.

Case Description: We present a case of passively transfused anti-D alloantibodies in two red blood cell (RBC) units from the same donor given to D-negative recipients. Each recipient had a negative antibody screen prior to transfusion, followed by detection of anti-D on subsequent screening at different facilities. There was no patient harm, but additional workup was required in order to direct clinical management.

Conclusions: The purpose of this case report is to briefly review the screening of RBC blood donors for alloantibodies, identification of units from such donors from a regulatory framework, and the potential impact on patient care after transfusion of these blood products. Without a national surveillance system or adequate transfusion history, patients undergoing transfer of care are at risk for erroneous clinical management. This case highlights the importance of proper inter-institutional communication in order to avoid such mistakes.

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Introduction

The donation and transfusion of blood and blood products is well established as a standard of health care for a variety of clinical indications (1,2). Prior to transfusion, a recipient's blood is analyzed via type and screen to determine their blood type and the presence of any significant alloantibody. If an alloantibody is detected, the blood bank will select a unit of blood that is devoid of the corresponding antigen (3). The compatibility of units is further assessed with a physical crossmatch where donor cells and patient plasma are combined to see if they will agglutinate. In those cases where ABO and Rh blood group antigens are known (through duplicate testing) and where the recipient does not demonstrate acquired alloantibodies, physical crossmatch may not be required. There is no requirement for donor plasma of a red blood cell (RBC) unit to be tested against host cells.

In the US, the Association for the Advancement of Blood and Biotherapies (AABB) requires universal donor screening for RBC alloantibodies but testing methods vary by blood center. Food and Drug Administration (FDA) regulations require that when alloantibodies are present, the antigen specificity be listed clearly on the unit label (21 Code of Federal Regulations 606.121). The distribution

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of these products is blood center dependent. In many centers, units with alloantibodies are quarantined and never put into the blood supply whereas other centers send these units for transfusion at selected hospitals (4). When hospitals or transfusion centers transfuse units from these donors, subsequent positive antibody screens from the patient must be interpreted with caution to distinguish passive alloantibody from true alloimmunization. We present the following case in accordance with the CARE reporting checklist (available at https://aob.amegroups.com/article/view/10.21037/aob-21-68/rc) (5).

Case presentation

A 69-year-old male presented with symptoms consistent with acute gastrointestinal (GI) bleeding. His blood pressure was 94/54 mmHg and a complete blood count revealed significant anemia with a hemoglobin of 5.4 g/dL and hematocrit of 18%.

RBC transfusion was requested, and a type and screen was performed. Using column agglutination technology (ABO-Rh gel testing) the patient was determined to be O via forward and reverse typing and RhD negative on forward type. The patient also had a negative pre-transfusion antibody screen by testing the patients serum in the presence of Panoscreen reagent cells, Immucor (Norcross, GA, USA), using Ortho Vision Analyzer, Ortho Clinical Diagnostics (Raritan, NJ, USA). Over the next 12 hours the patient received six units of O Rh-negative blood, each of which were retyped and confirmed to be Rh-negative prior to transfusion per AABB requirements. The units were crossmatched by immediate spin at room temperature resulting in no reactivity and thus considered compatible. One of the units was identified on the label as containing anti-D. At the time of receipt of the unit, the label was noticed, and the outside blood supplier was contacted who said that the unit was safe to transfuse. The implicated unit was one of a double RBC collection (via apheresis) and was determined to have anti-D by using solid phase/NEO Iris Capture-R Ready Screen, Immucor.

Three days later, the patient was transferred to an outside facility. A transfusion was again requested, and type and screen were performed using gel testing. As before, the patient was determined to be O Rh-negative, but the new antibody screen detected anti-D with 2+ reactivity (0–4+ scale) in the presence of anti-human globulin (AHG). Upon notification of new antibody screen positivity in the recipient, an antibody screen was performed on a segment from all six transfused units. The segment from the unit labelled as containing anti-D was confirmed as positive for the antibody. Follow-up antibody screens for anti-D in this patient revealed minimal positivity at 13 days and no reactivity at 110 days.

The second recipient of the other implicated unit from the same donor was a 56-year-old female admitted to her local hospital for workup of ascites with positive CA 125 concerning for malignancy. The patient was transferred after an acute hypotensive episode for intensive care support. The malignancy workup was negative, but the patient continued to have persistent anemia, hemoglobin 6.6 g/dL and hematocrit 21.3%. The patient was also typed via identical methodology and found to be O negative with a negative antibody screen. During a 25-day hospitalization she received 5 units of RBCs to include the implicated unit, which was the last unit transfused 2 days prior to transferring back to her community hospital for rehabilitation.

The patient was readmitted 6 days after discharge for anemia and further evaluation for positive testing for anti-D at an outside laboratory evaluation. Blood type revealed ABO/Rh, which was consistent with prior transfusion. Anti-D was detectable in plasma, but a direct antiglobulin test (DAT) was negative, ruling down the possibility of acute or delayed hemolytic transfusion reaction and making passive anti-D transfusion the most likely explanation. No additional blood bank workup occurred after the admission and the patient was lost to further follow-up.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

In the laboratory scenario we describe, both patients demonstrated detectable anti-D antibodies. In most circumstances, this would indicate immunization to D antigen through prior exposure to allogeneic blood such as a previous transfusion or pregnancy (6,7), although alloimmunization through other sources is described in the literature (8,9). In pregnant patients, passive anti-D through Rh immune globulin (RhIG) must be differentiated from alloanti-D to guide management, an issue which can

be complicated by a lack of history and poor information exchange (10). Without a detailed transfusion history, a positive screen from passively transfused alloantibodies can be mistaken for actively produced alloantibodies. This may lead to the recommended use of antigen-negative units for all future transfusions. While this may be appropriate at first, erroneous selection of antigen-negative units after the alloantibody has diminished may reduce the donor pool and delay transfusion.

When blood is donated by eligible donors, samples are tested for ABO group, Rh type (including weak/partial D status), transmittable transfusion-related diseases, and unexpected alloantibodies (3). Recent analysis of the recipient epidemiology and donor evaluation study-III (REDS-III) database was done to assess the prevalence and risk factors for RBC alloantibodies in healthy US donors over a 4.5-year period. It showed that 0.51% of blood donations and 0.77% of blood donors have a positive unexpected antibody screen. The most common alloantibodies detected by the REDS-III were anti-D (26.4%), anti-E (23.8%) and anti-K (21.6%). Anti-D prevalence is overrepresented in previously pregnant but never transfused females, despite widespread use of RhIG, while anti-K is more common in previously transfused but never pregnant females. In males, anti-K is more common than any other alloantibody. They concluded that positive associations for alloimmunization include prior transfusion, previous pregnancy, female sex, Rh-negative status, and increased age (4). Additional analysis shows that the majority of donor alloantibodies are persistent, although 35% may become evanescent. Anti-D was persistent in 72% of cases (11).

Currently, the FDA does not regulate donor screening for unexpected RBC alloantibodies at the level of the blood center; instead, the AABB requires that serum/plasma of donors be tested for RBC alloantibodies, and if this is not completed the FDA requires a pre-transfusion minor crossmatch (recipient cells with donor serum) to exclude incompatibility (21 Code of Federal Regulations 606.151) (3). While most centers follow the AABB requirements, testing methodologies vary by center which induces differences in the sensitivity and extent of antibody identification (4). Furthermore, if an unexpected alloantibody is detected the FDA requires the label includes its presence, although the usage of such blood is dependent on the blood center (3,4). Products of high antibody concentration (platelets, plasma, or cryoprecipitate) are generally not distributed, but some centers still release alloantibody-positive RBC units, appropriately labelled, because they are still of value and generally safe (11,12).

Transfused alloantibodies against non-self antigens are not commonly seen in the clinical transfusion literature. Physiologic modeling would suggest no clinical impact, but studies in this field are limited. Additional methods of interpersonal transmission need to be reviewed for comparison. Recently, Sostin *et al.* (12) published a 7-case series of passive anti-C from RhIG administration over a 2-year period. None caused a positive DAT or clinically detectable hemolysis. Positive antibody screens were seen from 27–167 days post-infusion.

In conclusion, a small percentage of healthy US blood donors are positive for a clinically significant alloantibody, with anti-D being the most common. The FDA requires proper labeling and evidence of compatibility, but the distribution of such blood depends upon policies of the blood center itself. In cases of need, either medical or financial, these units may be released into the blood supply system with appropriate labelling. After transfusion, these passive alloantibodies are unlikely to cause an adverse reaction but may produce positive lab results on subsequent screening and require additional workup that can delay transfusion. To avoid such a situation relies on adequate detection of alloimmunized donors, recognition of the uncommon products from these donors, and understanding of consequences after transfusion of alloantibodies against non-self antigens. Inter-institutional transfers of care after transfusions further complicate the situation. With the lack of a national surveillance system, good interpersonal and institutional communication is vital to guarantee safe blood component therapy and avoid delays in testing and transfusion therapy.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://aob.amegroups.com/article/view/10.21037/aob-21-68/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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