Evaluation of a Possible Transfusion Reaction With a Positive Direct Antiglobulin Test in a 29-Year-Old Male

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DOI: 10.1309/W8A6EN2CV2X67F2D

Clinical History
Patient
29-year-old male.

Chief Complaint/History of Present Illness
The patient underwent orthopedic surgery for a left tibia/fibula fracture sustained in a motor vehicle collision. Postoperatively, he simultaneously received 2 units of red blood cells. Towards the end of the transfusion, the patient developed fever and chills. His temperature increased from 100°F to 102.1°F, pulse increased from 123 to 125, and oxygen saturation decreased from 100% to 92% on room air. His blood pressure was stable and there was no dyspnea.

Past Medical History
Negative.

Past Surgical History
Previous surgery of the left lower extremity.

Principal Laboratory Findings
Table 1.

Table 1. Transfusion Reaction Workup Results

<table>
<thead>
<tr>
<th></th>
<th>Pretransfusion</th>
<th>Posttransfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO/Rh</td>
<td>O Positive</td>
<td>O Positive</td>
</tr>
<tr>
<td>Plasma Color</td>
<td>Red</td>
<td>Straw</td>
</tr>
<tr>
<td>DAT</td>
<td>Negative</td>
<td>Weak positive</td>
</tr>
<tr>
<td>(confirmed microscopically)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine Hgb</td>
<td>Trace</td>
<td>Negative</td>
</tr>
<tr>
<td>Antibody screen (Gel)</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Antibody screen (PEG)</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Urine RBCs</td>
<td>0–2/HPF</td>
<td>Not performed</td>
</tr>
<tr>
<td>Abbreviated crossmatch (Unit 1)</td>
<td>Compatible</td>
<td>Compatible</td>
</tr>
<tr>
<td>Abbreviated crossmatch (Unit 2)</td>
<td>Compatible</td>
<td>Compatible</td>
</tr>
<tr>
<td>Full crossmatch Unit 1</td>
<td>Compatible</td>
<td>Incompatible</td>
</tr>
<tr>
<td>Full crossmatch Unit 2</td>
<td>Incompatible</td>
<td>Incompatible</td>
</tr>
<tr>
<td>Elution</td>
<td>Not applicable</td>
<td>Panreactive (1+)</td>
</tr>
</tbody>
</table>

*An improperly-collected, hemoglobin-tinged specimen was used for pretransfusion testing due to difficulty of recollection. Normal haptoglobin and indirect bilirubin levels support the absence of in vivo hemolysis.

*Positive (1+) with all panel cells tested.

DAT, direct antiglobulin test; Hgb, hemoglobin; PEG, polyethylene glycol; RBCs, red blood cells; HPF, high power field.

Questions
1. Why was an elution performed?
2. Which laboratory test should be performed next?
3. Did the transfusion of the second unit cause the patient's symptoms?
4. Did a transfusion reaction occur and, if so, what kind of reaction was it?
5. How should the clinician be advised regarding the cause of the patient's symptoms?
6. What further actions are necessary on the part of the laboratory?
7. Why was this not detected prior to the transfusion of blood products?
8. How common is this occurrence?

Possible Answers

1. In order to identify the nature of the antibody bound to the patient's red blood cells, an elution should be performed whenever a positive direct antiglobulin test (DAT) is encountered. A panreactive antibody, as seen in this case, suggests a warm autoantibody; however, other possibilities, such as an antibody to a high incidence antigen, should be considered. In this case, an alloantibody to high incidence antigen is not a possibility, since this would have been identified by the antibody screen performed routinely by the blood center.

2. In this case, there are seemingly conflicting results. The posttransfusion DAT is weakly-positive, and the elution is consistent with a warm autoantibody. However, the pre- and posttransfusion antibody screens were negative by 2 different methods. The origin of the antibody bound to the red cells in the posttransfusion sample, which was not in the pretransfusion sample, is unclear. The appropriate next step is to run a DAT on the full crossmatch-incompatible unit. As expected, the DAT on this unit was positive (2+); thus, the antibody was bound to the red cells in the donor unit and remained bound to the donor cells after the transfusion. This explained both the weak-positive DAT in the posttransfusion sample as well as the full crossmatch incompatibility. The donor in this case likely had a warm autoantibody bound to his red cells, thereby explaining the positive posttransfusion DAT and the panreactive elution results. If the DAT on the transfused unit had been negative, a plausible next step would be a full minor crossmatch, although an antibody in the donor's serum should have been discovered at the originating blood center unless that antibody showed specificity to a low-incidence antigen.

3. The transfusion of the “incompatible” unit was no more likely to have caused the patient's symptoms than the first unit. Since the autoantibody remained bound to the donor red cells,
if it were to cause hemolysis only the donor red cells would be affected. Furthermore, the autoantibody would only cause hemolysis in the recipient if it caused hemolysis in the donor. The donor did not have a hemolytic anemia, or he would have been ineligible to donate on the basis of his hematocrit. Therefore, it is highly unlikely that there will be hemolysis in the recipient, and it is safe to conclude that the autoantibody is clinically insignificant.

4. It is difficult to answer this question with the given information. The differential diagnosis includes 2 possibilities: febrile transfusion reaction, and coincidental fever. Although the donor units were leukoreduced, a febrile transfusion reaction is a distinct possibility; however, it is also possible that the patient’s symptoms were coincident with the transfusion. This is especially likely given that less than 24 hours had elapsed since the patient’s surgery. Follow up revealed that the patient continued spiking fevers over the next 24 hours, and atelectasis was seen on his chest radiograph. This information suggests that the patient’s symptoms were coincident with the transfusion, stressing the importance of reviewing the vital signs prior to, during, and following transfusion. The patient’s fever subsided, and he was discharged to home 4 days later.

5. The clinician should be advised that a hemolytic transfusion reaction did not occur. The autoantibody bound to the red cells of the donor unit caused the positive posttransfusion DAT. It should also be emphasized that the transfusion of a DAT-positive donor unit is not likely to be clinically significant. The competing possibilities of coincidental fever, versus febrile transfusion reaction, should be discussed with the advice to consider giving the patient acetaminophen prior to future transfusions if fever seems clinically likely. It should be noted that the posttransfusion DAT was very weakly positive. Routine microscopic examination of the DAT is not required. In this case, the technologist was suspicious of a weak reaction on visual examination and confirmed the weak reaction microscopically. It is open to debate whether such reactions should be reported or whether they are so weak as to be clinically insignificant. It is the policy of the authors’ institution to investigate and report such findings, especially given the gravity of a possible hemolytic transfusion reaction.

6. No further testing is necessary, although the blood center from which the unit in question was obtained should be informed that the unit had a positive DAT, and a review of the donor’s records is warranted. In this case, the donor was a 39-year-old male with a negative antibody screen. The incidence of warm autoantibodies increases with age. Even though the donor in question is relatively young, a warm autoantibody is not an unreasonable proposition.

7. Required pretransfusion compatibility testing includes an ABO and Rh type and antibody screen on the donor unit. A DAT is not routinely performed. The recipient must have a current type and antibody screen. If the antibody screen is negative, and the recipient does not have a history of any clinically-significant antibodies, an abbreviated crossmatch may be performed. Alternatively, if sufficient history is available, the recipient may be eligible for an electronic crossmatch. If the patient’s current antibody screen is positive, or if there is a history of a clinically-significant antibody, a full crossmatch is required. As stated above, antibody screening of donor units is required transfusion practice, but, in this case, an antibody was not detected in the donor unit. It is likely that it was negative because the autoantibody was bound to the patient’s red cells and not present in the serum. Since a DAT is not routinely performed on donor units, the antibody was not detected.

8. It has been estimated that between 1 out of 1,500 and 1 out of 14,000 donors are DAT positive. A relatively large percentage of DAT-positive individuals have negative antibody screens. One study found that 13 out of 20 DAT-positive units from healthy donors had a negative antibody screen because antibodies are bound to red cells and are not free in the serum at detectable levels. Because blood centers do not routinely perform a DAT on donor units, these would not be detected during component preparation. Furthermore, since this is clinically insignificant for the recipient, it would likely only be detected if there was a coincidental transfusion reaction or an unexplained incompatible full crossmatch. Therefore, the rate at which cases like this come to the attention of a transfusion medicine service is low.

Acknowledgements: The authors would like to acknowledge Dr. Marisa B. Marques for her helpful suggestions on the preparation of this manuscript.

Keywords: transfusion reaction, direct antiglobulin test, elution, blood donation