Ask a Pathologist: Delayed Hemolytic Transfusion Reaction

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Question: My patient received a cross-match compatible red blood cell transfusion last week, and now he has developed a new alloantibody to blood. The Blood Bank says it was caused by the transfusion last week, and that he is having a delayed hemolytic transfusion reaction. Could this have been prevented?

Answer: This patient experienced a delayed hemolytic transfusion reaction (DHTR) which usually occurs three to ten days after a transfusion that at the time appeared serologically compatible. This type of reaction usually happens in patients who have been previously exposed to foreign red cell antigens, either through transfusion or pregnancy. A red blood cell alloantibody is made after the initial exposure, but without ongoing exposure to the foreign antigen the alloantibody titer decreases over time to undetectable levels. When antibody levels are undetectable, the antibody screen will be negative and crossmatch testing performed in the blood bank will appear compatible even when the red blood cell units being tested express the offending antigen. After re-exposure to the antigen through transfusion, there is a rapid increase in alloantibody production, called an amnesic response, which binds transfused red cells and leads to hemolysis.

Delayed hemolytic transfusion reactions occur in approximately 1 in 1500 transfusions, and typically present as either an unexplained drop or a less than expected increase in hemoglobin after transfusion. They may also manifest as an unexplained increase in indirect bilirubin or an otherwise unexplained fever. DHTRs may vary significantly in severity. Although most reactions are mild or even sometimes clinically silent, occasionally these reactions may be quite severe. In 2013, there were 2 FDA reported fatalities attributed to delayed hemolytic transfusion reactions.

If a DHTR is suspected clinically, the blood bank should be notified to perform a transfusion reaction work-up including antibody identification and direct antiglobulin (DAT) testing. Once an alloantibody has been identified, the blood bank will select red blood cell units that are negative for the offending antigen for all future transfusions to prevent additional reactions.

Since the pre-transfusion blood bank work-up is usually negative in these cases, the only way to prevent this type of reaction is through a careful clinical history. It is very important for the blood bank to know about all patients with a history of antibodies to red cell antigens which may have been identified at other institutions. With clear communication between the blood bank, pathologist, and clinical team, patients with antibodies to red cell antigens and delayed hemolytic transfusion reactions can promptly identified and managed effectively through the reaction and for future transfusions.

References:

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