Rautenberg Factor: Transfusion Constraints During Cardiac Surgery

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THE KELL SYSTEM is a complex protein in the cell membrane of red blood cells (RBC), with 34 different surface antigens having been identified.[1] Antibodies develop to Kell antigens that are absent on an individual's RBCs in the same manner that antibodies develop to ABO blood system antigens. Kell antigens, including Kp^b, are prone to polymorphism due to mutations in the gene that encodes these antigens.[2] More than 99.9% of people have the wild type Kp^b+ Kell protein, also known as Rautenberg. Rare individuals who are Kp^b-, however, may develop the antibody to the Kp^b antigen, called Rautenberg factor (anti-Kp^b).[3] This antibody then may predispose a patient to a severe immune-mediated reaction if incompatible Kp^b+ blood is transfused. Herein the authors present the unusual case of an anemic individual with the rare Kp^b- phenotype and anti-Kp^b (Rautenberg factor) in need of urgent cardiac surgery.

CASE REPORT

An 84-year-old man presented to the hospital with acute chest pain and elevated myocardial enzymes in keeping with acute coronary syndrome. An echocardiogram revealed severe aortic stenosis with a mean transaortic gradient of 40 mmHg. A coronary angiogram demonstrated stenotic left anterior descending and circumflex coronary arteries. On the basis of these findings, coronary artery bypass graft (CABG) surgery and aortic valve replacement were indicated. The patient's hemoglobin level was 10.8 g/dL.

Surgery was scheduled, and 4 units of A+ cross-matched (ABO- and Rh-compatible) RBC units were made available by the local blood bank. During preoperative discussions with the patient, however, he questioned the compatibility of his cross-matched blood. He explained that his brother had suffered a severe hemolytic reaction to ABO- and Rh-compatible blood during surgery years earlier. Blood testing subsequently revealed that both the patient and his brother were Kpb- and each had Rautenberg factor (anti-Kp^b) in their serum. Presumably, the patient's current anti-Kp^b antibody titers were too low to be detected during conventional preoperative cross-matching.

Surgery subsequently was postponed in order to solicit the input from the blood bank and hematology teams. Due to the recent coronary event, the patient was a poor candidate for preoperative erythropoietin. The state blood bank agency was contacted (OneBlood). Since Kp^b- RBC units are extremely rare, a state-wide search of rare donor registries was performed to gather 4 frozen RBC units. A fifth unit was solicited fresh from a donor in the state who shared the same rare blood type. Issues regarding transfusing donor platelets or fresh frozen plasma were discussed with the blood bank and hematology teams and judged to be potentially safe to administer, should they be necessary. However, since these products contain a small amount of residual (incompatible) RBCs despite processing, a theoretical risk of a minor hemolytic reaction remained with their use.

Following several days of preparation, surgery was performed. The 4 frozen Kp^b- RBC units were thawed (deglycerolization) early in the morning before surgery. This process can take several hours and may decrease the red blood cell content of a donor unit by 15%, lessening the expected rise in the recipient's hemoglobin. Given the rarity and expense of these units and their 24-hour shelf-life after thawing, the plan was to consider administering all 4 units to the patient on the day of surgery if necessary. In the operating room, the patient's hemoglobin level was 9.9 g/dL. A decision was made to autologously harvest a unit of whole blood from the patient at the beginning of surgery. This unit of whole blood, with platelets and factors not disturbed by cardiopulmonary bypass, would be administered at the conclusion of surgery in hopes of avoiding donor platelets and plasma should the patient become coagulopathic. As the unit of whole blood was procured, 2 thawed donor RBC units were administered to prevent volume depletion and more severe anemia.

The surgical procedure was completed without incident. Two coronary grafts were performed, with the mammary artery grafted to the left anterior descending and saphenous vein grafted to a circumflex branch. The aortic valve was resected and replaced with a bovine bioprosthesis. A cell saver was employed to minimize RBC loss. Surgical adhesives were applied along the suture lines, and the unit of whole blood was returned to the patient after the heparin was reversed with protamine. With adequate hemostasis, no additional blood products were needed. Upon arrival in intensive care, the initial hemoglobin level was 8.8 g/dL. With low blood pressure and to facilitate weaning from vasopressor support, the remaining 2 thawed donor RBC units were administered in the hours that followed, achieving a hemoglobin level of 9.6 g/dL. The patient was extubated shortly after surgery and had a straightforward recovery. Prior to discharge from the hospital, the fifth (fresh) donor RBC unit was administered to increase the patient's hemoglobin in the context of a minor hypotensive episode (hemoglobin 8.5 g/dL). More than 12 months later, the patient remains alive and well.

DISCUSSION

More than 30 different surface antigens have been identified for the Kell RBC system.[1] One such antigen is Kp^b, with over 99.9% of the population being Kp^b+.[4] Among the very rare individuals who are negative for the antigen (Kp^b-), anti-Kp^b antibody (Rautenberg factor) may develop, posing a problem should the need arise for future blood transfusion.[3] Of interest,

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whereas the ABO system was first evaluated in 1900, Kp^b was not discovered until 1958.[3]

The potential for severe immune-mediated transfusion reactions to incompatible donor antigens long has been recognized. The ABO and Rh antigens are the most immunogenic and are tested routinely and matched prior to the transfusion of a blood product. Mismatches in the phenotypes between a donor and recipient may cause a severe hemolytic reaction in which recipient isoagglutinins recognize and attack donor RBC antigens, causing intravascular hemolysis. The release of tissue factor from lysed RBCs into the bloodstream may trigger a systemic inflammatory response, leading to hypotension, disseminated intravascular coagulation and, ultimately, death.[5]

The Kell system is second in immunogenicity to the Rh system. The rarity of low-frequency Kell phenotypes has accounted for its relative lack of recognition. Nevertheless, despite this rarity, severe immune reactions to Kell antigens have been reported.[4,6,7] In general, precautions must be taken to avoid transfusion-related reactions and provide Kp^b-compatible RBC units in the context of known Kp^b-status. However, cases in the literature have described successful emergency transfusion of Kp^b+ blood to Kp^b- patients, sometimes with the use of intravenous gamma globulin and hydrocortisone to mitigate the immune response.[4] In 1 interesting case, transfusion of Kp^b incompatible blood without immunosuppression inexplicably resulted in no adverse reaction. While the Kp^b antibody titers initially were low, after the transfusion of Kp^b+ blood, the authors noted a dramatic increase in the Kp^b antibody titer. This would have mandated the use of immunosuppression should further incompatible blood transfusion have been necessary.[8] Although the authors did not measure antibody titers in the current patient, they did consider immunosuppressive therapies if emergency transfusion of Kp^b+ blood had been needed.

This case highlights that major surgery in patients with rare RBC phenotypes is both safe and feasible, underscoring the importance of careful preoperative planning and stocks of rare blood phenotypes for perioperative transfusion.

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