To the editor:

Severe hemolysis following administration of Rh_o(D) immune globulin in an ITP patient associated with anti-C

In a recent issue of *Blood,* Gaines[1] reported on disseminated intravascular coagulation associated with acute hemoglobinemia or hemoglobinuria following intravenous administration of Rh_o(D) immune globulin as a treatment for immune thrombocytopenic purpura (ITP). Previously, the same author reviewed 15 cases of acute hemoglobinemia or hemoglobinuria following intravenous administration of Rh_o(D) immune globulin for ITP.[2] The author postulated that passively acquired blood group antibodies other than anti-Rh_o(D) might contribute to the severe hemolysis. We would like to support this hypothesis by describing a recent case of ours.

A 67-year-old Rh_o(D)–positive woman with a 5-month history of ITP was admitted for bleeding from the lower gastrointestinal tract. Upon admission, her platelet count was 16×10^9/L and her hemoglobin was 116 g/L (11.6 g/dL). The next day, her bleeding stopped, but her platelet count fell to 9×10^9/L and she received 3500 μg (50 μg/kg) Rh_o(D) immune globulin (WinRho, Cangene, Winnipeg, MB). The day following Rh_o(D) immune globulin administration, her hemoglobin fell to 69 g/L (6.9 g/dL). Laboratory data at that time were consistent with an acute hemolytic episode: increased LDH (632 U/L), increased bilirubin (total, 82.1 μM [4.8 mg/dL]; direct, 10.26 μM [0.6 mg/dL]), and severely decreased haptoglobin (< 0.2 μM [20 mg/dL]). Coagulation function tests were within normal limits. Her urine was noted to be cloudy but was not tested for blood. One unit of packed red blood cells (RBCs) was requested for transfusion. A routine pretransfusion serologic workup showed a positive direct antiglobulin test (DAT) that was 3+ for IgG and weakly positive for complement. The antibody screen was positive with both screening cells. An antibody workup identified an anti-D alloantibody in the patient's undiluted serum sample. In addition, an eluate obtained from the patient's RBCs revealed the presence of anti-D and anti-C alloantibodies. The patient's Rh phenotype was C+c-D+E-e+ (most probable genotype: R1R1). These results were consistent with severe hemolysis induced by Rh_o(D) immune globulin. The patient was then treated with pulse steroids and with an anti-CD20 monoclonal antibody (ie, rituximab), and her laboratory values slowly improved. She was discharged 10 days after receiving Rh_o(D) immune globulin, with a platelet count of 23×10^9/L and a hemoglobin level of 84 g/L (8.4 g/dL). A follow-up visit 2 weeks later as an outpatient showed a similar platelet count and a hemoglobin level of 108 g/L (10.8 g/dL).

Rh_o(D) immune globulin contains more than 90% polyclonal IgG anti-Rh_o(D), as well as low titer anti-A, anti-B, anti-C, and anti-E alloantibodies.[3] Other low titered blood group antibodies (eg, anti-Fy^a and anti-Jk^a) have also been reported to occur in this product.[4] It is possible that the combination of passively acquired blood group antibodies, in this case both anti-Rh_o(D) and anti-C (in a correspondingly antigen-positive patient), will cause sensitization of a critical mass of circulating RBCs, resulting in complement activation and acute intravascular hemolysis. Transfusion services should be aware that Rh_o(D) immune globulin can cause severe hemolysis and that other alloantibodies in addition to anti-Rh_o(D) may be transferred with the administration of this therapeutic product. In addition, if RBC transfusions are indicated in this clinical setting, it may be warranted to determine the RBC antigen phenotype of the recipient, or at least the Rh phenotype; the use of Rh_o(D)-negative RBCs for transfusion should also be considered.

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