Autoimmune hemolytic anemia (AIHA) has been reported in 15-20% of patients with hematological disorders, as leukemia and lymphoma. The incidence of direct antiglobulin test (DAT) positivity is even greater than overt clinical AIHA. The pathogenesis of AIHA is still unknown, but an imbalance of CD4/CD8 T lymphocytes ratio is believed to play a central role, in addition to a weakened expression of red blood cell (RBC) antigens. Autoantibodies rarely show specificity against antigens of the Kell system. However, when an anti-Kpb antibody is detected, the selection of compatible blood is extremely difficult, as the frequency of Kpb is 99.9%. This difficulty may be clinically relevant, because the transfusion of incompatible RBC may be associated with acute or delayed hemolytic reactions. The aim of this letter is to report the reassuring evidence of an uneventful transfusion of Kp(a-b+) RBC to a Kp(a-b+) patient with anti-Kpb antibodies without evident signs of post-transfusion in vivo hemolysis.

Case report

A 39-year-old white man with non-Hodgkin lymphoma was referred to our immunohematology laboratory for serological study when routine compatibility tests gave positive results. The year before he had been transfused with 2 RBC units. No irregular antibodies had been detected and the transfusion had been uneventful. On admission hemoglobin was 6.6 g/dL, total bilirubin 0.44 mg/dL, lactate dehydrogenase 282 IU/L. The reticulocyte count was 2%. AB0 and RH typing was performed on an EDTA blood sample using standard commercial reagents according to the manufacturer's instructions (Ortho Clinical Diagnostics, Raritan, Inc., NJ, USA; Spectra Biologicals, Viareggio, Italy). Typing was performed also on RBC treated with chloroquine (Gamma-Quin, Gamma Biologicals Inc., Houston, TX, USA). Blood group typing was: O, CcDee, Cw-, Jk(a+b+), Kk+, Kp(a+b+), Js(a+b+), phenotype and no reduction of the Kell antigenicity was observed. A direct antiglobulin test (DAT) was performed by tube technique, using polyspecific anti-human globulin and monospecific anti-IgG and anti-C3 of three manufacturers (Gamma; Ortho; Immucor Inc., Norcross, GA, USA). DAT was positive (3+) for IgG (titer 32, score 35). Screening for unexpected RBC antibodies was performed using a 3-cell commercial panel (Surgiscreen Ortho) by microcolumn agglutination technology (CAT BioVue System, Ortho) according to the manufacturer's instructions. As the screening was positive, patient's plasma was tested against 11-cell commercial panels (Panel One and Twenty, Gamma; Panel C and B, Ortho) by CAT and by tube technique using polyethylene glycol (PEG, Gamma) as potentiating agent. Due to panreactive results with all RBCs tested with a strength of 3+, additional tests were performed with selected cells including frozen RBC samples from our own rare phenotype cell collection lacking a variety of high-incidence RBC antigens. They showed a negative reaction only with Kp(a+b)- RBC. Alloantibodies were absent in patient's plasma autoadsorbed with two different aliquots of patient's RBCs. An eluate, prepared by acid EDTA elution with a commercial kit (Elu-kit II, Gamma), was tested by tube technique without additive against commercial and in-house RBCs panels. It showed strong reactivity and anti-Kpb specificity, as identified in plasma. Four additional Kp(b-) RBC samples from different donors gave negative reactions with plasma and eluate.

The patient's KELL genotype was identified as Kpa1b1Kpbo1 (Kpa1b1). Genotype results obtained from DNA of peripheral blood were in agreement with serological Kell typing. Genotype was Kpa1b1Kpbo1. Due to a rapid hemoglobin decrease during chemotherapy and the development of symptomatic anemia on day 5, since no Kp(b-) donors were available, two incompatible group O, CCDee, Cw-, K-, Fya-, Kp(a-b+), Js(a+b+) RBC units were administered in sequence, with careful monitoring. We extensively discussed the choice to transfuse two units sequentially with the attending clinician. The clinician's concern was related to the possibility that the patient could rapidly decompensate for his anemic condition. He considered that the advantages of a rapid and significant hemoglobin rise outweighed the risk of acute hemolysis, that we could define as low in view of our serological findings. To reduce the risk of acute hemolytic reaction the patient was given dexamethason. Plasma hemoglobin, lactate dehydrogenase and total bilirubin did not show modifications during transfusions. Figure 1 shows patient's hemoglobin during hospital stay. Administration of cyclophosphamide was added to steroid therapy, as part of chemotherapy cycles. The patient's condition remained stable and further transfusion was avoided. The DAT and irregular RBC antibody screening remained positive during hospital stay. The patient was discharged on day 7. One month after the initial findings, serological tests were still positive with a similar titer and score and hemoglobin was 8.7 g/dL. Implication of the Kell blood group system in some patients with RBC autoimmunity has been well established. Advani et al. found such specificity in 1 of 170 patients. Few reports of autoantibodies with specificity directed towards Kpb antigen have been described, more frequently in adults than in infants. Because autoimmunity associated with the Kell system may cause severe in vivo hemolysis, it may seem logical to provide Kp(b-) blood for transfusion support in these patients. Nonetheless, the risk of acute or chronic hemolysis should be balanced with that of anemia. It is therefore important for the scientific community to document cases in which red cell transfusions performed under conditions of apparent incompatibility are not associated with clinically significant side effects, as this
can facilitate the management of future immunized patients in need of transfusion support. In summary, our case supports the prevalent opinion\cite{12,13} that incompatibility for RBC autoantibodies is an infrequent cause of clinically relevant complications of RBC transfusion and that careful and accurate detection of alloantibodies remains the cornerstone of effective RBC support.

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References