A delayed hemolytic transfusion reaction due to anti-Co^b

J. E. SQUIRES, P. J. LARISON, W. T. CHARLES, AND P. F. MILNER

A delayed hemolytic transfusion reaction precipitated by anti-Co^b is described in a multiple transfused primigravida woman with sickle-cell disease. Sixteen days after the prophylactic transfusion of the first of 4 units of red cells, she experienced a fall in hemoglobin concentration accompanied by a newly positive antibody screen and direct antiglobulin test. Anti-Co^b was identified both in the patient's serum and in an eluate prepared from her red cells. **TRANSFUSION** 1985;25:137-139.

THE COLTON BLOOD group system was first described by Heisto et al. in 1967.[1] These workers reported the presence of an antibody, anti-Co^a, in the sera of three patients which reacted with an antigen on the red cells of most people. Antibody to the antithetical antigen, Co^b, was reported 3 years later by Giles et al.[2] Since that time, several examples of anti-Co^a and anti-Co^b have been reported. These antibodies are immune in origin, enhanced by enzyme techniques, and frequently identified in sera containing multiple antibodies.[3] Anti-Co^a has been associated with both hemolytic disease of the newborn[4,5] and in vivo hemolysis.[6] However, only one previous report addressed the clinical significance of anti-Co^b.[7]

Case Report

A 23-year-old black woman with a diagnosis of sickle-cell disease had been followed for 11 years. The course of her disease was complicated by multiple painful crises requiring medical attention 10 to 12 times each year. While the patient previously had received multiple transfusions of red cells, she did not require transfusion during the past 4 years.

Following the onset of her first pregnancy, 4 units of red cells were administered prophylactically. The first 2 units were transfused at approximately 22 weeks of gestation, followed 7 days later by the second 2 units. Blood bank evaluation prior to each of these transfusions showed a group O Rh-negative patient with a negative antibody screen and autocontrol. Sixteen days after the initial 2-unit transfusion, she reported to the clinic complaining of pain in her legs and right arm. She had tenderness over the upper shaft of the right humerus and over both tibia; she was afebrile but slightly icteric. Her pulse was 128 beats per minute and blood pressure, 100/80 torr. Prothrombin and the activated partial thromboplastin times were normal. Urinalysis showed only an elevation in bilirubin. Blood samples submitted to the blood bank at this time revealed a positive antibody screen and autocontrol. The direct antiglobulin test was positive with both the broad-spectrum and anti-IgG reagents, but not with anti-C3d. A 56° C ether eluate showed anti-Co^b reactivity. Further study of the serum showed a relatively strongly reactive anti-Co^b at the antiglobulin phase, as well as several additional weakly reactive antiglobulin phase reactions, which could not be identified. Pretreatment of the panel cells with ficin enhanced those reactions attributable to anti-Co^b; the additional antiglobulin phase reactions were not affected.

The patient was admitted to the hospital, and during the ensuing week (days 16–23 following transfusion), she showed a marked decrease in hemoglobin concentration (Fig. 1) accompanied by a simultaneous but smaller decline in the concentration of hemoglobin A. Twenty-seven days after the initial transfusion, the antibody screen remained unchanged; however, the direct antiglobulin test at this time was positive only with the broad-spectrum and anti-C3d reagents. A 56° C ether elution was negative at this time. No further transfusions were administered during her pregnancy. Repeat antibody screens performed at 52 and 68 days after the initial 2-unit transfusion continued to show the anti-Co^b, as well as the additional unidentifiable antiglobulin phase reactions; no additional antibody specificities were detected. At 34 weeks of gestation (68 days after the initial transfusion), a cesarean section was performed due to the possibility of hemolytic disease of the newborn as suggested by the increasing optical density of the amniotic fluid. A group A Rh-positive infant was delivered with a weakly positive direct antiglobulin test. A 56° C ether eluate prepared from the infant's red cells revealed only anti-A and anti-D (due to previously administered Rh-immune globulin). During the delivery, 1 unit of red cells compatible on crossmatch were transfused without adverse reaction.

Discussion

Several reports delineated the immunohematologic characteristics of anti-Co^b. Lee and Bennett,[7] however, were the only authors to describe a transfusion

From the Department of Pathology, Medical College of Georgia, Augusta, Georgia.

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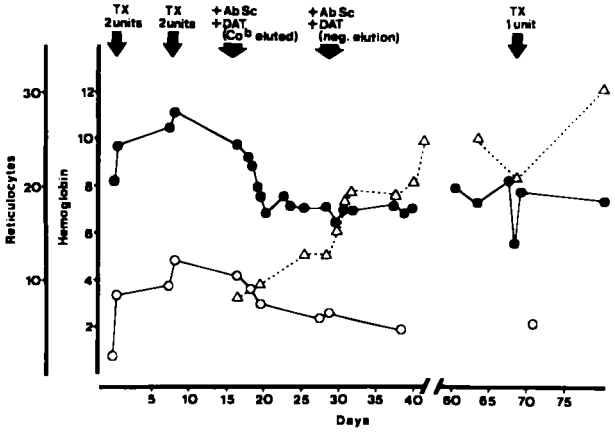

FIG. 1. Total hemoglobin concentration (●) and hemoglobin A concentration (○) in g per dl. "Tx" represents the time at which red cells were transfused. The reticulocyte count, in percentage, is indicated by the open triangles (△).

reaction precipitated by this antibody. They reported the case of a 74-year-old man with no history of previous blood transfusion who developed the clinical and laboratory picture of an acute hemolytic transfusion reaction. While no elution was performed, it was considered probable that anti-Co^b was the cause of the transfusion reaction. The current report describes a young primigravida woman with sickle-cell disease who began to complain of leg and arm pain approximately 16 days after the first of 4 units of blood were transfused. While these symptoms could have represented a sickle-cell crisis, her subsequent serologic evaluation supported the possibility of a delayed transfusion reaction. Diamond et al.[8] emphasized the clinical similarity between painful crises and delayed transfusion reactions in sickle-cell patients. They noted that while many laboratory tests useful in documenting delayed transfusion reactions are already abnormal in sickle-cell patients, the disappearance of transfused cells, hemoglobin electrophoresis, and the appearance of alloantibodies may lead to the correct diagnosis. No specific red cell labeling studies could be carried out in this case; however, the pattern of results obtained in sequential direct antiglobulin tests suggests the disappearance of transfused cells. The negative autocontrol found prior to each transfusion became positive 16 days after the first transfusion. A direct antiglobulin test performed at this time was positive with the anti-IgG reagent but not with the anti-C3d reagent. Importantly, an elution carried out at this time revealed only anti-Co^b. During the following 10 days, the direct antiglobulin test remained positive; however, by day 27 it was positive only with the anti-C3d reagent and negative with the anti-IgG reagent, and anti-Co^b could no longer be eluted from the red cells. The observation that the direct antiglobulin test remained positive with an anti-C3d reagent even several days after the apparent red cell destruction had ceased was initially a somewhat anomolous finding. However, the recent report by Salama and Mueller-Eckhardt[9] suggested that following delayed hemolytic transfusion reactions, C3d may be demonstrated on red cells for long periods of time, and further, that this C3d sensitization may involve autologous red cells.

Second, Diamond et al.[8] also noted that hemoglobin electrophoresis may provide evidence of a delayed transfusion reaction in sickle-cell patients. The coincident decline in both total hemoglobin and hemoglobin A during the time immediately following the development of a newly positive direct antiglobulin test is highly suggestive of such a reaction. However, the fall in total hemoglobin was quantitatively much greater than that of hemoglobin A. Three of the four units of blood transfused to this patient were Co(b−). The apparent Co(b+) unit was 1 of 2 units transfused on day 7, as shown in Figure 1. Thus, it is likely that only a minority of the transfused red cells were hemolyzed in a delayed reaction caused by anti-Co^b. Nevertheless, the disparity between the rather large decline in total hemoglobin as compared to the somewhat more modest fall in hemoglobin A may be explained in two ways. Mollison[10] cited two cases in which the destruction of autologous red cells were noted during delayed hemolytic transfusion reactions. A similar mechanism may have been responsible, in part, for the destruction of autologous hemoglobin S-containing cells in the current case. It may be more important that the transfusion of sickle-cell patients is associated with some degree of bone marrow suppression.[10] Reticulocyte counts of less than 10 percent during the episode of hemolysis in our patient were below the reticulocute counts carried by her throughout the remainder of pregnancy and were also below those recorded during the previous year when an average of three reticulocyte counts was 20.23 percent. Thus, it appears probable that the marked decline in total hemoglobin was the result both of the destruction of 1 unit of Co(b+)-positive red cells as well as the patient's transient inability to adequately replace autologous sickle cells, which even under usual conditions have an extremely short half-life.[11]

Finally, Diamond et al.[8] indicated that delayed, hemolytic transfusion reactions in sickle-cell patients can be recognized by the appearance of new alloantibodies. This patient has been evaluated in this blood bank on 27 separate occasions during the past 4 years. On all occasions, her autocontrol has been negative with the exception of the current hemolytic episode. In addition, her antibody screen was positive only once previously when an anti-Le^a was identified; all 4

transfused units were Le(a−). Further evaluation of the weak antiglobin phase reactions at 52 and 68 days after the initial transfusion failed to reveal any identifiable additional alloantibodies. The probability of certain antibodies traditionally associated with delayed hemolytic transfusion reactions can be eliminated on the basis of the patient's partial phenotype which in this case showed that she carried red cell antigens C, Fy^b, Jk^a, Jk^b, S, s, and M but lacked the E, K, Fy^a, N, Le^a, and Co^b antigens.

In summary, we believe that the data presented here strongly suggest that this sickle-cell patient suffered a delayed hemolytic transfusion reaction precipitated by anti-Co^b.

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Jerry E. Squires, PhD, MD, Blood Bank, Department of Pathology, Medical College of Georgia, Augusta, GA 30912. [Reprint requests]

P. Joyce Larison, MT(ASCP) SBB, MA, Blood Bank, Department of Pathology, Medical College of Georgia.

William T. Charles, MT(ASCP), Blood Bank, Department of Pathology, Medical College of Georgia.

Paul F. Milner, MD, Professor of Pathology and Medicine, Medical College of Georgia.