Brief Reports

Delay in the Onset of Immune Hemolysis *in Vivo* Apparently Due to Heparinization

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A 55-year-old type B patient inadvertently received one unit of type A_1 blood following the administration of 14 units of type B blood while heparinized for cardiopulmonary bypass. Agglutinated erythrocytes were present in a Wright stained film of venous blood after the transfusion of the A_1 unit, but they were absent three hours after administration of protamine sulfate when hemolysis ensued. Heparin may have temporarily prevented rapid early lysis of the transfused incompatible cells.

AGGLUTINATED erythrocytes were discovered in the blood of a type B patient after he received a unit of type A_1 blood while heparinzed for cardiopulmonary bypass. Three hours after protamine sulfate was given the agglutinates were absent and brisk hemolysis occurred.

Rosenfield, Vitale, and Kochwa[2] demonstrated in rats that transfused lysin-sensitized erythrocytes were protected from rapid early destruction *in vivo* by heparinizing the recipient. Heparinization may have prevented rapid early lysis of the transfused cells in our patient.

Case Report

A 55-year-old white man was hospitalized for repair of partial dehiscence of an aortic valve prosthesis. He had had operative correction of symptomatic aortic valvular stenosis four months earlier. However, two months postoperatively there was evidence of regurgitation around the prosthesis and associated mild traumatic hemolysis.

The dehiscence of the aortic valve prosthesis was obliterated with teflon pledgets during cardiopulmonary bypass and Halothane anesthesia. The procedure required over nine hours, and bypass was utilized for two hours. The patient was type B, Rh_o (D) negative. He received 14 units of such blood during the procedure. However, one unit of type A_1, Rh_o (D) positive blood inadvertently was included among the transfused units. The patient received 15,000 units of heparin in the solution used for modification of the five units of blood used for priming the pump oxygenator. In addition, 20,500 units of heparin were injected into the heart just before, and 7,000 units were given via the pump oxygenator during the transfusion of the A_1 blood. One hour later the error was discovered and the Blood Bank was notified.

Fifty minutes after completion of the transfusion of the A_1 unit, 270 mg of protamine sulfate was given. Twenty minutes later his blood was examined. The serum was pink in comparison with the normal-appearing preoperative specimen. The direct antiglobulin test was weakly positive. The erythrocytes gave a weak mixed field reaction with anti-A serum, reacted strongly with anti-B serum, and failed to react with anti-Rh_o (D) serum. The patient's serum strongly agglutinated A_1 cells, but did not react with B cells or with a panel of Group 0 cells. A Wright-stained smear of EDTA anticoagulated blood revealed scattered

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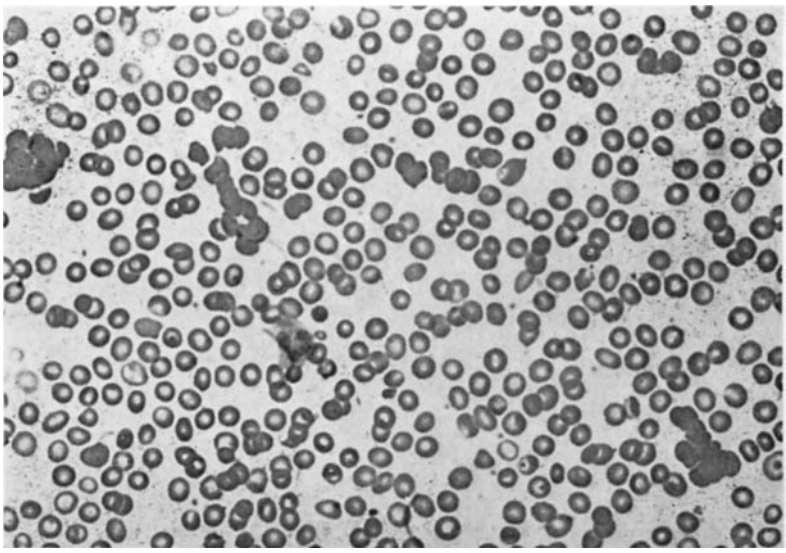

FIG. 1. Blood smear prepared during heparinization. The transfused incompatible cells are seen as scattered agglutinates of 3-8 cells in a sea of free cells. Agglutinates were absent in smears prepared after the administration of protamine sulfate.

clumps of 3-8 agglutinated erythrocytes, amid a background of nonagglutinated cells (Fig. 1). About 5 per cent of the cells were agglutinated.

Consideration was given to the continuation of heparin therapy; however, the surgeon was reluctant to do so because of bleeding in the operative field. Therefore, 270 mg of protamine sulfate was given in two doses, 85 and 115 minutes after the transfusion. Two hours and forty minutes after the second dose, the direct antiglobulin test was negative and circulating erythrocytes did not react with anti-A serum. The serum was light red, in contrast to the earlier posttransfusion specimen, and agglutinated erythrocytes could not be found on a Wright-stained blood smear. Urinary output fell to 10 ml per hour during the next 12 hours, despite intravenous therapy with fluid, mannitol, and five units of type B blood. Hemoglobinuria was present.

On the first postoperative day, he was obtunded and continued to be oliguric. The serum bilirubin was 21 mg/100 ml and the arterial oxygen saturation 62 per cent. Congestive heart failure was evident on day 2 and the bilirubin rose to 30 mg/100 ml. The prothrombin time was 21 seconds and the partial thromboplastin time was 81 seconds, findings which persisted until death.

On the fourth postoperative day, his urinary output returned to normal but on the eighth day oliguria recurred and the serum bilirubin was 58 mg/100 ml. Peritoneal dialysis was attempted but the dialysate had a packed red cell volume of 26 per cent. Intraperitoneal hemorrhage continued, he became hypotensive and died on day nine. No unexpected antibodies were detected in the patient's serum during the postoperative course.

Necropsy disclosed hemoperitoneum (3,000 ml), right hemothorax (800 ml) and generalized petechiae. No grossly identifiable ruptured vessels were present. The liver weighed 1,350 gms and there was severe centrilobular congestion, hemorrhage, and necrosis. Hepatic necrosis was believed to be the most important cause of the terminal bleeding disorder. The kidneys weighed 190 and 180 gms. The cortices were green and bile and hemoglobin casts were present in renal tubules. Hemosiderin was present in tubular epithelium.

Discussion

The finding of agglutinated red blood cells in our patient demonstrated that heparinization did not prevent binding of anti-A to transfused A_1 cells. In the studies of Rosenfield, Vitale, and Kochwa[2] the presence of heparin neither demonstrably blocked uptake of antibody by erythrocytes *in vitro* nor was associated with noticeable dissociation of antibody *in vivo*. The disappearance of the agglutinates and the onset of rapid hemolysis within three hours following the administration of protamine sulfate demonstrated the ability of re-

cipient and/or transfused anti-A to lyse the A_1 cells when heparin was neutralized by protamine. The apparent delay in the onset of hemolysis in the presence of heparin in our patient may be analogous to the observations of Rosenfield, Vitale, and Kochwa[2] that transfused erythrocytes sensitized with lysins were protected from rapid early destruction *in vivo* by heparinizing the recipient. Their data suggested that this protection was transient, lasting approximately two hours, and was clearly absent by 24 hours. They believed the mechanism of protection to be heparin's anticomplementary action, because erythrocytes sensitized with lysins in the presence of fresh serum were not protected. We have no data concerning complement activity in our patient during the transfusion but it is conceivable that a similar mechanism was operative.

Nalbandian, *et al.*[1] found agglutinated erythrocytes in the marrow but not in the blood of a patient with an anti-Kell antibody reactive 2+ by the antiglobulin technic. Their patient had received 260 ml of Kell-positive packed cells two days before the marrow examination. They believed that the agglutinates were the transfused cells and that a slow hemolytic transfused reaction was occurring. They ascribed the apparent infrequency of such observations to, among other things, the possible requirement of a low recipient complement level.

References

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