Traumatic Hemolysis with Hemoglobinuria Due to Ball Variance

By Elaine Eyster

POSTIMPLANTATION ALTERATION of the physicochemical properties of the silastic poppet (ball variance) has been reported in some patients with aortic ball valve prostheses. Clinical recognition of this situation is difficult, and the diagnosis is usually made at autopsy. This report concerns a patient with ball variance manifested primarily by traumatic intravascular hemolysis and hemoglobinuria. The hemolysis subsided following replacement of the swollen ball component (poppet).

CASE REPORT

A 23 year old nulliparous white woman was admitted to The New York Hospital in April 1964 because of congestive heart failure secondary to rheumatic heart disease with severe aortic insufficiency. The hematocrit was normal when the aortic valve was excised and replaced with a Starr-Edwards artificial ball valve prosthesis in May 1964. Following surgery she resumed normal activities, and her hematocrit one year later was 41 per cent. Medications included digitoxin and sodium warfarin.

She felt well until July 1966 when she was admitted for the second time because of anemia, with symptoms of light-headedness of several weeks duration. There was no history of excessive menstrual bleeding or loss. Physical examination revealed pallor and scleral icterus. The blood pressure was 120/70. The heart was enlarged, and faint aortic systolic and diastolic murmurs were heard. The lungs were clear. The liver edge and the spleen tip were palpable. There was no edema. The hematocrit was 16 per cent and the hemoglobin 4.9 g/dL. The red blood cells were markedly hypochromic and microcytic. Many fragmented forms (89 per 1000 cells) including helmet, burr and triangle forms as well as numerous microspherocytes were noted. A reticulocyte count was 5.9 per cent. Routine urinalysis was normal. Repeated examinations of the stool for occult blood were negative. The serum iron was 33 mcg/dL, and the total iron binding capacity was 333 mcg/dL. Serum haptoglobins were absent, methemalbumin was present in the serum, and the serum lactic dehydrogenase was 2000 U (normal 150-350 U.). The direct Coombs' test and the sucrose hemolysis test for paroxysmal nocturnal hemoglobinuria were negative. There was stainable hemosiderin in the urine sediment and the supernatant contained free hemoglobin. Bone marrow examination revealed erythroid hyperplasia with no stainable iron.

The patient was treated with intramuscular iron dextran, oral ferrous gluconate and...
folic acid, and the hematocrit rose from 15 per cent to 37 per cent without transfusion. A \textsuperscript{51}chromium red cell survival study performed when she was iron repleted showed a half life of 11 days. Red cell osmotic fragility was increased (Fig. 1). Because of a severe allergic reaction, iron dextran was discontinued. Over the course of one year, urinary iron losses rose progressively from 6.0 to a high of 18.8 mg. per 24 hours. The patient was maintained on oral iron and ascorbic acid in a partially compensated hemolytic state with a hematocrit of 30 per cent and a reticulocyte count of 15 per cent.

In October 1967 the patient again became severely anemic and was readmitted for further study. There was no history of angina or syncope. Physical examination revealed brownish discoloration of the sclerae. The blood pressure was 115/60. The heart was not enlarged. There was a grade 4/6 systolic precordial murmur and a grade 3/6 blowing diastolic murmur along the left sternal border. No systolic click was heard. The lungs were clear. The liver edge and spleen tip were palpable. There was no edema. The electrocardiogram showed changes indicative of left ventricular hypertrophy. Cardiac series revealed normal heart size with no specific chamber enlargement. The hematocrit was 18 per cent and the peripheral blood smear was unchanged. A reticulocyte count was 23.6 per cent. The urine was dark brown and contained \textsuperscript{4+} protein. No red cells were seen and the reaction with Hemostix was strongly positive for hemoglobin. The platelet count was normal. The stool was negative for occult blood. Serum haptoglobins were absent. Serum bilirubin was 0.1 per cent in the direct fraction and 0.7 mg. per cent in the indirect fraction. Serum lactic dehydrogenase was 6,925 U. and the plasma heme pigments were 140 mg. per cent (normal < 2 per cent). The direct Coombs' test was negative. A \textsuperscript{51}chromium red cell survival study showed a half life of 4 days. Surface counting revealed a spleen-precordial ratio of 0.45 at day 0 increasing to 1.2 at the half life, with a liver-precordial ratio of 0.25 increasing to 0.55, indicating splenic sequestration. Twenty-four hour urea and creatinine clearances were normal. Consecutive twelve hour urinary iron determinations revealed that greater amounts of iron were excreted during the day than during the night. When the patient was placed on bed rest during the day and ambulated at night, greater amounts of iron were excreted during the night (Fig. 2). On limited activity over the 17 day period of hospitalization, 24 hour urine iron excretion fell from 34 mg. to 9 mg., and plasma heme pigments decreased to 60 mg. per cent.

It was felt that the patient had traumatic intravascular hemolysis and hemoglobinuria secondary to a malfunctioning aortic ball valve prosthesis with outflow tract obstruction.
and regurgitation. She was transfused with 4 units of red cells and an aortotomy was performed on December 11, 1967. The mean systolic gradient across the aortic valve was increased (40 mm. Hg). The prosthesis was noted to be firmly fixed in proper position and a clot was adherent to the anterior rim. The ball component (poppet) was swollen and yellow, and could be moved within the cage only with difficulty. The poppet was replaced with a new one of comparable size. It weighed 4.4 Gm. compared to 3.5 Gm. for an unused poppet. Indentations from the metal struts were visible (Fig. 3). On cut surface the entire poppet was opaque and discolored. Following surgery a grade 2/6 diastolic murmur along the left sternal border was again noted. In addition, a grade 3/6 systolic murmur along the left sternal border was heard. Opening and closing clicks were present. One month later the hematocrit was 43 per cent and the reticulocyte count was 1.4 per cent. Serum haptoglobins had risen to 28 mg. per cent and the lactic acid dehydrogenase had fallen to 490 U. The urine was negative for protein and hemoglobin but still contained hemosiderin. A 24 hour urine iron excretion was 5.2 mg. Four months after surgery the hematocrit was 44 per cent, the reticulocyte count was 2.4 per cent, and the peripheral smear showed only 5 fragmented forms per 1000 cells.

**DISCUSSION**

Traumatic hemolysis can be accompanied by urinary iron loss and is increased during periods of activity. This patient presented two years after the insertion of a prosthetic aortic ball valve prosthesis with hemoglobinuria and iron deficiency anemia secondary to traumatic hemolysis. As previously reported, oral iron, ascorbic acid and folic acid maintained the patient in a partially compensated hemolytic state. Subsequently the hematocrit fell when urinary iron losses increased and hemolysis became more severe. Hemolysis decreased when activity was restricted presumably related to a decrease in cardiac output. Urinary iron excretion was greater during the day than during the night. This pattern was reversed when the patient was ambulated at night and placed on bed rest during the day. Renal function remained normal twelve months after onset of hemoglobinuria. At operation a swollen discolored poppet was found to be obstructing the aortic outflow tract. After the poppet was re-
placed hemolysis ceased and urinary iron loss subsided. However, the murmur of aortic regurgitation persisted, probably indicating continued leakage around the cage of the prosthesis.

Ball variance has been observed almost exclusively in patients with aortic ball-valve prostheses. In most instances it has been associated with an abnormality of implantation such as leakage around the cage of the prosthesis that might account for increased trauma to the ball. Fatty acids or fatty acid esters have been found on analysis of these poppets, suggesting that lipids may be driven into the ball when the velocity of blood flow in the aortic root is increased by obstruction or regurgitation.

Although the cause of ball variance is unknown, it seems likely that it results from surface interaction between the silastic ball and plasma, red cell or platelet lipids. Because of the association of traumatic hemolysis and ball variance in this patient, it is tempting to postulate that the red cell may be the source of such lipids. Of particular interest in this regard are the osmotic fragility studies similar to those seen in hereditary spherocytosis. In this disorder the red cell loses surface lipid as it spheres. The spherical cell is predisposed to both splenic trapping and fragmentation hemolysis. This same sequence of events may have occurred in this patient who showed fragmented cells, micro spherocytes and massive intravascular hemolysis with hemoglobinuria in addition to extravascular hemolysis with splenic sequestration. Also of interest is the finding that hemosiderinuria persisted after hemolysis ceased, suggesting that hemosiderin is slowly excreted by the kidney when hemoglobin is no longer presented to the tubule.
TRAUMATIC HEMOLYSIS

SUMMARY
A patient with an aortic ball valve prosthesis who had traumatic hemolysis, hemoglobinuria and iron deficiency secondary to ball variance has been reported. Hemolysis and urinary iron loss decreased when activity was restricted. A diurnal pattern of urinary iron excretion was observed. This was reversed when the patient was placed on bed rest during the day and ambulated at night. Hemolysis ceased and urinary iron loss slowly subsided after outflow tract obstruction was corrected by replacement of the swollen poppet.

SUMMARY IN INTERLINGUA
Es reportate Ic caso de un patiente con un prosthese de valvula aortic a balla qui habeva hemolyse traumatic, hemoglobinuria, e carentia (Ic ferro secundari a irregularitates del balla. Le hemolyse e le perdita urinari de ferro declinava quando le activitate del patiente esseva restringite. Un rhythmo diurne del excretion urinari de ferro esseva observate. Isto esseva revertite quando le patiente esseva allectate durante le die, durante que on le faceva ambular se durante le nocto. Le hemolyse cessava e le perdita urinari de ferro subsdieva gradualmente post que le obstruction del tracto de effluxo esseva corrigite per le re-implacemento del defective parte del prosthese.

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REFERENCES
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