Chronic Intravascular Hemolysis (Renal Hemosiderosis) after Incomplete Prosthetic Closure of a Ventricular Septal Defect and Noncalcific Aortic Regurgitation

THOMAS J. LIDDY, M.D., AND WILLIAM C. ROBERTS, M.D.

Pathologic Anatomy Branch, National Cancer Institute and Section of Pathology, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland 20014

ABSTRACT

Liddy, Thomas J., and Roberts, William C.: Chronic intravascular hemolysis (renal hemosiderosis) after incomplete prosthetic closure of a ventricular septal defect and noncalcific aortic regurgitation. Amer. J. Clin. Path. 53: 839-842, 1970. Clinical and pathologic features of the case of an 11-year-old boy who underwent operative repair of tetralogy of Fallot nine months before death are described. Aortic regurgitation was produced inadvertently at operation during an unsuccessful patch closure of the ventricular septal defect. Postoperatively, the child developed severe cardiac failure and mild anemia. During a second operation seven days before death, aortic blood, which regurgitated through the aortic valve, was observed to contact the nonendothelialized ventricular septal patch, which only partially closed the septal defect. Erythrocytes were traumatized by the jet of blood contacting the nonendothelialized patch, liberating free hemoglobin, which was filtered by glomeruli and reabsorbed by renal tubules (renal hemosiderosis). Intravascular hemolysis after patch closure of ventricular septal defect has not been described previously.

CHRONIC INTRAVASCULAR HEMOLYSIS occurs occasionally in patients with severe calcific aortic valvular stenosis and regurgitation. After replacement of aortic valves with a caged-ball or Teflon-leaflet prosthesis, however, intravascular hemolysis invariably occurs, but it usually is not clinically significant. Chronic intravascular hemolysis also occurs occasionally in patients with partial atrioventricular canals after prosthetic closure of the atrial septal defects, with or without repair of the cleft anterior mitral leaflets. The hemolysis in these patients has been attributed to contact of erythrocytes regurgitated from the left ventricle at high velocity and pressure against the prosthetic atrial septal patch. A review of the literature disclosed that intravascular hemolysis after operative closure of ventricular septal defect with prosthetic material has not been described. However, intravascular hemolysis did develop in a patient studied by us, in whom aortic valvular regurgitation was produced inadvertently while a ventricular septal defect was being closed incompletely. Clinical and autopsy findings in this patient are described.

Report of a Case

An 11-year-old boy had undergone repair of tetralogy of Fallot eight months before admission to the National Heart Institute.
The ventricular septal defect allegedly had been closed by an Ivalon patch and the valvular and infundibular pulmonic stenosis was thought to be alleviated. During closure of the septal defect, a suture had caught an aortic valvular cusp and aortic regurgitation occurred. Severe right-sided congestive failure, evident immediately after operation, became progressively more severe. Catheterization a month after operation disclosed a residual large left-to-right shunt at the ventricular level.

When admitted to the National Heart Institute for the first time eight months later (a month before death), the patient was severely ill (class IV). A grade 5/6 ejection-type systolic murmur was audible over the entire precordium and a grade 4/6 decrescendo diastolic blowing murmur was heard along the left sternal border. The hematocrit was 37%, hemoglobin 11.3 Gm. per 100 ml., platelet count 59,000 per cu. mm., and leukocyte count 6,000 per cu. mm. Serum iron was 86 μg. and the total iron-binding capacity, 330 μg. The direct Coombs’ test proved negative. Total serum bilirubin was 2.7 mg. per 100 ml. and blood urea nitrogen, 10 mg. per 100 ml. Urine was normal. Repeat cardiac catheterization disclosed a left-to-right shunt (1.5 to 1) at the ventricular level and elevated right ventricular (60/20 mm. Hg) and right atrial pressures (mean, 17; a wave, 23; v wave, 23 mm. Hg). The femoral arterial pressure was 110/48 mm. Hg. At reoperation (seven days before death), two perforations, each about 0.5 cm. in diameter, were found in the noncoronary aortic valvular cusp. The aortic valvular cusps were fibrotic, smooth, and free of calcific deposits; the two perforations, which were responsible for the severe aortic regurgitation, were closed by sutures. It was apparent that the regurgitant stream was in direct line with the ventricular septal patch, which was not covered by endothelium. The residual shunt resulted from partial detachment of the ventricular septal patch; the detached portion was reapproximated to the margin of the defect by sutures. Postoperatively,
Fig. 2. Kidney. Upper left, cut section. Upper right, same kidney after soaking in Prussian blue solution for 2 min. The cortex stained dark blue, indicating heavy deposits of iron, whereas the medulla did not stain. Lower left, photomicrograph of a section of kidney stained by the Prussian blue method. The dark-stained tubules indicate deposits of iron. The medulla (bottom) is free of iron deposits. × 20. Lower right, close-up showing that the iron deposits are situated predominantly in the cytoplasm of the proximal convoluted tubules, although some iron-positive material is present in Bowman’s space and in the lumen of the proximal tubules. × 280.

the patient had prolonged periods of hypotension, grand mal seizures, and hyperbilirubinemia (17 mg. per 100 ml.), and died.

At autopsy, the ventricular septal defect and the aortic valvular perforations were well closed (Fig. 1). The erythroid elements in the bone marrow were hyperplastic and large deposits of iron were present in the cytoplasm of the proximal convoluted tubules of the kidney (Fig. 2). No stainable iron was present in the liver or spleen.
Comments

The intravascular hemolysis almost certainly resulted from damage to erythrocytes which contacted the nonendothelialized ventricular septal patch. Blood which regurgitated from the aorta through the perforated aortic valvular cusp and ejected from the left ventricle through the residual ventricular septal defect had direct contact with the prosthetic patch. Although few clinical tests for hemolysis were performed, there is unequivocal anatomic evidence, i.e., renal hemosiderosis, that chronic intravascular hemolysis had occurred. Chronic intravascular hemolysis is the only condition which causes severe renal hemosiderosis without associated deposits of iron in the liver or spleen. Acute hemolysis (resulting from cardiopulmonary bypass, for example) may cause glomerular filtration of hemoglobin, but hemosiderin in these patients is present only in the tubular lumens and in Bowman's spaces. Prolonged periods of intravascular hemolysis are necessary before stainable iron can be detected in the cells of the proximal convoluted tubules. The amount of intravascular hemolysis required to produce severe renal hemosiderosis is not precisely known, but the extracorpuscular hemoglobin, at least initially, must exceed 100 to 140 mg. per 100 ml. plasma for hemoglobin to filter through renal glomeruli. Prolonged intravascular hemolysis, however, depletes the serum haptoglobin, and this threshold falls accordingly. The hemolysis in the patient described was well compensated, since he was only mildly anemic. The pronounced erythroid hyperplasia of the bone marrow in the presence of normal arterial oxygen saturation, however, indicates an active stimulus to erythropoiesis.

References