Delayed Onset of Hemolytic Anemia in a Child
An Indicator of Ball Variance of Aortic Valve Prosthesis

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SUMMARY
Severe intravascular hemolysis is described as a complication of implantation of an aortic Starr-Edwards ball-valve prosthesis and insertion of a Teflon patch in the ascending aorta in a 9-year-old boy with severe aortic valvar stenosis. This progressive hemolysis of delayed onset was the sole indicator of extreme degeneration of the silicone rubber ball of the prosthetic aortic valve, a potentially lethal condition requiring surgical intervention. The phonocardiographic signs of aortic ball variance were not present, and there was no overt valvar incompetence.

A lesser but noteworthy aspect in this case was the occurrence of an "aplastic crisis" superimposed on the severe hemolysis. This transient bone marrow, red cell aplasia, which was unrelated to drugs, precipitated an acutely severe anemia which accounted for the presenting symptoms of the patient and required transfusion.

Additional Indexing Words:
Cardiac intravascular hemolysis
Aplastic crisis
Starr-Edwards aortic valve prosthesis
Silicone rubber ball degeneration

CHRONIC intravascular hemolysis is a known complication of prosthetic replacement of aortic or mitral valves and of Teflon patch repair of endocardial cushion defects. Severe hemolysis has generally been associated with a significant hemodynamic defect. When associated with incompetent aortic ball valves, hemolysis usually appears early in the postoperative course. Ball variance, in other words, degeneration of the silicone rubber poppet of a ball valve, is a common, but difficult to diagnose, late complication of certain aortic valve prostheses. This report documents progressive hemolysis of late onset as the sole indicator of extreme aortic ball variance in a child.

Methods
Standard hematologic methods were used as given by Dacie and Lewis. Autologous red cell life spans were estimated by the chromium technic. Urinary iron and serum iron and iron binding capacity were determined. Plasma hemoglobin was measured with a normal control. Fibrin-split products were investigated by an immunoelectrophoretic technic, using rabbit antihuman reagent. The phonocardiograms were re-
corded with a Cambridge* Model MC-IV photographic recorder, employing a paper speed of 75 mm/sec. The frequency response of the system is from 0.1 cycles/sec to 100 cycles/sec. A Sanborn diaphragm microphone was used, and the patient was placed in the supine position.

Report of Case

This 9-year-old boy with a history of subacute bacterial endocarditis, successfully treated, developed exertional syncope. He had signs of left ventricular outflow obstruction, mild left ventricular hypertrophy with positive left precordial T waves on the electrocardiogram, and a left ventricular contour on chest x-ray. At catheterization there was a peak systolic pressure difference of 130 mm Hg across the aortic valve and a left ventricular pressure of 230 to −5 to 10 mm Hg. The aortogram showed a localized saccular aneurysm in the ascending aorta and signs of aortic valve stenosis.

At surgery the aortic valve was a thickened solid mass with early calcification near the 3 mm ostium. Valvuloplasty was not feasible, and an infant 6A Starr-Edward Model 1000 ball valve, the largest that could be accommodated in the narrow annulus, was inserted. The 2 cm diameter aneurysm in the ascending aorta was excised, and a woven Teflon patch was inserted. After an uncomplicated postoperative course, the patient was discharged; at that time he was receiving no medication and was asymptomatic.

One year postoperatively he had a blood pressure of 130/90 mm Hg, a grade II/VI ejection systolic murmur, and no diastolic murmur. The AO (aortic opening)/AC (aortic closing sound) ratio at the second right intercostal space was 1.7. The heart was of normal size on x-ray. The electrocardiogram showed a shift of the QRS axis from +45° to −10° but positive left precordial T waves and loss of voltage criteria of hypertrophy. Catheterization demonstrated a 38 mm Hg peak systolic pressure difference across the aortic ball valve with a cardiac output of 5.1 L/min, a value at the upper limits of normal in this laboratory. A cineaortogram showed the expected ‘puff’ of aortic incompetence seen with normally functioning aortic ball valves.

Two years postoperatively the patient developed paleness and lethargy 2 weeks after an upper respiratory infection. He was afebrile but severely anemic with a hematocrit of 17% as compared to 35% 6 months earlier. The reticulocyte count was 0.5%. He had received no medications, and three blood cultures were negative. His hyperdynamic cardiovascular state in the absence of a murmur of aortic incompetence was thought to be secondary to the anemia. He was transfused.

Hematologic data are summarized in table 1. Peripheral blood smear showed characteristically abnormal fragmented red blood cells. Other peripheral blood elements were normal. Four days after the initial markedly low value, the reticulocyte count had spontaneously risen to 11.5%. Bone marrow aspirate at this time showed marked erythroid hyperplasia. Red cell life span, estimated by 51Cr survival studies, was markedly shortened (fig. 1). Serum iron saturation was low, indicating concomitant iron deficiency. Excessive urinary iron loss was confirmed. Direct and indirect Coombs tests were negative. An acid hemolysin test was negative. Forty-eight hour autohemolysis, incubated red cell osmotic fragility, prothrombin time, partial thromboplastin time, and thrombin time

Table 1

<table>
<thead>
<tr>
<th>Hematologic Data</th>
<th>After insertion</th>
<th>2-4 wk after reoperation</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25 mo</td>
<td>30 mo</td>
<td></td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>17</td>
<td>27</td>
<td>35</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
<td>0.4</td>
<td>15.9</td>
<td>1.3</td>
</tr>
<tr>
<td>Fragmented RBCs (%)</td>
<td>8</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>RBC survival (51Cr T 1/2)</td>
<td>9.2</td>
<td>6.1</td>
<td>23.0</td>
</tr>
<tr>
<td>Hemoglobinuria</td>
<td>Neg.</td>
<td>Pos.</td>
<td>—</td>
</tr>
<tr>
<td>Urinary iron (mg/12 hr)</td>
<td>2.2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Serum iron (µg/100 ml)</td>
<td>62</td>
<td>57</td>
<td>—</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>399</td>
<td>281</td>
<td>—</td>
</tr>
<tr>
<td>(µg/100 ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron saturation (%)</td>
<td>16</td>
<td>20</td>
<td>—</td>
</tr>
<tr>
<td>Plasma hemoglobinemia (mg %)</td>
<td>—</td>
<td>27.2</td>
<td>—</td>
</tr>
</tbody>
</table>

*Cambridge, 73 Spring Street, Ossining, N. Y. 10562

Circulation, Volume XL, July 1969
were normal. Fibrin-split products were not detected.

In spite of oral and parenteral iron, folic acid, and multiple vitamin supplementation, hemolysis increased as shown by increasing reticulocytosis and further shortening of the $^{51}$Cr. Repeated examination revealed neither an early diastolic murmur nor peripheral signs of valvar incompetence. The AO/AC ratio of 1.8 (fig. 2), unchanged from 1 year postoperatively, suggested a normal aortic ball-valve poppet. However, in view of the increasing rate of hemolysis, reoperation was recommended.

At surgery marked ball variance was found. A well-organized 3 cm long thrombus originated from a deep crevice in the sphere. The markedly deteriorated ball showed opacification, discoloration, and multiple areas of surface damage (fig. 3). The entire prosthetic valve was removed, and the nonendothelialized Teflon patch in the ascending aorta was excised. The aortic annulus was incised in the region of the noncoronary sinus, and a pericardial patch was inserted across the left ventricular outflow tract, aortic annulus, and the ascending aorta encompassing the area of the previous Teflon patch. A new 8A Starr-Edwards valve prosthesis, with a hollow metal ball and struts covered with Dacron velour, was implanted.

Postoperatively, fragmented red blood cells were no longer seen on the peripheral blood smear, and $^{51}$Cr survival indicated a nearly normal red blood cell life span. A persistent surgically induced heart block was treated with a trans-
Phonocardiograms recorded 30 months after implantation of an aortic Starr-Edwards ball valve. (A) At the apex there is a discrete high intensity aortic opening sound (AO). (B) At the 2nd right intercostal space the AO/AC (aortic closing sound) ratio is 1.8 suggesting that the AO is of normal intensity and that ball variance is not present. Use of this criterion would have led to an erroneous conclusion in this case.

Discussion

Severe intravascular hemolysis appeared 25 months after insertion of a Starr-Edwards aortic ball valve in this patient. Although the non-endothelialized Teflon patch in the aorta may have contributed to this hemolysis, the fact that it had been in situ for 2 years suggests that it was not responsible for the timing and progressive nature of the hemolysis.

Aortic ball variance may progress to ball fracture and dislodgement or swelling with impaction. Signs of ball variance include altered character of the valve opening sounds, intermittent or late onset of aortic incompetence, embolic episodes, and hemolytic anemia. Either an AO/AC ratio less than 0.5 or loss of the discrete high spiking frequencies of both AG and AC has been reported to identify most cases. In spite of marked sphere deterioration, this patient had neither of these phonocardiographic signs.

Progressive cardiac intravascular hemolysis beginning late in the postoperative course was the sole indicator of advanced aortic ball variance in this case. Scalabrini and associates reported a case of aortic ball variance which presented with hemolytic anemia followed by...
embolic episodes. And recently, Garcia and co-workers have reported a patient with severe and progressive hemolysis due to a markedly enlarged aortic sphere which obstructed aortic outflow. Surgery to replace the deteriorated sphere or the entire value is the only treatment for ball variance.

The severe degree of anemia which was seen as the initial indication of hemolysis in our patient is best explained by an "aplastic crisis," a syndrome which commonly occurs with hemolytic states of many types. The sequence of an upper respiratory tract infection, followed by anemia with reticulocytopenia, and subsequent spontaneous recovery with reticulocytosis, as occurred in this patient, is typical. Although aplastic crises have not been reported in association with cardiac intravascular hemolysis prior to this case, they are a possible serious secondary complication of such hemolysis in both children and adults. The treatment of the severe anemia that may result is transfusion with packed red cells or blood until spontaneous recovery occurs.

References


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Platitudes

... out of the riches with which his mind was dowered in his youth, something that was real and true and of good repute rises through the shattered shell of his self-confidence, and he rests on it. He examines it again in a new light and finds it in its new meaning. It is no longer old or trivial or meaningless. It is not somebody else's thought, but his own. It is not a platitude, but a living truth. All that he once heard and accepted and then neglected or rejected takes on a new meaning, comes trooping back with new light and glory shining from its facets. ... The platitude being dead, yet liveth. The seed at last finds soil and the husbandman is justified of his sowing.—Guy Stanton Ford: On and Off the Campus. Minneapolis, University of Minnesota Press, 1938, p. 431.
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Circulation. 1969;40:55-60
doi: 10.1161/01.CIR.40.1.55

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