Spontaneous Partial Remission of Postoperative Hemolytic Anemia in a Case with Ostium Primum Defect

By S. K. Sanyl, M.B.B.S., H. F. Polesky, M.D., Michael Hume, M.D., and M. J. Browne, M.D.

Severe hemolytic anemia after surgical correction of congenital endocardial cushion defects is a rare clinical entity, first described by Sayed et al. in 1961. Since then five more cases have been reported. All of these patients had an endocardial cushion defect with a cleft in the mitral valve. All defects were repaired with a Teflon patch, and the patients developed hemolytic anemia in the postoperative period. The hemolysis was considered to be mechanical in origin caused by regurgitation of blood through the residual cleft in the mitral valve against the Teflon patch. Only one patient is reported to have demonstrated spontaneous remission although, after 8 months, splenomegaly and elevated reticulocyte count still persisted. Sayed's patient had an immediate cessation of hemolysis after a second operation at which the bare Teflon patch was covered with endocardium. The remaining four patients were reoperated upon. Of the two patients reported by Sigler et al., one showed a complete remission and one died on the third postoperative day. Of the two cases reported by Verdon et al., one patient did not show remission and died 6 months after the second operation from massive pulmonary embolism. The other patient died 6 hours after the second operation.

The purpose of this paper is to describe the spontaneous remission of a hemolytic anemia that developed after repair of an ostium primum defect with a Teflon patch. Remission occurred during adequate medical management of cardiac failure.

Case Report

J.B., a 15-year-old white girl, product of an uneventful gestation, had been observed in the Pediatric Cardiac Clinic, Grace-New Haven Community Hospital, since the age of 2 1/2 years. Because of an episode of congestive cardiac failure at the age of 2 years, she was digitalized. Digitalis was maintained until the time of open-heart surgery. During the succeeding years, poor growth and occasional exertional dyspnea were her chief complaints.

Physical examination revealed no distress, cyanosis, or clubbing. The habitus was asthenic, and the height and weight were below the third percentile. The blood pressure was 110/70 in the arm and 130/80 in the leg.

The pertinent cardiac findings were the presence of a left precordial bulge and cardiomegaly on percussion. A loud ejection systolic murmur, accompanied by a systolic thrill, was best appreciated over the second and third left intercostal space, parasternally. The murmur was widely transmitted over the precordium and to the back. There was an apical mid-diastolic rumble. The second heart sound was split over the third left intercostal space, parasternally, was widely split and fixed.

Electrocardiogram revealed first-degree heart block, right ventricular hypertrophy, and incomplete right bundle-branch block (fig. 1). X-ray of the chest showed enlargement of all cardiac chambers and increased pulmonary vascular markings (fig. 2a). Right heart catheterization demonstrated a left-to-right shunt at the atrial level, moderate pulmonary hypertension, and absence of a right-to-left shunt. The pulmonary flow was five times the systemic flow (table 1). The hemoglobin, hematocrit value, reticulocyte

From the Departments of Pediatrics, Pathology, and Surgery, Yale University School of Medicine, Grace-New Haven Community Hospital, New Haven, Connecticut.

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count, and liver function tests, including serum bilirubin, were within normal limits.

At open-heart surgery two atrial septal defects were seen, a small one of the secundum type and one below it with no lower border and an associated cleft in the mitral valve. The cleft was repaired by sutures reinforced with pledgets of Teflon patch. The ostium primum defect was closed with a Teflon patch and the secundum defect with interrupted sutures.

Toward the end of the first postoperative week, the patient developed progressive icterus and anemia. During the second week she developed low-grade fever, anorexia, abdominal pain, and hepatosplenomegaly.

During this period abnormal cephalin flocculation and thymol turbidity tests, high levels of serum glutamic oxaloacetic transaminase and alkaline phosphatase reflected hepatic impairment. These, however, returned to normal levels within 1 week. Repeated blood cultures were sterile. There was no hematuria.

Antihuman globulin (Coombs) test, both direct and indirect, antibody screening tests, tests for autoagglutinin and hemolysins were negative. Plasma protein level, hemoglobin electrophoresis, and osmotic fragility tests revealed normal patterns. Studies of red blood cell survival with the patient's Cr$^{51}$-tagged red blood cell revealed reduction in survival time (chromium T½).

Because of the progressive drop in hemoglobin and hematocrit levels, the patient was given several blood transfusions. Gradually the jaundice receded, and the patient became afebrile and was discharged 7 weeks after surgery, with a hemoglobin level stabilized at 7 Gm. per cent. Decrease in the heart size was noted in follow-up visits. For the next few months the patient maintained a hemoglobin level of about 7 Gm. per cent.

Toward the end of 7 months there was a sudden, further drop in the values of hemoglobin and hematocrit, the fall in hematocrit level being more rapid (fig. 3). The patient reported shortness of breath and increasing weakness. Physical examination at this time revealed severe anemia and congestive cardiac failure. The patient appeared pale, the apical systolic murmur which had persisted following surgery was more prominent, and x-ray of the chest revealed recent increase in heart size (fig. 2b). The patient was admitted to the hospital. Peripheral blood smear exhibited marked hypochromia, microcytosis, anisocytosis, poikilocytosis, and fragmented red blood cells (fig. 4). Red-cell survival studies showed further reduction in survival time of the patient's red blood cells (fig. 5). The serum iron was low with high iron-binding capacity. The hemoglobin was 5 Gm. per cent and the hematocrit level was 17 per cent. The patient was given digitalis and repeated blood transfusions, with marked improvement. At the time of discharge, the hemoglobin was 11.4 Gm. per

**Table 1**

<table>
<thead>
<tr>
<th>Position of the catheter</th>
<th>Oxygen saturation per cent</th>
<th>Pressure (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior vena cava</td>
<td>67</td>
<td>m = 10</td>
</tr>
<tr>
<td>Right atrium</td>
<td>79</td>
<td>a = 13-15*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60-70</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>83</td>
<td>12-18</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>82</td>
<td>40-60</td>
</tr>
<tr>
<td>Wedge (pulmonary artery)</td>
<td>15-18</td>
<td>106-110</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>98</td>
<td>69-76</td>
</tr>
</tbody>
</table>

* m, mean atrial pressure; a, atrial systolic pressure.

**Figure 1**

Electrocardiogram showing superiorly oriented axis of $-50^\circ$, prolongation of P-R interval, rSR pattern and evidence of right ventricular enlargement.

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Figure 2

Roentgenograms showing the size of the heart and pulmonary vascular markings. A, before surgery. B, 6 months after surgery during the acute episode. C, 18 months after operation, during state of remission. Note the decrease in heart size and the pulmonary vascular markings at the present time.

Figure 3

Course after surgery. Note the sharp fall in hemoglobin and hematocrit levels at 7 months and the response to adequate treatment. Broken line, hematocrit level. Solid black line, hemoglobin level. Horizontal hatched column, iron therapy. Vertical hatched columns, reticulocyte count. Vertical white columns, direct bilirubin levels. Vertical black columns, indirect bilirubin level. Arrows indicate blood transfusions.
Then followed an acute episode characterized by further fall in hemoglobin and hematocrit values, acute congestive cardiac failure, and increased mitral insufficiency. The peripheral blood smear and the serum iron level during this admission revealed that, in contrast to most of the other forms of hemolytic anemias, the body iron stores of this patient were low. Urine examination showed the presence of a large amount of hemosiderin, indicating abnormal loss. It would appear, therefore, that chronic hemolytic anemia further aggravated by the presence of iron-deficiency anemia, secondary to increased loss or poor dietary intake, leads to high-output cardiac failure, progressive dilatation of the heart with the development of a greater degree of mitral insufficiency, and a larger high velocity jet of blood in contact with the Teflon patch. The contact brings about further hemolysis, thereby causing an exacerbation of the anemia. Thus a viscous cycle is established from the anemia, hemolytic in nature, aggravated fur-

Discussion

The acute onset of anemia and evidence of increased blood destruction following the prosthetic closure of a low atrial septal defect associated with cleft mitral valve indicated the presence of a hemolytic process. In all the reported cases including the present one, an extensive search for other etiologic factors failed to demonstrate any of the usual causes of hemolytic anemia.1–4

For 7 months after surgery, the patient was in a state of compensated hemolytic anemia.

Figure 4

Peripheral blood smear during acute episode, showing hypochromic microcytic red blood cells and occasional irregularly shaped red-blood-cell fragments.

Figure 5

Red-cell survival studies. The dotted line represents the survival of the patient's Cr\(^{51}\)-tagged red cells during the clinical remission 18 months after operation (T\(_{50}\) = 16 days) and 1 month after operation (T\(_{50}\) = 15 days). The solid line represents the survival of fresh donor cells during the episode of acute congestive failure (T\(_{50}\) = 8 days). The normal red cell T\(_{50}\) by this technic is 28 to 32 days.

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ther by the iron-deficiency state; to high-output cardiac failure with dilatation of the heart; to increased regurgitation resulting in an increased rate of hemolysis. Bringing the hemoglobin and hematocrit levels to normal by blood transfusions and maintaining it by iron therapy appears to have broken the cycle in our patient.

At present, 19 months after surgery and 12 months since her acute episode of congestive cardiac failure, the patient is in a state of clinical remission. Her serum iron level and the iron-binding capacity are normal. There is still, however, laboratory evidence of compensated hemolysis, namely, an elevated reticulocyte count, the presence of hemosiderin in the urine, and shortened red-cell survival time.

Correction of any existing anemia and maintenance of hemoglobin and hematocrit at normal relative levels by repeated blood transfusions or iron therapy, as required, would appear to be an important factor in the management of these cases.

A high mortality rate has been observed in the cases that have been subjected to second operation.1-4 The good response to adequate management of anemia and congestive cardiac failure in two cases,2 including the one under discussion, indicates that vigorous medical management should be given an adequate trial before resorting to reoperation.

Conclusion

A case of hemolytic anemia that developed after open-heart surgery has been presented. The hemolysis appears to be mechanical in origin, caused by regurgitation of blood against the Teflon patch. The patient showed evidence of iron-deficiency anemia, which, by further aggravating the chronic hemolytic anemia, led to high-output cardiac failure, progressive dilatation of the heart, increased mitral regurgitation, and a greater impact of a high-velocity regurgitant jet of blood against the Teflon patch, resulting in more hemolysis. Correction of the anemia by blood transfusions and iron therapy broke the vicious cycle. Thus, intensive medical management to maintain hemoglobin and hematocrit at normal levels should be given a fair trial before resorting to reoperation.

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References


Acquire the art of detachment, the virtue of method, and the quality of thoroughness, but above all the grace of humility.—Sir William Osler. Aphorisms From His Bedside Teachings and Writings. Edited by William Bennett Bean, M.D., New York, Henry Schuman, Inc., 1950, p. 68.
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