Spontaneous Closure of Physiologically Advantageous Ventricular Septal Defects

By P. SYAMASUNDAR RAO, M.D., AND NORMAN J. SISSMAN, M.D.

SUMMARY
The clinical and pathological features of two cases in which physiologically advantageous ventricular septal defects closed spontaneously are presented. The first patient, with tricuspid atresia, Type I(c), developed symptoms and signs of increasing systemic hypoxemia, decreasing pulmonary blood flow, and a systolic murmur of decreasing intensity. His ventricular septal defect, previously demonstrated angiographically, could not be found at autopsy; it is presumed to have closed by fusion of its muscular rims with subsequent covering by endocardial proliferation. The second patient, with a double-outlet right ventricle, demonstrated progressive left ventricular enlargement and congestive failure despite increasing pulmonary vascular resistance. Postmortem examination showed that this defect was sealed by adherence of the septal leaflet of the tricuspid valve to the edges of the defect. Appreciation of the true nature of the changing anatomical situation would have resulted in more rational effective therapeutic approaches.

The cases presented and review of pertinent literature contribute to more complete understanding of circumstances surrounding the spontaneous closure of ventricular septal defects.

Additional Indexing Words:
Tricuspid atresia    Double-outlet right ventricle    Congestive heart failure
Ventricular septal defect, spontaneous closure

SPONTANEOUS closure of isolated ventricular septal defects is well documented.1-3 Even defects of this type large enough to require banding of the pulmonary artery in infancy have been reported to close naturally.4-6 Such occurrences are clinically desirable. Spontaneous closure of ventricular septal defects, which if open would be physiologically advantageous components of multiple defect complexes, is more rare; there are only a few reports of such anatomic events in cases of tricuspid atresia7,8 and double-outlet right ventricle.9 The purposes of this paper are the documentation of spontaneous closure of ventricular septal defects in one case of tricuspid atresia and one case of a double-outlet right ventricle, and a discussion of some of the unusual ensuing diagnostic and therapeutic problems.

Case Reports
Case 1 (S.U.H. 25-61-13)
J. W., the product of a normal pregnancy and delivery, was noted to be cyanotic during the first week of life. Physical examination at the age of 5 months revealed moderate cyanosis. Pulses and blood pressures were normal. The heart sounds were normal; there was a systolic thrill and a grade 4/6 holosystolic murmur maximal at the left lower sternal border. Cardiac series X-rays revealed an enlarged heart with right atrial enlargement and increased pulmonary vascular markings. The electrocardiogram showed a mean frontal plane QRS axis of +10 deg and right

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Table 1

<table>
<thead>
<tr>
<th>Site</th>
<th>Oxygen saturation (%)</th>
<th>Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior vena cava*</td>
<td>57</td>
<td>-</td>
</tr>
<tr>
<td>Right atrium</td>
<td>57</td>
<td>a = 11, v = 7, m = 6</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>Not entered</td>
<td></td>
</tr>
<tr>
<td>Pulmonary vein</td>
<td>95</td>
<td>-</td>
</tr>
<tr>
<td>Left atrium</td>
<td>76</td>
<td>a = 11, v = 7, m = 6</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>76</td>
<td>82/10</td>
</tr>
<tr>
<td>Right femoral artery</td>
<td>76</td>
<td>110/70 m = 87†</td>
</tr>
<tr>
<td>Pulmonary: systemic flow ratio†</td>
<td>1:1</td>
<td></td>
</tr>
</tbody>
</table>

*Persistent left superior vena cava was also entered.
†Obtained after angiocardiogram.
‡We assume pulmonary arterial saturation to be the same as those in the left ventricle and the femoral artery (76%).

atrial and left ventricular hypertrophy. Hematocrit was 45%. Cardiac catheterization was performed at age 5½ months (table 1). Left ventricular cineangiography revealed a large left ventricle and filling of a small right ventricle through a ventricular septal defect (fig. 1). A normal sized pulmonary artery opacified simultaneously with the ascending aorta. The great arteries were in normal anatomical position. Right atrial injection revealed findings typical of tricuspid atresia. The diagnosis at the catheterization was tricuspid atresia without transposition of the great arteries, ventricular and atrial septal defects, and a 1:1 pulmonary-systemic flow ratio.

The patient was not examined at Stanford again until the age of 2½ years, at which time his parents reported increased cyanosis and diminished exercise tolerance. Squatting was noted; however, no hypoxic spells had occurred. Examination at this time revealed marked cyanosis and clubbing. The first heart sound was normal, the second sound was single. Only a grade 1/6 ejection systolic murmur was noted at the left midsternal border. The patient's chest X-ray showed a normal sized heart with a concave pulmonary artery segment and a lung-field pattern of marked bronchial collateral circulation. The electrocardiogram continued to show left ventricular hypertrophy. His hematocrit was 77%. It was concluded that he had decreased pulmonary blood flow, and he was scheduled for a surgical systemic-pulmonary anastomosis. However, prior to the scheduled surgery he abruptly had a severe hypoxic spell and died at home.

Autopsy findings were limited to the heart and the lungs. There was a persistent left superior vena cava that united with the coronary sinus and entered the left atrium. An extensive unusual Chiari-like network was found in the left atrium. The right atrium was large and hypertrophied; the tricuspid valve was atretic. There was a large atrial septal defect of the secundum type. The left ventricle was large and hypertrophied; the right ventricle was hypoplastic. No ventricular septal defect was found, nor could any trace of a previous defect be found by inspection of the endocardial surfaces of the septum (fig. 2). The aorta and pulmonary arteries were normal in size and anatomical position. The pulmonary valve was normal. The ductus arteriosus was not patent. Numerous large bronchial collateral arteries were seen.

Case 2 (S.U.H. 21-78-47)

R. B. was a product of normal pregnancy and delivery. A heart murmur, cyanosis with crying, and congestive heart failure were noted at the age of 3 weeks, and he was digitalized. Physical examination at the age of 3 months revealed obvious cyanosis and normal blood pressures and pulses. There was a right ventricular heave. The first heart sound was normal and the second heart sound was split, with accentuation of the pulmonary component. A systolic thrill was palpated, and a grade 4/6 holosystolic murmur at the left lower sternal border and a grade 2/6 middiastolic rumble at the apex were noted. Hematocrit was 39%. A chest X-ray revealed mild cardiomegaly with left atrial and right ventricular enlargement (fig. 3A). The electrocardiogram showed a normal frontal plane QRS axis and right ventricular hypertrophy. Cardiac catheterization data obtained at age 3 months are recorded in table 2. Biplane cineangiograms were interpreted as showing a double-outlet right ventricle and a large ventricular septal defect. Because of the degree of arterial oxygen desaturation, increased pulmonary flow, and elevated pulmonary arterial and wedge pressures,
Case 1. Cineangiogram at age 5½ months; injection into the left ventricle. Passage of contrast material through a ventricular septal defect into the right ventricle is demonstrated clearly. (a) Anteroposterior projection. (b) Left lateral projection. RV, right ventricle; LV, left ventricle; A, aorta; PA, main pulmonary artery.

Figure 1

surgical atrial septostomy and pulmonary banding were recommended, but the parents refused consent. Periodic follow-up examinations revealed continued cyanosis and marked failure to thrive. Between 2 and 2½ years of age increasing symptoms of congestive heart failure and progressive cardiomegaly were noted. Cardiac examination at age 2½ years revealed marked cyanosis, clubbing, and signs of severe congestive heart failure. The apical impulse was in the fifth intercostal space in the anterior axillary line. There was a right ventricular heave, and a systolic thrill associated with a grade 5/6 holosystolic murmur were present at the left lower sternal border. A grade 3/6 mid-diastolic murmur was also heard at the apex. There was marked accentuation of the pulmonary component of the second heart sound. Chest X-rays at this time revealed massive cardiomegaly and pulmonary vascular congestion (fig. 3B). The electrocardiogram showed marked left ventricular enlargement with T-wave inversion over the lateral chest leads. Cardiac catheterization was repeated with results recorded in table 2. The left side of the heart was not entered. Right ventricular and pulmonary artery cineangiograms confirmed the diagnosis of double-outlet right ventricle. On the levocardiographic phase the left ventricle was noted to be extremely large in size, to contract poorly, and to show prolonged opacification (fig. 3C). The left atrium contracted well.

Again surgery was recommended although the increased risk because of the altered physiologic

Figure 2

Photograph of the heart of case 1. The right ventricle is open and no trace of the previously present ventricular septal defect is seen. There is no pulmonary stenosis. Abbreviations as in figure 1.
**Table 2**

*Cardiac Catheterization Results in Case 2*

<table>
<thead>
<tr>
<th>Site</th>
<th>Age 3 months</th>
<th>Age 2½ years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oxygen saturation (%)</td>
<td>Pressure (mm Hg)</td>
</tr>
<tr>
<td>Superior vena cava</td>
<td>43</td>
<td>-</td>
</tr>
<tr>
<td>Right atrium</td>
<td>43</td>
<td>a = 8 v = 4 m = 3</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>72</td>
<td>80/7</td>
</tr>
<tr>
<td>Pulmonary artery*</td>
<td>86</td>
<td>75/40 m = 50</td>
</tr>
<tr>
<td>Pulmonary artery wedge</td>
<td>-</td>
<td>18 (mean)</td>
</tr>
<tr>
<td>Aorta*</td>
<td>60</td>
<td>75/38 m = 53</td>
</tr>
<tr>
<td>Pulmonary: systemic flow ratio†</td>
<td>4.7</td>
<td>(mm/liter/min/m²)</td>
</tr>
</tbody>
</table>

*Both great arteries were entered from the right ventricle.
†We used assumed pulmonary venous saturation of 96% and assumed oxygen consumption of 150 ml/min/m².

status was recognized. However, before surgery could be performed, the patient, in whom signs of severe hypoxemia and pulmonary congestion persisted despite intensive medical treatment, was found dead in his crib one morning.

The autopsy showed that both atria were large and that the foramen ovale was sealed. Both great arteries arose directly from the right ventricle. The left-right relative positions of the aorta and pulmonary artery were normal, but the aorta was anteriorly situated. The left ventricle was markedly hypertrophied and dilated. The ventricular septal defect, which had been the only outlet from the left ventricle, was situated below the level of crista supraventricularis and was closed (except for a 1–2-mm diameter opening) by adherence of the septal leaflet of the tricuspid valve to its margins. Marked endocardial proliferation covered the area of the previously patent ventricular septal defect, which had been approximately 1.0 × 1.0 cm (fig. 4). Microscopy of the lung showed moderate pulmonary arterial changes, classified as Heath-Edwards grade III.

**Discussion**

The first case was diagnosed in early infancy as tricuspid atresia, Type I(c), according to the classification of Keith et al.10 The patient had unequivocal angiocardiographic evidence of patency of a ventricular septal defect at the age of 5 months. Even though no direct measurement of pulmonary pressure was made, subsequent examinations,

**Figure 3**

Case 2. (a) Chest X-ray in anteroposterior projection at age 3 months. (b) Chest X-ray at age 2½ years. Note the great increase in heart size. (c) Frame from the levocardiographic phase of a cineangiogram performed at about the same time as the film in (b). Film taken toward the end of systole shows the large end-systolic volume. LA, left atrium; LV, left ventricle.
including autopsy, demonstrated no valvular or infundibular pulmonary stenosis. Although its size could not be accurately assessed, it must be concluded that the largest area of the ventricular septal defect was less than that of the aortic orifice in view of the fact that pulmonary blood flow did not exceed systemic flow despite a probable normal or low pulmonary vascular resistance. When the patient was examined at age 2½ years the decreased intensity of his holosystolic murmur and his increased cyanosis, dyspnea, and fatigue on exertion were correctly interpreted clinically as being caused by further diminution of pulmonary flow. Gallaher and Fyler discussed three patients in whom a similar sequence of events occurred; they concluded, in their discussion of possible explanations, that narrowing or complete closure of the ventricular septal defect was the most likely cause.

We have found only two reports in the literature in which complete closure of ventricular septal defects in tricuspid atresia was proven anatomically. Roberts et al. described a 27-year-old man who died after a Glenn procedure. At autopsy the diagnosis of tricuspid atresia was confirmed; the ventricular septal defect was closed by progressive apposition of myocardial fibers followed by endocardial proliferation over the united surfaces. The second report was that of Meng whose 28-month-old patient had tricuspid atresia demonstrated at autopsy. In her case, the ventricular septal defect was narrowed by endocardial sclerosis and proliferation and finally sealed off by an occluding mural thrombus.

In case C of Gallaher and Fyler, catheterization of the patient at age 18 months revealed that dye-dilution curves showed no apparent left-to-right shunt at the ventricular level although a cineangiogram showed a shunt. There appeared to be marked diminution in the size of the ventricular septal defect compared with a previous study. None of these authors' three cases was examined at autopsy.

Brock has discussed methods of surgical treatment of patients with tricuspid atresia without transposition of the great arteries in whom there is no valvular pulmonary stenosis.

Figure 4

Photographs of the heart of case 2. (a) From the right ventricular aspect. Arrow points to the very small remaining opening of the ventricular septal defect. Above this is seen the abnormal insertion of the chordae tendineae of the tricuspid valve onto the crista supraventricularis. (b) View from the right atrial aspect. The extent of the previous ventricular septal defect can be seen as an area of light transmitted through the translucent valve leaflet. The defect was approximately 1.0 x 1.0 cm in size. Orientation relative to the view in (a) can be made by noting the chordae tendineae of the papillary muscle of the conus indicated by an arrow. (c) The previous ventricular septal defect as seen from the left ventricular side. Arrow points to area where strands of thickened endocardium cover the site of the defect.

RV, right ventricular endocardial surface; A, aorta; PA, main pulmonary artery; TV, tricuspid valve leaflets; MV, mitral valve leaflets; LV, left ventricle.
He advocated enlarging the ventricular septal defect, and actually performed this type of surgery in a 5-year-old girl. She died on the fifteenth postoperative day, and autopsy revealed that the defect had not been enlarged adequately. The difficulties of surgical creation of ventricular septal defects are well known from animal experiments. The insertion of cored plastic buttons does maintain a satisfactory communication, but this has not yet been attempted in humans to our knowledge. Systemic-pulmonary anastomoses are at present still the most practical means of increasing pulmonary blood flow in an anatomical situation such as the one in our patient; an anastomosis of the Blalock-Taussig type would seem preferable to a Glenn procedure, as the latter would leave the left lung without any pulmonary artery flow if the ventricular septal defect were to close completely. Should a satisfactory means of creating or enlarging a ventricular septal defect become practical, it would be the preferred method of treating patients of this type; accurate assessment of the size and location of the left-to-right shunt and the presence or absence of infundibular or valvar stenosis then would be even more essential than at present.

The catheterization data obtained from our second patient led us to conclude that his double-outlet right ventricle anomaly was of Neufeld's Type II, in which the ventricular septal defect lies "above" the crista supraventricularis beneath the pulmonary valve, and thus the pulmonary circulation receives a greater portion of left ventricular output than does the systemic circulation, and the oxygen saturation of the pulmonary artery is higher than that of the aorta. Because of this diagnosis, the later clinical situation, in which he appeared to be developing progressive left ventricular enlargement and failure in the presence of increasing pulmonary vascular resistance, was particularly difficult to interpret because of the usual large size of such subpulmonic defects and the consequently small likelihood of their closing spontaneously. We postulated that he had developed additional disease of the left ventricle, such as endocardial fibroelastosis, and this seemed to be confirmed by the observation of a markedly dilated and poorly contracting left ventricular chamber on the levocardiographic phase of the cineangiocardio gram.

The autopsy revealed that the defect lay "beneath" the crista (fig. 4); thus the anomaly clearly was of Neufeld's Type I. The explanation of the physiologic findings at the first catheterization lay in the unusually short vertically oriented insertion of chordae tendineae of the medial leaflet of the tricuspid valve onto the crista supraventricularis itself (fig. 4A). This directed the major portion of the ventricular septal defect flow into the right ventricular outflow tract and hence into the pulmonary artery. This anatomical arrangement also must have predisposed this leaflet of the tricuspid valve to becoming "plastered" over the major portion of the defect during systole and to the eventual almost complete sealing of the defect by adherence of the leaflet to the rim of the defect. Creation of an atrial septal defect, if it had been performed during the first few months of life, would have resulted in higher systemic arterial oxygen saturation by permitting a left-to-right shunt to flow into the inflow tract of the right ventricle; it might have retarded the rapidity of development of increased pulmonary vascular resistance by decreasing the left atrial, and thus the pulmonary venous, pressure; but it probably would have had no effect on the progressive diminution of the size of the ventricular septal defect. Had the true anatomical situation been appreciated it would seem that enlargement, or at least reconstitution, of the septal defect by excision of the obstructing portion of the tricuspid valve leaflet would have been possible, although the effect of this type of surgical intervention on the function of the valve would be problematic.

To our knowledge, only one case of spontaneous closure of a ventricular septal defect in double-outlet right ventricle has been reported previously. The case of Edwards et al. was that of a 4½-month-old.
female in whom a membranous ventricular septal defect was closed by apparent adhesion of the anterior leaflet of the mitral valve to the margins of the defect. Associated lesions in this case were double orifice of the mitral valve and a single coronary artery. Lauer et al.\textsuperscript{15} reported one case of double-outlet right ventricle with left ventricular obstruction caused by a small \((6 \times 4\) mm\) ventricular septal defect in a 13-year-old girl who died after corrective surgery. She also had infundibular and valvular pulmonary stenosis and a small atrial septal defect. Three cases of double-outlet right ventricles with congenitally intact ventricular septa have been reported.\textsuperscript{16-18} Associated lesions in these cases were endocardial fibroelastosis of the left ventricle,\textsuperscript{16} congenital mitral stenosis,\textsuperscript{17} and hypoplastic mitral valve;\textsuperscript{18} all three patients had hypoplastic left ventricular chambers and small but patent anatomical communications between the left and right atria.

Several different mechanisms for spontaneous closure of ventricular septal defects have been postulated. These include apposition to and eventual fusion with the rims of the defects by leaflets of the tricuspid\textsuperscript{22, 4, 19-21} or mitral\textsuperscript{19} valves, progressive muscular "encroachment" of the margins of the defects with subsequent fibrosis and covering by endocardial proliferation,\textsuperscript{2, 7, 8, 23, 24} aneurysmal formation of the membranous septum,\textsuperscript{26} and occlusion by thrombus\textsuperscript{8} or vegetations of bacterial endocarditis. In our second case, the first of these mechanisms was obviously the operative one; although the explanation in case 1 is less clear, muscular encroachment of the margins of an initially rather small muscular defect with subsequent complete obliteration by endocardial proliferation seems most likely. This may happen more often in tricuspid atresia than is generally appreciated: Suzuki\textsuperscript{24} concluded that spontaneously closed ventricular septal defects are most likely those of the muscular septum, and, in all ten cases of Type I tricuspid atresia described by Guller and Titus,\textsuperscript{26} the ventricular septal defect was entirely surrounded by muscle.

\textbf{References}

1. \textsc{Evans Jb}, \textsc{Rowe Rd}, \textsc{Keith Jd}: Spontaneous closure of ventricular septal defects. \textit{Circulation} \textbf{22}: 1044-1054, 1960

2. \textsc{Bloomfield Dk}: The natural history of ventricular septal defects in patients surviving infancy. \textit{Circulation} \textbf{29}: 914-955, 1964

3. \textsc{Hoffman Jje}, \textsc{Rudolph Am}: The natural history of ventricular septal defects in infancy. \textit{Amer J Cardiol} \textbf{16}: 634-653, 1965

4. \textsc{Mukty K}, \textsc{Arcilla Ra}, \textsc{Moulder Pv}, et al.: Functional closure of a ventricular septal defect after pulmonary artery banding. \textit{JAMA} \textbf{205}: 592-594, 1968

5. \textsc{Edgett Jw Jr}, \textsc{Nelson Wp}, \textsc{Hall Rj}, et al.: Spontaneous closure of ventricular septal defects after banding of the pulmonary artery. \textit{Amer J Cardiol} \textbf{22}: 729-732, 1968

6. \textsc{Stark J}, \textsc{Tynan M}, \textsc{Aberdeen E}: Spontaneous closure of ventricular septal defects following pulmonary artery constriction (banding). \textit{Amer Heart J} \textbf{76}: 548-551, 1970

7. \textsc{Roberts Wc}, \textsc{Morrow Ac}, \textsc{Mason Dt}, et al.: Spontaneous closure of ventricular septal defects, anatomic proof in an adult with tricuspid atresia. \textit{Circulation} \textbf{27}: 90-94, 1963

8. \textsc{Meng Ccl}: Spontaneous closure of ventricular septal defects in tricuspid atresia. \textit{J Pediat} \textbf{75}: 697-700, 1969

9. \textsc{Edwards Je}, \textsc{James Jw}, \textsc{DuShane Jw}: Congenital malformations of the heart: Origin of transposed great vessels from right ventricle associated with atresia of the left ventricular outlet, double orifice of the mitral valve, and single coronary artery. \textit{Lab Invest} \textbf{1}: 197-207, 1952


11. \textsc{Callaher Me}, \textsc{Fyler Dc}: Observations on the changing hemodynamics in tricuspid atresia without associated transposition of the great vessels. \textit{Circulation} \textbf{35}: 381-388, 1967

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\textbf{Addendum}

Since the submission of this manuscript for publication, our attention has been directed to two recent additional reports of cases of double-outlet right ventricle with obstruction to left ventricular outflow.\textsuperscript{22, 27} In none of the four cases described was there evidence of progressive diminution of the size of the ventricular septal defect as in our case 2.
17. AINGER LE: Double-outlet right ventricle; intact ventricular septum, mitral stenosis and blind left ventricle. Amer Heart J 70: 521-525, 1965
27. MASON DT, MORROW AG, ELKINS RC, ET AL: Origin of both great vessels from the right ventricle associated with severe obstruction to left ventricular outflow. Amer J Cardiol 24: 118-124, 1969
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