Congenital Stenosis of Individual Pulmonary Veins

By JOHN D. SHONE, M.B. (Lond.), KURT AMPLATZ, M.D.,
RAY C. ANDERSON, M.D., PAUL ADAMS, JR., M.D., AND JESSE E. EDWARDS, M.D.

Congenital stenosis of individual pulmonary veins as they join the left atrium is a rare cause of pulmonary venous and arterial hypertension.

Cases have been reported by Reye,1 Ferencz and Dammann,2 Andrews,3 Bernstein and associates,4 and Edwards.5, 6 Emslie-Smith and associates7 reported a patient with membranous occlusion of the pulmonary veins associated with pulmonary hypertension. The purpose of this report is to correlate the clinical, pathologic, roentgenographic, and hemodynamic data in a case of congenital stenosis of the individual pulmonary veins. The report also comments on the possibility of surgical correction of this malformation.

Report of Case

Clinical Features

A 5-month-old male infant was referred to the University of Minnesota Hospitals on June 1, 1961. He had gained weight poorly from birth. At the age of 4 months, cyanosis, easy fatigability, and profuse perspiration were noted.

Physical examination revealed a malnourished, moderately dyspneic and cyanotic male infant. Tachypnea (80/min.) and tachycardia (160/min.) were present. The lungs were clear to auscultation. No precordial thrill was palpable. The sounds over the base of the heart were of diminished intensity. Splitting of the second sound was noted only in the apical area. A grade 2 (on the basis of 1 to 6) short, harsh, midsystolic murmur was heard along the left lower parasternum, accompanied by an early systolic ejection click. Blood pressures obtained by simultaneous flush technic were 100 mm. of mercury in the right arm and leg. The hepatic margin lay 1 cm. below the right costal margin in the midepigastic line. The hemoglobin concentration of the blood was 13.3 Gm. per 100 ml.

From the Departments of Pediatrics, Radiology, and Pathology, University of Minnesota, Minneapolis, Minnesota, and the Department of Pathology, The Charles T. Miller Hospital, St. Paul, Minnesota.

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A diagnosis was made of pulmonary hypertension of unknown etiology associated with a right-to-left shunt at atrial level on the basis of studies described below. The infant was discharged but readmitted on July 28, because of anorexia, irritability, loss of weight, increasing cyanosis, and dyspnea. The physical findings were essentially the same as on the first admission. His general condition had deteriorated, so he was digitalized with digoxin and given chloramphenicol and penicillin. The infant died on August 11, at the age of 7 months, with no definitive anatomic diagnosis having been made clinically.

Electrocardiographic Features

The first electrocardiogram showed a mean manifest electrical axis of the QRS complex (A QRS) of +140 degrees in the frontal plane, narrow, peaked P waves measuring 0.3 millivolt in lead II, and a pattern of marked right ventricular hypertrophy of the systolic (pressure) overload type (fig. 1).

In subsequent tracings there was a slight increase in P wave voltages in lead II and also a slight increase in R wave voltages in the right precordial leads.

Hemodynamic Findings

Right-sided cardiac catheterization was done on both admissions (table 1). No positive evidence of a left-to-right shunt was obtained. On the second admission right-sided catheterization was repeated, primarily to obtain pulmonary arterial and pulmonary arterial “wedge” pressures but these could not be obtained.

The right ventricular pressure was higher than at the time of the first study. There also was evidence of a greater degree of desaturation of the systemic venous blood. A systemic arterial sample was not obtained.

Roentgenographic Findings

On both admissions, roentgenograms of the thorax showed a normal-sized heart without abnormalities of contour, except for some fullness of the main pulmonary artery segment. There was diffuse accentuation of the vascular markings in both pulmonary fields (fig. 2).

Prior to the first cardiac catheterization a venous angiocardiogram was performed from the right greater saphenous vein at the ankle (fig. 3). It showed opaque material passing from the right
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Electrocardiogram of patient at 5 months of age.

atrium into both the left atrium and the right ventricle, with simultaneous opacification of a normally situated aorta and pulmonary artery. The pulmonary arteries were enlarged and unduly tortuous, the right more so than the left. In the late phases of the study no abnormal features were apparent. This study did not preclude the clinical diagnosis of total anomalous pulmonary venous connection.

In conjunction with the first cardiac catheterization, a selective right ventriculogram (fig. 4) disclosed enlargement of the right ventricular chamber without pulmonary valvular or infun-

dibular obstruction. The right pulmonary artery was abnormally dilated and tortuous; the left appeared small. The left pulmonary field was more radiolucent than the right. Late views showed good filling of normal-sized left atrium, left ventricle, and aorta. The pulmonary veins appeared to connect normally with the left atrium.

After this study a diagnosis was made of pulmonary hypertension of unknown etiology associated with a right-to-left shunt at atrial level.

After necropsy on re-examination of these films, unusual tortuosity of the pulmonary veins and constriction of the veins at their veno-atrial junc-

Table 1

<table>
<thead>
<tr>
<th>Site</th>
<th>Pressure (mm. Hg)</th>
<th>Oxygen saturation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior vena cava</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Inferior vena cava</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Right atrium</td>
<td>17/10 (M 15)</td>
<td>19/11 (M 14)</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>150/0</td>
<td>185/15</td>
</tr>
<tr>
<td>Femoral vein*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Right pulmonary artery†</td>
<td>—</td>
<td>170/80</td>
</tr>
<tr>
<td></td>
<td>(M 110)</td>
<td></td>
</tr>
</tbody>
</table>

*In June 1961, oxygen content: 3.4 vol. per 100 ml.; oxygen capacity: 16.4 vol. per 100 ml.; Van Slyke oxygen saturation: 25 per cent.

†In August 1961, oxygen content: 4.5 vol. per 100 ml.; oxygen capacity: 14.8 vol. per 100 ml.; Van Slyke oxygen saturation: 31 per cent.
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Figure 3
Forward angiocardiogram in anteroposterior and lateral projections showing right-to-left shunt at the atrial level, with opacification of pulmonary artery (P.T.) and aorta (A.), which are in normal relationship. Enlarged and tortuous pulmonary arteries, especially in right lung. R.A., right atrium; R.V., right ventricle; L.A., left atrium.

Figure 4
Selective angiocardiogram from right ventricle showing enlarged right ventricular chamber with no evident pulmonary stenosis or right-to-left shunt at this level.

findings were thought to indicate a delay in passage of blood from the right pulmonary veins into the left atrium.

Pathologic Features
Gross Findings
The pertinent necropsy findings were confined to the heart and lungs. The pulmonary veins joined the left atrium at normal locations. At the ostium of each pulmonary vein a localized, circumferential collar of intimal fibrous thickening protruded into the venous lumen, narrowing it to a diameter hardly more than 1 mm. The lesions of the veins extended less than 3 mm along the length of the vessel from the left atrial junction. Peripheral to the stenotic lesions, each pulmonary vein was comparatively thick-walled but not dilated (figs. 6 and 7, left). No gross differences were noted between the arteries and veins of either lung.

At the fossa ovalis the atrial septum showed a large defect crossed by strands of septal tissue. The ductus arteriosus was obliterated normally. The ventricular septum was intact. The cardiac valves were normal. Right ventricular hypertrophy was marked. The right atrial chamber was moderately enlarged (fig. 7, right). The left atrium and left ventricle were normal.

Histologic Findings
Histologically, the zones of stenosis in the pulmonary veins were represented by focal nonspecific fibrous thickening of the intima (fig. 8). The

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lungs showed engorgement of the capillaries. Within the alveolar spaces there were foci of fresh hemorrhage and accumulations of macrophages containing small amounts of iron pigment. The lymphatics of the visceral pleura and interlobular septa appeared somewhat dilated. The arterial and venous vessels were essentially similar in all lobes. The arterial vessels showed prominent, parallel and continuous elastic laminae in the elastic arteries (fig. 9, upper left). The large muscular arteries exhibited prominent medial hypertrophy (fig. 9, upper right). Some large muscular arteries contained isolated bands of elastic tissue within the muscular media. At their proximal muscular portions, the arteriolar vessels showed distinct hypertrophy of the wall producing significant luminal narrowing. The venules and arterioles showed rare foci of intimal fibrous thickening (fig. 9, lower). The large venous trunks within the parenchyma showed mild degrees of medial hypertrophy (fig. 10).

Discussion

The pulmonary venous stenotic lesions observed in this case are rare. The pathologic aspects of congenital pulmonary venous stenosis have been reviewed previously.\(^5\) This review emphasized that this type of lesion may occur either in pulmonary venous channels that course anomalously, or in those that join the left atrium at normal locations. In general, experience with stenotic pulmonary venous lesions is limited. This prevents the formulation of broad conclusions. Nevertheless, it seems that localized fibrous intimal lesions of pulmonary veins are more common in vessels that join structures other than the left atrium than in those that connect at normal sites with the left atrium.
lesions occur under the latter circumstances, the pulmonary veins may be involved either bilaterally or unilaterally.

Several factors favor a congenital basis for the pulmonary venous stenosis observed in our case, as well as in cases reported. They include (1) the frequent association with other congenital anomalies (atrial septal defect in our case); (2) the young age at which symptoms referable to the lesion became apparent; (3) the similarity of the lesion that occurs in normally inserting pulmonary veins and in those veins that insert into structures other than the left atrium; and (4) the absence of evidence of active inflammation in or around the involved segments of vein. While a congenital basis is favored for these cases, it is recognized that acquired functional pulmonary venous stenosis may occur as a complication of several congenital or acquired lesions, for example: (1) constrictive pericarditis, (2) mediastinitis, (3) pulmonary venous phlebitis (as in tuberculosis), and (4) invasion by tumor tissue. The functional pulmonary venous obstruction manifested in congenital or acquired stenosis of individual pulmonary veins is found in a number of other conditions. The etiologic conditions that may give rise to pulmonary venous obstruction in children may be classified in two anatomic groups:

Group I includes conditions in which the obstructive lesion is situated at or proximal to the mitral valve. Right ventricular hypertrophy and right atrial enlargement result from obstruction to the pulmonary venous flow as a primary functional effect. These conditions include atresia or stenosis of the mitral valve, cor triatriatum, stenosis of the individual pulmonary veins, tumor of the left

**Figure 7**

Left. Left side of heart and pulmonary veins viewed from behind. At each veno-atrial junction (points of arrows) is circumferential, intimal thickening. On the right side, both upper and lower veins are shown. On the left side, only the upper pulmonary vein is shown. The left atrium (L.A.) and the left ventricle (L.V.) are intrinsically normal, although an atrial septal defect is evident in the left atrium. Right. Right atrium (R.A.) and right ventricle (R.V.). The atrial septal defect is evident in the atrium. It lies at the fossa ovalis, above the ostium of the coronary sinus (C.S.). The right ventricular wall is hypertrophied.
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atrium, and total anomalous pulmonary venous connection with high resistance to flow of either the infradiaphragmatic or supradiaphragmatic types.

Group II includes conditions in which the lesion lies distal to the mitral valve. They are characterized, usually, by predominant left ventricular hypertrophy. In these conditions pulmonary venous hypertension occurs secondarily to left ventricular failure or insufficiency. They include aortic stenosis, coarctation of aorta, mitral insufficiency, and endocardial sclerosis. (Coarctation of the aorta is usually associated with right ventricular hypertrophy on the electrocardiogram.)

In congenital pulmonary venous stenosis there are a number of general manifestations shared with those conditions in Group I, i.e., conditions in which there is right ventricular hypertrophy and obstruction to pulmonary venous flow as a fundamental functional derangement. These general manifestations are (1) a history of progressive dyspnea and failure to thrive, which may be associated with increasing cyanosis, recurrent respiratory infections, and repeated hemoptysis; (2) clinical findings indicating pulmonary arterial hypertension and right ventricular hypertrophy; (3) electrocardiographic findings of right ventricular hypertrophy, which may be associated with right atrial enlargement; and (4) conventional roentgenograms of thorax showing a normal-sized or an enlarged heart with unilateral or bilateral increased pulmonary venous markings and with no left atrial enlargement. (Mitral stenosis is an exception as, also, are some cases of cor triatriatum.) An enlarged right ventricle and right ventricular outflow tract, together with an enlarged main pulmonary artery, may be demonstrated by selective angiocardiography. Characteristically, the pulmonary fields in pulmonary venous obstruction show a fine, reticulated vascular pattern, passive pulmonary congestion, or the “ground glass” appearance of frank pulmonary edema. In our experience with the pediatric age group, the heart may be normal in size or may be enlarged; there is no left atrial enlargement; Kerley’s lines are absent. In addition to these general features of obstruction, there are findings that tend to separate the condition being discussed from a larger group with functional similarities. These findings include (1) unilateral or bi-

Figure 8
Low-power photomicrograph of the right lower pulmonary vein and the left atrium. At the junction with the atrium the vein shows localized, non-specific intimal thickening. Elastic tissue stain; × 35.

Figure 9
Photomicrographs of pulmonary arterial vessels. Upper left. Lower lobe of right lung. An elastic artery is cut in cross section and a large muscular artery arises from it at right angles. The elastic artery shows prominent parallel and continuous elastic fibers, while the muscular artery shows a distinctly hypertrophied medial coat. Elastic tissue stain; × 100. Upper right. Lower lobe of left lung. A large muscular artery shows pronounced hypertrophy of its media. Isolated strands of elastic tissue are present among the muscle fibers. Elastic tissue stain; ≥ 300. Lower. Photomicrographs of arterioles showing intimal fibrous thickening. Each stained for elastic tissue; × 750. Lower left. Lower lobe of the left lung. Lower right. Upper lobe of right lung.
lateral increased pulmonary arterial wedge pressures in conjunction with (2) a normal left atrial pressure. This rules out stenosis or atresia of the mitral valve and, probably, a supravalvular stenosis in the left atrial cavity. Both findings may occur, however, in cor triatriatum, atresia of the common pulmonary vein,10 and total anomalous pulmonary venous connection with high degrees of resistance to flow.

The specific diagnosis of congenital stenosis of individual pulmonary veins can be established only by the identification of delay in the passage of opaque material from one or more of the pulmonary veins into the left atrium, coupled with evidence of constriction of the pulmonary veins at the veno-atrial junction. This can best be achieved, probably, by selective angiocardiography performed from the pulmonary artery. The major difficulty is in differentiating this defect from cor triatriatum, particularly if the left atrium is not well visualized. Since the constricted segments of the pulmonary veins in this anomaly extend for only a few millimeters from the veno-atrial junction, it appears feasible to excise the constricted segments and re-anastomose the pulmonary veins to the left atrium.

Summary

The case is reported of an infant with congenital stenosis of each of the four individual pulmonary veins near the left atrium. The characteristic features were failure to thrive, increasing cyanosis and dyspnea, and death in congestive cardiac failure at 7 months of age. A precordial systolic murmur and an early systolic ejection click were heard; the sounds over the base of the heart were diminished in intensity. Roentgenograms of the thorax revealed a heart of normal size with fullness of the main pulmonary artery segment and increased pulmonary vascular markings that had the reticulated appearance associated with pulmonary venous engorgement. Electrocardiography showed right axis deviation, right atrial enlargement, and a pattern of right ventricular systolic overload. Cardiac catheterization demonstrated increased right atrial pressure and markedly elevated right ventricular and pulmonary arterial pressures. Angiocardiographic studies revealed a right-to-left shunt at atrial level, enlargement of the right ventricle, and enlarged and tortuous pulmonary arteries. In the late films the left atrium appeared normal in size, but the pulmonary veins were tortuous and there was evidence of constriction of the pulmonary veins at the veno-atrial junctions, associated with delay in the passage of opaque material from the pulmonary veins to the left atrium.

It is suggested that the definitive diagnosis most likely is to be made by a selective angiocardiogram performed from the main pulmonary artery.

It would appear feasible, at least in theory, to obtain complete surgical correction of this anomaly.

References


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It has somewhere been said that true science is like a flowering and delectable plateau which can be attained only after climbing craggy steeps and scratching one's legs against branches and brushwood. If a comparison were required to express my idea of the science of life, I should say that it is a superb and dazzlingly lighted hall which may be reached only by passing through a long and ghastly kitchen.—CLAUDE BERNARD. An Introduction to the Study of Experimental Medicine. New York, The Macmillan Company, 1927, p. 15.
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