Extrapulmonic Stenosis of the Pulmonary Veins

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Pulmonary venous stenosis is a rare condition. A case combining unilateral stenosis and atresia was included by Ferencz and Dammann in a series of congenital abnormalities associated with pulmonary venous obstruction. The abnormality occurred in a child who developed severe recurrent hemoptysis at 1½ years of age and thereafter suffered from progressive dyspnea and orthopnea. The patient exhibited right heart failure with pulmonary arterial hypertension. Death occurred at the age of 2½ years. Postmortem examination disclosed atresia of the vein from the lower lobe and stenosis of the vein from the left upper lobe; the right pulmonary veins were normal. Arteriolar sclerosis was restricted to the left lung.

Bilateral obstruction was reported by Reye in the case of an 8-year-old girl, who was thought to have had congenital heart disease and who terminally developed right heart failure. She had stenosis of the veins from the left upper and lower and the right lower lobes. The vein from the right upper lobe was atretic.

The only comparable cases encountered in a review of the literature were those reported by Aust, Romberg, Posselt, and Hart as “primary” pulmonary arteriosclerosis. In these 4 cases in young adults, pulmonary arteriosclerosis was associated with diminution in caliber of the pulmonary veins and hypoplasia of the left side of the heart. Both Posselt and Hart thought that the venous abnormality was congenital, and Posselt attributed it to a form of fetal endocarditis. The onset of the disease in adult life would lead us to suspect, however, that the hypoplasia of the left ventricle and aorta and possibly the apparent constriction of the pulmonary veins were only relative to marked hypertrophy and dilatation of the right ventricle and dilatation of the pulmonary artery.

In the case reported below, marked constriction of all the pulmonary veins appeared to be the primary factor in the development of severe pulmonary arterial hypertension.

Case Report

The patient was a 6-year-old Negro boy admitted to Children’s Hospital of Michigan because of recurrent hemoptysis.

During the first 4 years of life the child had occasional respiratory infections. At 4 years of age a chest roentgenogram revealed cardiac enlargement and an electrocardiogram right ventricular hypertrophy. Later the child had repeated episodes of hemoptysis, which became progressively more severe and for which he was hospitalized. Angiocardiographic studies showed dilatation of the pulmonary artery and its major branches but no evidence of cardiovascular malformation (fig. 1). Bronchoscopic examination was initially negative, but on subsequent examination very hyperemic, “granulomatous” tissue was seen partially occluding the right upper lobe bronchus. A thoracotomy was undertaken and abnormally vigorous pulsations were present in the azygos and intercostal veins. A faint thrill, which could be obliterated by occluding the pulmonary artery, was present in the right upper lobe. This lobe was firmer than the others and was resected. Pathologic examination of the specimen revealed extensive arterial and venous thrombosis in varying stages of organization.

At 6 years of age, when he was readmitted because of increasing dyspnea, fatigue, and fever, he was slightly cyanotic with tachypnea and moderate dyspnea. Venous distention was present in the neck. Rales were heard and breath sounds were decreased in the left upper chest. The blood pressure was 100/40 mm. Hg and the pulse rate 144 per minute. A rumbling systolic and a soft diastolic murmur were heard at the apex. The pulmonary second sound was booming in character. A continuous hum was heard to the right of the sternum in the second intercostal space. The liver was felt 5 to 6 cm. below the costal margin in the right midclavicular line. It was smooth, firm, and quite tender. Laboratory data included a hemoglobin of 9.4 Gm. per 100 ml. and a red
rate fell to 86 to 92 per minute, and the liver was no longer palpable. He was more comfortable, but his cough was occasionally productive of considerable amounts of bright red blood. Approximately 1 month after admission he suddenly developed marked left anterior chest pain, rapidly rising temperature, profuse diaphoresis, cyanosis, and tachypnea. The patient died four hours after the onset of these symptoms.

At postmortem examination the heart was greatly enlarged and weighed 280 Gm. (normal weight approximately 95 Gm.). The right atrium and ventricle were greatly dilated and hypertrophied. The pulmonary artery was wide and presented atheromatous plaques on its intimal surface. There was dilatation of the left side of the heart in association with slight ventricular hypertrophy, and a moderately severe degree of endocardial sclerosis was present in the left atrium. There was no evidence, grossly or microscopically, of mural thrombosis to account for the endocardial thickening. The 3 remaining pulmonary veins were stenotic at their respective junctions with the left atrium. On the left, the 2 veins entered separately, and the lumen of each was only 1 to 2 mm. in diameter (fig. 2B). The atrial endocardium around the venous orifices was greatly thickened, and there was marked intimal sclerosis of the veins. On the right, the vein from the upper lobe had been ligated when the lobe was removed, and the vein from the lower lobe was both stenotic and partially occluded by an organizing thrombus (fig. 2A). The thrombus appeared to have resulted from the ligation of and marked proliferative reaction around the stump of the upper vein. Microscopic examination of the heart revealed, in addition to myocardial hypertrophy, a very slight ventricular infiltrate of mononuclear cells, insufficient to warrant the diagnosis of myocarditis. There were, however, prominent intimal fibrosis and moderate medial hypertrophy of the branches of both coronary arteries. There was no obvious relationship between the changes in the coronary arteries and those in the left atrium, unless both were the result of a common inflammatory process. The ventricular endocardium, on the other hand, was only minimally thickened.

The pulmonary changes were striking, and most prominent among them were innumerable arterial thrombi in all stages of organization and recanalization. The large arteries contained grossly visible, usually white thrombi, which partially occluded the lumina; the lumina distal to the thrombi were frequently dilated. The thrombi extended into the smallest vessels (fig. 3A) and were associated with focal necrosis and irregular areas of hemorrhage and organizing pneumonia. The degree of connective tissue proliferation exceeded

FIG. 1. A. Posteroanterior film, just prior to onset of illness, showing a relatively normal heart size with normal pulmonary vascularity and clear lungs. B. Angiocardiogram demonstrating marked dilatation of the main pulmonary artery and the hilar branches. Other films in study showed normal peripheral vascularity.

blood cell count of 3,080,000 per mm.³ A roentgenogram of the chest revealed further enlargement of the heart (11.3/18.8 cm.), rather marked prominence of the pulmonary artery segment along the left sternal border, vascular congestion of both lungs, and parenchymal infiltration of the left upper lobe. An electrocardiogram revealed a marked increase in the right ventricular hypertrophy pattern and nonspecific myocardial changes.

The patient was placed in oxygen and treated with digitalis and antibiotics. His temperature stabilized between 99 and 100 F. orally, his heart
that usually seen in pulmonary infarction, but the reaction was conspicuously bland. It was apparent microscopically that some of the thrombosed vessels were veins (fig. 3C), and in a few areas there were necrosis and inflammatory cell infiltration of arterial walls (fig. 3D). Extremely dilated bronchial vessels, approximating varices, appeared to represent collateral circulation, and the bronchial arteries had thickened walls (fig. 3E, F). No extrapulmonic source of emboli was found, and the inflammatory arterial changes are regarded as hypertensive. Intimal sclerosis was present in the arterioles and seemed to be due in good measure to the recanalization of thrombi (fig. 3A). Medial hypertrophy of the small vessels existed both together with and apart from the intimal fibrosis (fig. 3B).

In summary, there was extrapulmonic stenosis of the pulmonary veins, in association with pulmonary arteriolar sclerosis and pulmonary arterial and venous thrombosis. A marked degree of cor pulmonale was present and was associated with hypertensive pulmonary arteritis.

**DISCUSSION**

Structural alterations in the pulmonary vascular system are commonly associated with and attributed to sufficiently prolonged and severe obstruction to the flow of blood from the lungs through the left side of the heart. Gross dilatation and sclerosis and microscopic alteration of the pulmonary arteries have long been recognized as an accompaniment of acquired mitral stenosis, and as early as 1927 Moschcowitz\(^7\) singled out hypertension of the lesser circulation as the factor common to cases of pulmonary arteriosclerosis associated with both obstructive lesions in either the heart or lungs and vascular shunts in either the heart or great vessels. Congenital mitral stenosis,\(^1\) cor triatriatum with stenosis of either the common pulmonary vein\(^8\) or intrapulmonary veins,\(^9\) constrictive endocardial sclerosis,\(^10\) tumors of the left atrium,\(^11\) and extrinsic pressure on the pulmonary veins\(^12\) have all been related to the development of pulmonary arterial and arteriolar sclerosis.

In the case of acquired mitral stenosis some evidence has been offered that the extent of the vascular changes in the lungs correlates with the severity of the obstruction at the mitral valve\(^13\) and the duration\(^14\) and degree\(^15,16\) of pulmonary hypertension, and that severe hypertension may lead to vascular necrosis in the lungs.\(^15,17-20\) Other evidence, both clinicopathologic\(^21\) and experimental,\(^22\) has been adduced to show that increased resistance and pressure are due to reversible vascular spasm, and that anatomic changes in the pulmonary vessels are largely the result of thromboembolic phenomena, even in association with obstruction of the pulmonary venous flow.
The alterations in arterioles and small arteries are generally compounded of medial hypertrophy and intimal fibrosis or proliferation. The former may reasonably be attributed to increased vascular tension, and although the problem of persistence of fetal vascular structure need not concern us here there seems to be ample evidence for muscularization of arterioles and medial hypertrophy in response to obstruction of the pulmonary venous flow.\textsuperscript{15, 23, 24} Intimal fibrosis in the smaller vessels has also been regarded as a consequence of pulmonary hypertension.\textsuperscript{15, 24} In the case reported herein, the intimal thickening is irregular and seems to have arisen at least in part from thrombosis and recanalization of the smaller vessels. The presence of such widespread thrombosis is regarded as a direct complication of hypertension and vascular sclerosis, possibly mediated by an arteritis, rather than as an embolic phenomenon.

The development of arteritis in this case must be regarded as the consequence of hypertension. Inflammatory lesions occurred independently of thrombi, although they may have preceded them. In several areas there appeared to be a healing or healed arteritis, but "fibrinoid" necrosis of the very small vessels was not seen.

The venous thrombi present an unusual complication that is not easily explained. Previously described instances of pulmonary venous thrombosis in association with pulmonary thrombophlebitis\textsuperscript{25} and primary vascular sclerosis,\textsuperscript{26} or as an anatomic finding in infants dying unexpectedly\textsuperscript{27} offer little to the understanding of this case. In the case reported by Schonlebe\textsuperscript{28} of a 4-month-old child with endocardial sclerosis and pulmonary venous thrombosis there were also transposition of the great vessels, pulmonic stenosis, and an interventricular septal defect. It is possible that the venous thrombosis in our case may have been enhanced by stasis due to obstruction at both ends—arterial thrombosis and venous stenosis—but there is no direct evidence to support this view. The alternate supposition that venous thrombosis led to phlebosclerosis and constriction does not make the case any more plausible or less unique. In the case of a young child who developed diffuse interstitial fibrosis of the lungs during infancy, reported by Diamond\textsuperscript{29} as a case of Hamman-Rich syndrome, there were extreme constriction of the pulmonary artery and vein and severe arteriolar sclerosis in one lung. Complete constriction of the pulmonary vein was present at its junction with the left atrium, and because of the inflammatory process in the lungs and the hilar adventitial tissue the abnormality of the vessels was attributed to inflammation and scarring rather than to a congenital malformation. More than a slight degree of pulmonary inflammation was not seen in our case and significant scarring in the hilar structures was limited to the stump of the right upper lobe vein.

More satisfactory is the view that the venous stenosis, uncommon as it might be, was the primary factor in the development of pulmonary hypertension and vascular disease. The 2 cases cited above\textsuperscript{1, 2} combined stenosis and atresia, indicating that the abnormality was a congenital malformation. Despite the age of the patient and the relatively late onset of symptoms in our case, the abnormality might still be regarded as congenital. The clinical course suggests that it may have been progressive, and possibly it bore some relationship to the endocardial sclerosis of the left atrium and to the intimal changes in the branches of the coronary arteries. However, as commonly as we see involvement of the left atrial endocardium in both primary and secondary endocardial sclerosis we have not seen it associated with pulmonary venous stenosis in either reported\textsuperscript{30} or observed cases. Indirect evidence in support of venous obstruction was the early development of extensive collateral circulation. Hemoptysis, the initial complaint, appears to have been due to bleeding from bronchial mucosal varices, a condition similar to that seen in acquired mitral stenosis.\textsuperscript{31} At the time of the pulmonary resection there were abnormally dilated, pulsatingazygos veins. Arterial and venous thrombosis was seen in the resected portion of lung, but the initial cause of venous obstruction could not be determined.
Summary

A case is reported of a 6-year-old boy who had developed pulmonary hypertension because of obstruction to the pulmonary venous flow by severe stenosis of the pulmonary veins at their junction with the left atrium. The development of collateral circulation through the bronchial vessels led to early, severe hemoptysis. The course was complicated by the development of pulmonary arterial and venous thrombi and hypertensive arteritis.

Acknowledgment

The authors are indebted to Mr. Charles L. Zinser for the photographs and photomicrographs.

Summary in Interlingua

Es reportate le caso de un puero de 6 annos de etate qui habeva disveloppate hypertension pulmonar in consequentia de obstruction del fluxo pulmono-venose per sever grades de stenosis del venas pulmonar al sito de lor junction con le atrio sinistre. Le disveloppamento de un circulation collateral via le vasos bronchial resultava tosto in sever hemoptysis. Le curso clinic del caso esseva complicate per le disveloppamento de thrombos pulmono-arterial e -venose e arteritis hypertensive.

References

EXTRAPULMONIC PULMONARY STENOSIS


In a study of the effects of stress on serum cholesterol levels, the serum cholesterol, total circulating eosinophils, body weight, blood pressure, and heart rate were measured at 3 different periods that were associated with varying degrees of stress. The first set of data was collected 3 weeks after starting the first year course in anatomy, the second set at the time of the final examination period in anatomy which was felt to be the period of maximal stress, and the final set of data was collected at a varying interval after the anatomy examination period at the convenience of the subject. Subjects were 52 male first-year medical students. The highest mean cholesterol value was found to occur at the time of the anatomy examination. It was 225.7 mg./100 ml. It was significantly greater than the value of 204.7 mg./100 ml. found at the examination made at random with presumably little stress. The mean cholesterol level of 224.4 mg./100 ml. found 3 weeks after starting medical school was not significantly lower than the value at the time of the anatomy examination. The mean eosinophil count at the time anatomy examination was 97 per cm. while at the time of the third or random examination the mean was 129 per cm., which was thought to be a significant difference. The measurements of pulse rate and systolic and diastolic blood pressures showed a significant difference only in the measurement of the diastolic blood pressure, which was highest at the time of the anatomy examination, next highest at the time of the initial examination, and lowest at the time of the random examination. Variations in body weight were effectively excluded as a cause for variation in cholesterol levels.

Maxwell
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Circulation. 1959;19:891-897
doi: 10.1161/01.CIR.19.6.891
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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