Pathogenesis of Pulmonary Hypertension in Congenital Heart Disease

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THE following is a list of major congenital heart diseases which associate with pulmonary hypertension: large ventricular septal defect (VSD) with a diameter of 1.5 cm or more, large patent ductus arteriosus (PDA), aorto-pulmonary septal defect, complete transposition of great vessels with VSD, single ventricle, persistent truncus arteriosus communis, and total anomalous pulmonary venous return (TAPVR) with pulmonary venous obstruction. Pulmonary hypertension in congenital heart disease is more frequent and severer than in acquired heart disease. There are several reasons for this. The first reason is persistent prominent pulmonary vasoconstriction in infants with some congenital heart disease. Strong pulmonary vasoconstriction is characteristic feature in fetus, and this feature tends to persist in congenital heart disease after birth. The second reason is common systolic ejection pressure in both aorta and pulmonary artery in some congenital heart diseases such as large VSD and large PDA. The third reason is large increase in pulmonary blood flow due to left to right shunt.

Four factors contributing to pulmonary hypertension should be evaluated by cardiac catheterization study in each patient. The first factor is increase in pulmonary blood flow which causes hyperkinetic pulmonary hypertension. This is the major factor in large portion of VSD, PDA, and ASD with pulmonary hypertension. Surgical repair is usually successful in these cases and pulmonary hypertension subsides after operation^{1,2}

Key Words:

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Tolazoline test

The second factor is increase in pulmonary venous pressure, which causes passive pulmonary hypertension. This is the major factor of pulmonary hypertension in TAPVR with venous obstruction, cor triatriatum, congenital mitral stenosis or insufficiency.

The third factor is pulmonary vasoconstriction, which is characteristic in infants with pulmonary hypertension and increased pulmonary vascular resistance. Pulmonary vasoconstriction is evaluated by accurate cardiac catheterization combined with 100% oxygen inhalation or injection of vasodilator such as tolazoline or acetylcholine^{6,9,10}

The fourth factor is organic pulmonary vascular obstruction^{3,4}. Physiologically it causes increased pulmonary vascular resistance which is not reactive to vasodilators such as 100% oxygen, tolazoline and acetylcholine. Histologic examination reveals intimal proliferation and fibrosis and obstruction of the lumen of small pulmonary arteries⁵. The progress of pulmonary vascular obstruction is variable in each congenital heart disease and in each individual^{7,8}. It is expected that the following paper will clarify the nature of these factors in pulmonary hypertension of congenital heart disease.

PULMONARY HYPERTENSION IN VSD

Four factors in pulmonary hypertension associated with VSD were analysed by cardiac catheterization study. Fig. 1 shows pulmonary to systemic flow ratio (Q_p/Q_s) in 227 cases of uncomplicated VSD with pulmonary hypertension, and systolic pressure ratio of more than 0.79. Vast majority of the cases under the age of 10 years had Q_p/Q_s more than 2.0, and increased pulmonary blood flow was the major factor of pulmonary hypertension. After the age of 10

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Fig.1. Pulmonary to systemic flow ratio (Q_p/Q_s) in VSD with pulmonary hypertension.

Fig.2. Pulmonary to systemic resistance ratio (R_p/R_s) in VSD with pulmonary hypertension.

VSD with PH — Progress of Pulmonary Vascular Obstruction

Fig.3. Distribution of hemodynamic groups in five age groups.

Fig.4. Reactivity of R_p/R_s to tolazoline in VSD with pulmonary hypertension.

Fig.5. Natural history of pulmonary vasculature in VSD with pulmonary hypertension.

years hyperkinetic factor was minor in most cases. Left atrial pressure was normal or only slightly elevated in these cases.

Pulmonary to systemic resistance ratio (R_p/R_s) in these 227 cases are illustrated in Fig. 2. Under 6 years of age resistance ratio was usually less than 0.6, and only one case had R_p/R_s more than 0.75. The incidence of high resistance ratio increased at ages over 6 years, especially over 12 years. In adult patients R_p/R_s had a wide distribution; the highest was 2.4 and the lowest was 0.1.

These patients were divided into four hemodynamic groups in Fig. 3. In group 1 were patients who had low pulmonary to systemic resistance ratio (less than 0.20). Fifteen of the total 227 patients fell into this group. 152 patients had mildly increased R_p/R_s (0.20–0.44), and these were classified into group 2. 37 patients had moderately increased R_p/R_s (0.45–0.75), and these are classified into group 3. 23 patients had severely increased R_p/R_s (more than 0.75), and these were classified into group 4 (Eisenmenger complex). Eisenmenger complex was not present in the first two years, and increased in number after two years of age, up to 55% at the age of 12 to 19 years (Fig. 3).

Pulmonary vasoconstrictive factor was evaluated in 30 patients with VSD and pulmonary

hypertension ranging 1 month to 17 years of age by cardiac catheterization combined with injection of tolazoline hydrochloride. 26 out of 30 patients had R_p/R_s less than 0.7 and predominant left to right shunt. The other 4 patients had high R_p/R_s ranging 0.9 to 1.2 and bidirectional shunt. Tolazoline, 1 mg/Kg body weight injected into the main pulmonary artery, caused remarkable fall of R_p/R_s in all cases less than 2 years old. The reactivity to tolazoline was variable and less remarkable in older children over 3 years of age (Fig. 4). In conclusion pulmonary vasoconstriction is the major factor of increase in pulmonary vascular resistance in these infants. After the age of three years pulmonary vasoconstriction is less and organic pulmonary vascular obstruction becomes more prominent.

Changing pattern of pulmonary vascular resistance in VSD with pulmonary hypertension is illustrated schematically in Fig. 5. In fetus strong pulmonary vasoconstriction causes suprasystemic pulmonary vascular resistance. After birth some pulmonary vasoconstriction persists and maintains increased pulmonary vascular resistance in infants. After childhood pulmonary vasoconstriction subsides gradually and organic vascular obstruction develops. The degree of pulmonary vasoconstriction and organic obstruction is much different from case to case. Precise catheter

study combined with study of pulmonary vascular reactivity is essential in patients with congenital heart disease, pulmonary hypertension and increased pulmonary vascular resistance.

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