FAMILIAL VALVULAR PULMONIC STENOSIS INVOLVING THREE SIBLINGS

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This report describes the cases of three mentally and physically well-developed siblings, 12, 10, and 8 years of age, with varying degrees of isolated valvular pulmonic stenosis not related to age. The severest lesion occurred in the middle patient and was associated with a right-to-left shunt through a patent foramen ovale. The three children had no other siblings, and there was no history of congenital heart disease among close relatives. These cases support the conclusion that genetic factors play a significant role in the development of certain congenital cardiac disorders.

The role of genetic mutation is frequently implicated in the etiology of congenital heart disease. Reports of familial involvement appear with increasing frequency in the literature, and the hereditary predisposition is of major concern to parents and prospective parents.[1-5] Although the familial occurrence of stenosis of the pulmonary artery and its branches and of myxomatous dysplasia of the pulmonic valve is well known, familial valvular pulmonic stenosis is rarely mentioned.[2,3] This report presents an unusual instance of valvular pulmonic stenosis in a single generation of three siblings.

FAMILY HISTORY

This family included three siblings, a 12-year-old boy, a 10-year-old girl, and an 8-year-old boy. These children had varying degrees of valvular pulmonic stenosis, the severity of which was unrelated to age, sex, or body weight. The severest lesion was present in the girl and the mildest was in the youngest boy. The parents were not related prior to marriage. The father died in an accident, but was not known to have had congenital heart disease.

PHYSICAL EXAMINATION

The girl, who had the severest lesion, complained of effort intolerance and blue coloration on exertion. The two boys were asymptomatic. All three children were mentally and physically well developed and showed no signs of

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chromosomal abnormalities. Although the peripheral pulses and blood pressures were normal, a prominent "A" wave in the cervical veins was noticed in the girl and in the 12-year-old boy. A precordial examination revealed signs of right ventricular hypertrophy in the same two children. The girl (who had the severest lesion) had the faintest and most delayed pulmonary second sound. The youngest patient (who had the mildest lesion) had the loudest and most delayed pulmonic ejection sound. Although a pulmonic click was heard in the oldest and youngest patients, no pulmonic ejection click was heard in the middle patient with the severest lesion (Fig. 1). An ejection systolic murmur was heard over the second left intercostal space in all three, but was loudest and longest in the middle patient and shortest in the youngest.

Radiologic examination revealed post-stenotic pulmonary artery dilatation in all three children. Whereas an electrocardiogram showed right ventricular hypertrophy in both the 12-year-old boy and the 10-year-old girl, it was more marked in the girl (Fig. 2).

The right ventricular systolic pressure was 60 mm Hg in the oldest patient, 120 mm Hg in the second, and 35 mm Hg in the youngest. Systolic pulmonary artery pressures varied between 15 and 20 mm Hg in all three children. The right ventricular end-diastolic pressures were 1 to 2 mm Hg in the oldest and youngest patients and 6 mm Hg in the middle one. The right atrial "A" wave was 5 mm Hg in the first and third children and 8 mm Hg in the second child. An associated patent foramen ovale was also detected in the second sibling.

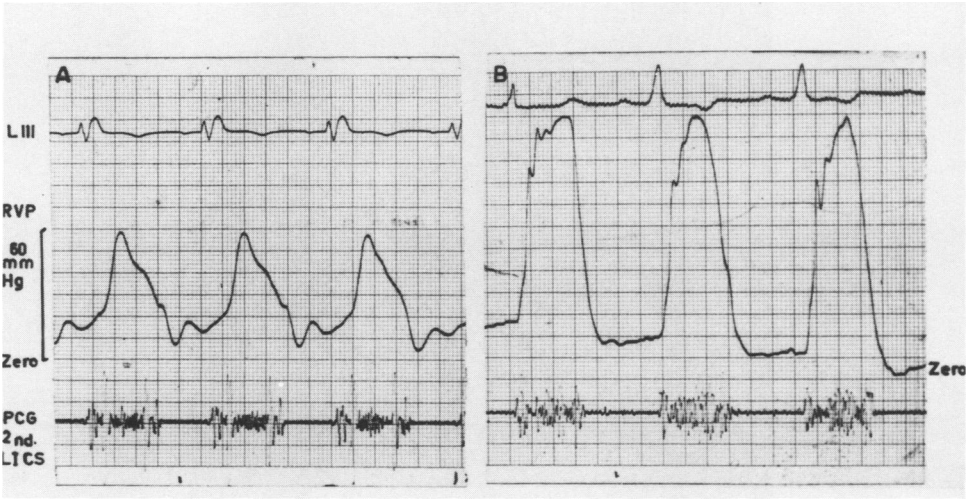

Fig. 1 Right ventricular pressure tracing and phonocardiogram from the first (A) and second (B) patients. A pulmonic ejection click and second sound were recorded only in A. B demonstrates a longer ejection systolic murmur.

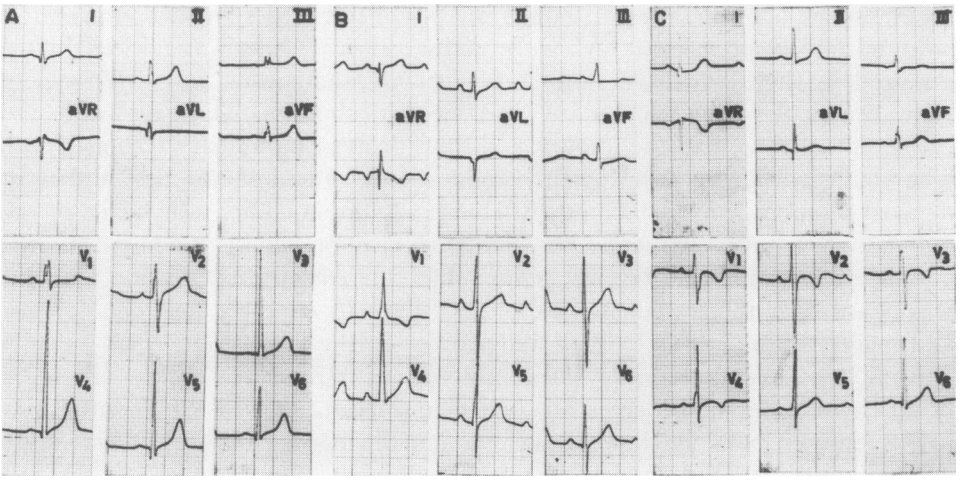

Fig. 2 Electrocardiograms from the three siblings arranged according to age (A, B, and C). B is from the second patient with the severest lesion, while C is from the youngest patient with the mildest lesion.

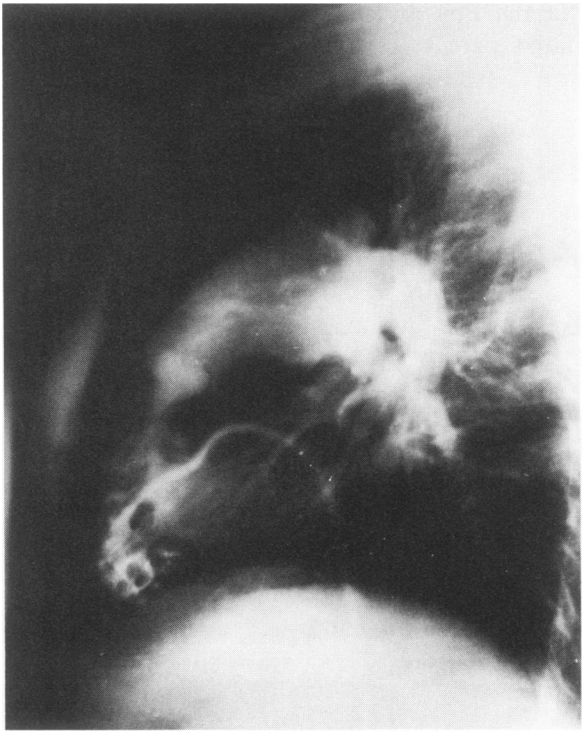

Fig. 3 Lateral right ventricular angiogram from the second patient, showing marked trabeculation, thickening and doming of the pulmonic valve, and post-stenotic pulmonary artery dilatation.

Right ventricular angiocardiography revealed valvular pulmonic stenosis in all three patients. The pulmonic valve was thickest and the pulmonic orifice narrowest in the second (Fig. 3). The right ventricle was normal in the youngest and oldest but showed marked hypertrophy in the second child. On recirculation, there were no abnormalities in the left side of the heart.

DISCUSSION

Although the etiology of congenital heart diseases is still unclear, the presence of a genetic factor is implicated by the high frequency of such disorders in twins and their prevalence within certain families. Animal experiments confirm a tendency towards familial involvement.[1-6]

Less than 1 percent of congenital cardiac anomalies are associated with single mutant gene syndromes,[7] and 4 percent arise from developmental confusion produced by a chromosomal abnormality.[7,8] Most of the remaining 95 percent can be explained by a multi-factorial inheritance hypothesis, which states that some patients are genetically predisposed to congenital heart defects and that the actual malformation is triggered by certain environmental agents that act on the vulnerable individual at a critical period of cardiac development. Rubella,[9] Thalidomide,[10] and dextroamphetamine[11] are thought to be such triggering agents.

The exact pathogenesis in the three siblings described here cannot be clarified. The parents were not relatives, and there was no history of drug addiction. Although preceding generations within the same family were normal, there may have been a recessive inheritance pattern; cardiac lesions do not usually conform to Mendelian principles.[12] Also, no evidence of chromosomal or extracardiac abnormalities was encountered in the present case. The fact that the severity of the lesions was not age related confirms the findings of Levine and Blumenthal,[13] and Moller and associates,[14] who failed to prove that mild or moderate valvular pulmonic stenosis progresses with age.

The possibility of a genetic factor in the etiogenesis of congenital cardiac malformations should be considered by family counselors,[14,16] whose influence may be of considerable value in reducing the frequency of such family-related disorders.

Care of these children continues to be supervised at the Department of Cardiology, Cairo, Egypt.

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