Supravalvular Aortic Stenosis in Association with Mental Retardation and a Certain Facial Appearance

By A. J. Beuren, M.D., J. Apitz, M.D., and D. Harmjanz, M.D.

There has been an increased interest in the diagnosis and surgical treatment of supravalvular aortic stenosis since Denie and Verheugt1 again drew attention to this congenital malformation. Since 1957 several review articles on this subject appeared in the literature,2-7 and a small number of clinically diagnosed cases have been reported.5, 7-13 Recently Williams and co-workers14 published the findings on four patients with supravalvular aortic stenosis in association with mental retardation and a peculiar facial appearance. In three of these patients the diagnosis was suggested by the close facial resemblance to the fourth patient, who had been found to have supravalvular aortic stenosis. The facial appearance of all these mentally deficient patients was so striking the authors suggested that the findings might constitute a previously unrecognized syndrome. In this clinic we have seen four patients with this condition. Three of these children had essentially the same findings as reported by Williams and co-workers,14 whereas one patient was mentally normal and had a normal facial appearance. The first three patients had already been investigated prior to the report of Williams, and we also suggested in the latter patients the diagnosis on clinical grounds alone, because of the close facial resemblance.

Clinical Features

Three of these patients are boys and one is a girl. They are aged 10 years (U.G.), 5½ years (B.H.), 5½ years (H.K.), and 8½ years (K.P.). Leukocyte nuclear sex characteristics have been investigated and found to be normal in three of the four patients (B.H., H.K., K.P.). The 10-year-old boy has a normal face and is mentally normal. The remaining patients have intelligence quotients of 46 (B.H.), 46 (H.K.), and 58 (K.P.) (normal value: 100, Wechsler). All have the same kind of friendly nature—they love everyone, are loved by everyone, and are very charming. Their photographs are shown in figures 1 to 3. The facial resemblance of these children to the four children published by Williams14 is striking. The same full faces, broad foreheads, heavy cheeks, and pouting lips are apparent. The chins are pointed. Patient B.H. has an epicanthus on both eyes and a right-sided strabismus convergens concomitans. The retinal vessels are normal. The facial similarity among these patients was evident to everyone who saw them. The family histories are uneventful. B.H. is an only child, whereas the others have healthy siblings, and no additional case of congenital heart disease is known in the families.

Delivery of all four patients was normal. Their birth weight, however, was significantly below average and weight gain was slow, except for H.G. In contrast to the cases of Williams,14 a heart murmur was discovered in all four patients during the first weeks of life, and all had a significant limitation of their physical exercise tolerance. The physical findings were very similar to those found in valvular and subvalvular aortic stenosis. In two patients (H.K. and K.P.), however, the systolic thrill was best felt in the first right intercostal space and in the suprasternal notch. The systolic ejec-tion murmur in these two patients was also loudest in the first right intercostal space and not in the second. All murmurs were widely transmitted to the periphery. There were no diastolic murmurs. The intensity of the second sound in the aortic area was definitely diminished in all four patients. All four patients had differences in the blood pressures of the upper extremities ranging from 15 to 25 mm. Hg.

On roentgenograms the size of the heart was at the upper limits of normal or slightly enlarged with the apex pointed downward. In all four cases it was thought that the area of the ascending aorta and of the aortic knob was somewhat "empty" (fig. 4). The electrocardiograms exhibited left ventricular hypertrophy and T-wave changes in two of these patients (U.G. and B.H.), and in the remaining two patients only left ventricular preponderance (H.K. and K.P.) (fig. 5). Indirect

From the Department of Pediatrics, University of Göttingen, Göttingen, Germany (Director: Professor Dr. G. Joppich).

Supported by research grant H-5582 from the National Heart Institute, U. S. Public Health Service, and the Deutsche Forschungsgemeinschaft.

Circulation, Volume XXVI, December 1962

1235
carotid pulse tracings in all four patients show nothing to suggest aortic stenosis of the supravalvular type.

In the first patient (U.G.) the preoperative diagnosis was “aortic stenosis” without left ventriculography. At operation supravalvular aortic stenosis was found with a systolic gradient of 160 mm. Hg. The stenosis, being about 10 cm. in length, began directly above the sinus of Valsalva and extended high up into the aortic arch. The other three patients (B.H., H.K., and K.P.) were diagnosed by transeptal left heart catheterization and left ventriculography. The systolic pressure gradients were 50, 65, and 120 mm. Hg, respectively. Ventriculography in two planes clearly showed the localized narrowing of the aorta above the sinus of Valsalva without poststenotic dilatation. In patient B.H., the aorta did not regain a normal caliber beyond the stenosis and it was hypoplastic, whereas in the two patients H.K. and K.P. the aorta was of approximately normal size beyond the stenosis (figs. 6 and 7).

**Discussion**

With the advent of aortic valvular surgery, supravalvular aortic stenosis has been seen in several instances and will probably be encountered more frequently in the future. Even though the condition has been diagnosed pre-
operatively since 1959, the total number of reported cases is still very small. It has been stressed by Morrow and co-workers that simple measurement of a systolic pressure gradient between the left ventricle and the brachial artery does not determine the site of obstruction and is not sufficient for preoperative diagnostic work-up. Complete left heart catheterization, either with a pull-back pressure tracing across the aortic valve or left ventriculography, is necessary to determine the site and the size of the obstruction to left ventricular outflow. Correct preoperative differential diagnosis is desirable, since the risk of operation and the postoperative result may be very different in supravalvular, valvular, or subvalvular aortic stenosis. There are, however, some clues for clinical differentiation between valvular and subvalvular aortic stenosis and, according to the observation of Williams and co-workers and the cases presented here, it may be possible to recognize

supravalvular aortic stenosis on clinical grounds.

The four children reported by Williams,
Barratt-Boyes, and Lowe\textsuperscript{14} look alike and all have a low intelligence quotient. They are mentally and physically retarded. The same is the case in three of the four patients presented here. In addition to the close facial resemblance, the systolic murmur and thrill were best heard and felt high in the first right intercostal space and just below the clavicle, suggesting a stenotic lesion above the usual valvular level. We also found that the x-ray in the anteroposterior position shows a strikingly empty vascular pedicle usually not seen in valvular and subaortic stenosis. This can be seen also in the roentgenogram published by Wooley et al.\textsuperscript{7} The electrocardiograms of these cases do not offer any possibility of differentiation. As in patients with valvular and subvalvular aortic stenosis, there may be a very high systolic pressure gradient and only some left ventricular preponderance. Williams et al.\textsuperscript{14} also reported a very poor relationship between the degree of left ventricular hypertrophy and the pressure gradients. This observation may be better understood if one takes into consideration that the elevation of the left ventricular pressure always precedes the development of hyper-
SUPRAVALVULAR AORTIC STENOSIS

Our patient is a 9-year-old girl, with a systolic thrill and a grade 4/6 diastolic murmur. The electrocardiogram showed a right bundle branch block with left atrial hypertrophy. Our patient with the highest pressure gradient in the left ventricle and the highest gradient (K.P. LV 230/0, gradient 120 mm. Hg) had only slight left ventricular preponderance. Williams and co-workers suggested that in supravalvular aortic stenosis, an additional lesion like congenital mitral insufficiency or cardiomyopathy might influence the electrocardiogram. In three of our four patients, left atrial pressure curves have been recorded during transseptal left heart catheterization and there was no evidence of mitral incompetence. In one of the angiograms of Williams, taken after transthoracic puncture of the left ventricle, there is, however, some reflux of contrast medium into the left atrium.14

Injection of contrast medium into the left ventricle and biplane angiocardiography is the best method for demonstration of supravalvular aortic stenosis (figs. 6 and 7). If this is done by transseptal left heart catheterization, no pullback tracing across the stenosis can be obtained. Since the coronary arteries are the only branches of the aorta proximal to the stenotic lesion, it may be of interest to speculate whether there is collateral circulation between the coronary arteries and the mediastinal vessels similar to the collateral circulation in coarctation of the aorta. We believe that the angiocardiogram of patient H.K. (fig. 8) shows such collateral circulation.

The question still remains whether the association of supravalvular aortic stenosis and mental retardation with the facial characteristics pointed out by Williams and co-workers and also present in three of the four patients reported here, constitutes a clinical syndrome. There is also a physical retardation in these patients, which is usually not present in cases of valvular and subvalvular aortic stenosis. Apparently the peculiar facial appearance of these children, in addition to their mental retardation, is not present in all patients of supravalvular aortic stenosis, since it has not been described in the cases reported prior to the paper by Williams and co-workers.14 There may be also patients with a similar face and mental retardation with different cardiac malformations and no supravalvular aortic stenosis. Nevertheless, the relatively frequent occurrence of this combination with supravalvular aortic stenosis, now seen in seven children out of a total of about 20 reported patients with supravalvular aortic stenosis, is striking.

Summary

Four patients with supravalvular aortic stenosis are reported. In three of these patients a certain facial resemblance was striking, and these three patients were also mentally and physically retarded. The cases are very similar to the four cases recently reported in the literature. Supravalvular aortic stenosis in association with mental retardation and a certain facial appearance may constitute a previously unrecognized clinical syndrome.

A systolic thrill and murmur most pronounced in the first right intercostal space and just below the clavicle, with an empty vascular pedicle on the roentgenogram, may be a clue to the clinical diagnosis of supravalvular aortic stenosis.

Supravalvular aortic stenosis is best demonstrated by left ventriculography. A collateral circulation between the coronary arteries and the internal mammary artery has been shown in one patient.

Addendum

An additional child with supravalvular aortic stenosis and with mental retardation has been seen in this clinic since the submission of this paper. This additional patient, a girl, has an I.Q. of 80 and the same facial appearance as the reported patients (fig. 9). Supravalvular aortic stenosis could be demonstrated on angiocardiography. Meanwhile, two of these patients have been operated upon with the aid of extracorporeal circulation. There is no systolic gradient after operation and the patients are doing well. (Operated on by Dr. J. Konec, Department of Thoracic Surgery, Göttingen).

References


Rewards of a Scientist

Though the scientific explorer has no prospect of becoming rich in the worldly sense, as a result of his labors, he certainly enjoys a rich life. The enthralling pleasures of discovery, the opportunity to do what he would rather do than anything else in the world, the sense of security in his academic position, the freedom for study and investigation, the world-wide friendships, the homage from learned societies, the assurance that his efforts in teaching and seeking have social value—all these satisfactions are his. No man could ask for better recompense.—WALTER B. CANNON, M.D. The Way of An Investigator. New York, W. W. Norton & Company, Inc., 1945, p. 214.
Supravalvular Aortic Stenosis in Association with Mental Retardation and a Certain Facial Appearance

A. J. BEUREN, J. APITZ and D. HARMJANZ

Circulation. 1962;26:1235-1240
doi: 10.1161/01.CIR.26.6.1235

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/26/6/1235

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/