Corrected Transposition of the Great Vessels with Ebstein Malformation of the Left Atrioventricular Valve

An Embryologic Analysis and Two Case Reports

By Arentje Dekker, M.D., Ali Mehrizi, M.D. and Avinash S. Vengsarkar, M.D.

Corrected transposition is commonly considered to be the result of a leftward bending of the bulboventricular loop instead of a rightward bending, with concomitantly abnormal development of the truncus septum.1-3 Recently an embryologic study was carried out by one of us of normal eight to 19 somites human embryos (Streeter's age groups horizon X and XI) and a 6.6-mm. human embryo with an abnormally bent heart (age group horizon XIV*).4 From this study, interesting supplementary information was gained regarding the sequence of events in the formation of the bent heart-tube and the possible consequences in case of a disturbance in the first step of the bending. Moreover, the fate of the atrioventricular endocardial cushions was followed throughout horizons XVII to XX in order to understand some of the characteristics of the right and left atrioventricular valves in the normal heart, in the heart with corrected transposition, and in the heart with the Ebstein-type malformation.

The association of an Ebstein-like malformation of the left atrioventricular valve with corrected transposition was described by Edwards5 and has since been reported by others.6,7 The purpose of the present paper is to describe two cases of corrected transposition with a left-sided Ebstein-type malformation, to explain briefly the embryopathogenesis of corrected transposition and to elucidate the possible method of development of this combination of anomalies, namely, a left-sided Ebstein-type malformation in corrected transposition.

Case Reports

Case 1

J. C. (JHH No. 91 23 52). This 17-month-old white boy was referred to Harriet Lane Home...
Cardiac Clinic in 1959 at 4 months of age with mild cyanosis and cyanotic spells.

He was born following a normal pregnancy with a birth weight of 7 lb. 6 oz. The neonatal period was uncomplicated. About 1 month of age he began to vomit, and successful operation for hypertrophic pyloric stenosis was performed. He did well until 4 months of age, when tachycardia, rapid breathing, dyspnea, and mild cyanosis were noted. After digitalization the tachycardia improved but the dyspnea and dusky color were unchanged.

On physical examination at 4 months his weight was 5,310 Gm., the pulse was 150 per minute, and the respirations were 50 per minute. He was moderately ill and obviously dyspneic. There was a grade II to III harsh systolic murmur best heard in the third and fourth interspaces transmitted toward the axilla. There was also a mid-diastolic rumbling murmur, which at times simulated a continuous murmur. The pulmonary second sound was loud and single. Scattered moist rales were heard over the lungs.

The hemoglobin was 12.7 Gm. per cent and the hematocrit value 41.5. X-ray showed the heart to be enlarged and the left atrium moderately dilated. The pulmonary vascularity was within normal limits (fig. 1).

The electrocardiogram showed left axis deviation, left ventricular hypertrophy, and left bundle-branch block (fig. 2).

Right heart catheterization revealed moderate right ventricular hypertension and no evidence of a shunt. A venous angiocardioogram showed a dilated right atrium. The right-sided ventricle showed a smooth outline resembling that of a normal left ventricle and the pulmonary artery was displaced medially and to the right (fig. 3A). The levogram showed a dilated left atrium (fig. 3B), which emptied slowly and appeared to reopacify in ventricular systole; the visualization of the left ventricle was poor, and the left ventricular cavity was small. On this basis the diagnosis of corrected transposition of the great vessels with an anomaly of the left atrioventricular valve, probably of the Ebstein type, was made by Dr. C. Ferencz.

The patient showed progressive cardiac enlargement, frequent attacks of pulmonary edema, and increasing cyanosis and failure. Terminally he developed 2:1 heart block and died at home at 17 months of age.

*Circulation, Volume XXXI, January 1965*
in size and location. There was only one large valve guarding the inferior vena cava, i.e., the embryonic right venous valve was not divided into Eustachian and Thubesian valves.

The right atrioventricular valve had only two leaflets, which were somewhat thickened and led into a right-sided ventricle of normal size; it showed delicate trabeculae, a smooth surface on the interventricular septum and a high position of the atrioventricular valve adjacent to the arterial orifice, i.e., all the anatomic features of a normal left ventricle. The bundle of His was vaguely recognizable under the septal endocardium and had a dividing pattern of a left bundle branch.

The vessel arising from this ventricle was the pulmonary artery guarded by three normal valve cusps. The pulmonary orifice was normal; the pulmonary trunk, however, appeared to be wider than the orifice of the pulmonary artery. The pulmonary artery divided in the normal manner into two branches.

The pulmonary veins drained into the left atrium, which was extraordinarily dilated. The left atrioventricular valve was abnormally located: the level of insertion was displaced downward about 6 to 12 mm. The valve was malformed, so that there was some doubt as to the number of leaflets. The chordae tendineae were shortened. The septal leaflet of the valve was displaced.

Autopsy.* The heart was enormously enlarged especially the left side (fig. 4). The aorta was on the left of and anterior to the pulmonary artery. The superior and inferior venae cavae returned normally into the right atrium, which was normal in size. The foramen ovale was closed. The orifice of coronary sinus was normal.

*The heart specimen was sent to us through the courtesy of Dr. H. H. Jeter, Florence, South Carolina.

Circulation, Volume XXXI, January 1965
downward, whereas in classic Ebstein anomaly the posterior leaflet is the most displaced.

The cavity of the left-sided ventricle was rather large. The endocardium was yellow-white and somewhat thickened. The atrioventricular valve was placed low into this cavity and was separated from the aortic orifice by a muscular band, the crista supraventricularis. The left-sided ventricle had coarse trabeculae, rough surface of the ventricular septum, and a crista supraventricularis, i.e., the anatomic features of a normal right ventricle.

The aorta was rather small as compared to the pulmonary artery and had three normal semilunar cusps. The right coronary artery gave rise to the anterior descending branch, and the left coronary artery ran in the atrioventricular groove and extended over the posterior wall of the heart. The aortic arch was left-sided and the ductus arteriosus was closed.

The anatomic diagnosis was corrected transposition with Ebstein-like malformation of the left atrioventricular valve.

Case 2

T.M. (JHH No. 88 01 21): This 9-year-old white boy was seen at Harriet Lane Home Cardiac Clinic in 1949 with the chief complaints of increasing dyspnea and frequent upper respiratory infections. The history revealed that the pregnancy and delivery had been normal and the birth weight between 6 and 7 lb. At 3 weeks of age, when he developed dyspnea and intermittent cough, a heart murmur was heard and chest x-ray showed an enlarged heart. The dyspnea gradually increased, and he developed a mild persistent cyanosis. He was digitalized and maintained on digitalis throughout his life.

At 9 years his height was 110 cm., weight 22 Kg., pulse 130, and respiration 24. The blood pressure was 145/100 mm. Hg in the right and 150/90 mm. Hg in the left arm; it was not obtainable in the legs. The heart was markedly enlarged. A harsh systolic murmur accompanied by a thrill was audible in the third and fourth intercostal spaces along the left sternal border and was transmitted to the left axilla. An apical mid-diastolic murmur was also heard. The liver was palpable below the umbilicus, and was soft and pulsatile. The lungs were clear. There was minimal pitting edema of the ankles. The hemoglobin was 18.5 Gm. per cent and the hematocrit value 59.

Fluoroscopy and x-ray showed generalized cardiac enlargement involving both right and left ventricles. The pulmonary vascularity was within normal limits (fig. 5).

The electrocardiogram showed sinus tachycardia and right axis deviation. The patient was hospitalized, but failed to improve on medical treatment. Operation for relief of the coarctation was recommended. An infantile coarctation and a patent ductus arteriosus were found, but he died during surgery.

Autopsy. The heart was markedly enlarged, especially the right atrium and the right-sided ventricle. In the anteroposterior view, the left atrium was almost invisible because it was situated behind the great arteries. The great vessels ran parallel to each other; the aorta was to the left and anterior to the pulmonary artery, which was greatly dilated (fig. 6).

The right atrium received the superior and inferior venae cavae in a normal manner. The foramen ovale was widely patent. The coronary sinus orifice was large.

The right atrioventricular valve had two cusps. The anterior cusp was partly attached to the free upper edge of the ventricular septum and the posterior cusp was continuous with the left atrioventricular valve through a large ventricular septal defect.

The right-sided ventricle was dilated and hypertrophied and had the anatomic structure of a normal left ventricle. The defect in the ventricular septum was large and involved the posterosuperior part of the ventricular septum. The pulmonary artery was greatly dilated and overlapped the ventricular defect to a great extent as if it was mainly originating from the left-sided ventricle. The pulmonary trunk was dilated and was guarded by three normal cusps.

The pulmonary veins emptied into the dilated left atrium in the normal manner. The left atrioventricular valve was situated lower than normal
and its free edge was plastered against the posterior wall of the ventricle.

The left-sided ventricle showed the anatomic features of a normal right ventricle. The aortic orifice was separated from the left atrioventricular valve by a muscular band of crista supraventricularis.

The aortic valve cusps were normal. The right coronary artery gave rise to the anterior descending artery; the left coronary artery divided into a number of small branches distributed over the dorsal wall of the heart.

The anatomic diagnoses were corrected transposition of great vessels with considerable overriding of the pulmonary artery, malformed atrioventricular valves with fusion of both valves through a large ventricular septal defect, and history of surgical resection of infantile coarctation of the aorta and attempted ligation of a large patent ductus arteriosus.

Discussion

The cases described both have in common an Ebstein-type malformation of the left atrioventricular valve. They also show the anatomic characteristics of the so-called “corrected transposition,” namely:

(a) The ascending aorta and the pulmonary artery take a parallel course, with the aorta showing a left ventral origin.

(b) The aorta arises from a ventricle, situated on the left, which has the structure of a normal right ventricle, and the pulmonary artery arises from a ventricle located on the right, with the structure of a normal left ventricle.

(c) The left-sided or anatomic “right” ventricle connects with the normal left atrium and the pulmonary veins, while the right-sided or anatomic “left” ventricle connects with the normal right atrium and the caval veins.

(d) The right-sided coronary artery divides into an anterior descending ramus and a ramus circumflexus; the left-sided coronary artery branches into small rami supplying the anterior wall of the left-sided ventricle.

In a recent study of the Carnegie Collec-
tion of human embryos, an embryo (no. 7324, 6.6 mm.) was found in which the development of the heart had deviated from the normal pattern in such a way that it provided supplementary information regarding the possible embryopathogenesis of corrected transposition. The findings have been described in detail elsewhere and are in part summarized below.

Early Embryology of the Heart

In normal human embryos of seven to 14 somites the bending process of the originally straight heart tube is initiated by a leftward outgrowth of the caudal part of the ventricular loop (the future left ventricle), which thus comes to occupy the left half of the transversely rather spacious pericardial sac. This leftward outgrowth of the caudal part of the myocardium is recognizable in drawings of previous publications but was not mentioned by the authors: it can be clearly seen in a number of embryos of horizon X and XI in the Carnegie Collection.

A little later the cranial part of the heart tube (truncus and future right ventricle) undergoes a considerable increase in length and comes to occupy the still available space in the right half of the pericardial sac. In this way, the heart tube becomes bent upon itself and the ventricular loop is formed with its convexity toward the right side. This downward movement of the future right ventricle initiates a rotation in the frontal plane of the left ventricular loop and the atrioventricular canal. We then have the compound S configuration with the interventricular junction lying in a transverse direction (horizons XII and XIII). Still later (horizons XIII and XV), we see the ventromedial rotation of the trabeculated right ventricle, related to the marked enlargement of the right atrium. In the abnormally bent heart of embryo (no. 7324, horizon XIV), the striking abnormal features were the extreme left-sided position of the truncus and infundibulum, an acute bend between trabeculated right ventricle and infundibulum and above all the right-sided position of the left ventricle. Based on the above observations, therefore, the following explanation for corrected transposition is presented: the early cellular growth of the caudal part of the ventricular loop of the heart is toward the right side instead of the left. By the time the cranial part reaches its period of rapid growth the right half of the pericardial sac is occupied by the caudal part of the loop, whereas space is available in the left half; the cranial part of the ventricular loop thus moves leftward causing a rotation of and torsion in the truncus-infundibular wall in the opposite direction to normal. Viewed from the cranial position a counterclockwise rotation of the truncus and infundibulum is produced instead of the normal clockwise rotation; consequently, the future aorta-part of the truncus rotates to the left and ventrally, the future pulmonary artery to the right and posteriorly. Relative shifting processes will thereby make the pulmonary artery connect with the right-sided ventricle, the aorta remaining sinistroventral, i.e., coming off the left-sided ventricle. Thus the initial abnormal movement of the ventricular loop is the cause of the abnormal relation of the great vessels in corrected transposition. There is no reason to postulate an additional anomaly in the development of the truncus septum.

Development of the Atrioventricular Valves

There is a stage in the development of the heart in which the cranial part of the ventricular loop (i.e., the anatomic right ventricle) has no direct communication with the future right atrium. The atrioventricular canal is located between the atrial part of the heart and the adjacent future left ventricle (fig. 7).

Early in normal development, the atrioventricular canal undergoes a relative shift to the right and thereby contact is established between the right ventricle and the right portion of the atrioventricular canal by the outgrowth of ventrocranial and dorsocaudal endocardial cushions. The ring of the migrating orifice becomes attached to the right ventricular wall below the infundibulum and also to the wall of the ventricular septum. The mi-
migration takes place in horizons XVII and XVIII, and at the same time the atrioventricular endocardial cushions fuse and the ventricular septum unites with the endocardial cushions. The left part of the fused cushions forms a freely movable flap attached to the septum only with a part of its base; the right part, however, is attached to the right side of the ventricular septum along its entire margin. Later this attached mass will form the septal leaflet of the tricuspid valve. The mitral orifice never develops such a close and extensive attachment to the septum. From the beginning it remains to the left of the septum, especially after the aorta has established contact with the left ventricle: most of the anterior leaflet of the mitral valve extends across the left ventricle. The aortic orifice lies between this leaflet and the septum to which the leaflet or aorta is attached only for a short distance posteriorly. The relation of the mitral valve to the outer wall of the left ventricle is much closer than that of the tricuspid valve to the outer wall of the right ventricle. Thus the mode of migration of the atrioventricular canal is the deciding factor in the formation of the atrioventricular valves. Specifically, that portion of the atrioventricular orifice which migrates becomes closely attached to the septum, and, to a lesser extent, to the infundibular outflow tract. On the other hand, the non-migrating orifice, i.e., the orifice to the left atrium, is farther away from the septum and this distance is increased when the aortic orifice is incorporated into the left ventricle (fig. 8).

In corrected transposition the primitive atrioventricular communication leads into the right-sided ventricle. The left atrioventricular orifice is established by migration of this valve from right to left. As a result, the left part of the atrioventricular communication crosses the plane of the ventricular septum and contacts with the left-sided ventricle below its infundibulum. This valve is formed with all the characteristics of the tricuspid valve, i.e., (1) close relationship between the septal leaflet of this valve and the ventricular septum and (2) separation of this valve from the arterial orifice by the infundibulum.

Ebstein's Malformation. In the normal bending of the heart, the left atrioventricular orifice is in a favorable position, not subject to migration and connected from the very beginning to the proper chamber of the heart. The right atrioventricular orifice, however, is in an unfavorable position because of the relative complexity of the shifting process.

Figure 7
Diagram to show bending of cardiac tube.

Figure 8
Diagram to illustrate the relationship between endocardial cushion, the future mitral and tricuspid valve, and the ventricular septum.
and the incorporation of this orifice into the right ventricle. The close and extensive attachment of the right part of the fused endocardial cushions to the interventricular septum may have a pathogenic significance in the deformity of the septal leaflet of this valve, which is always involved in Ebstein's malformation of the tricuspid valve.

In corrected transposition, however, it is the left-sided atroventricular orifice which migrates, and the left-sided valve has all the characteristics of the usual tricuspid valve, including a close relationship between the septal leaflet and the ventricular septum and thus an inherent susceptibility to the development of Ebstein's malformation.

Summary and Conclusions

Two autopsy proven cases of corrected transposition with an Ebstein-type malformation of the left atroventricular valve are presented. Case 1 had no other defects but the valvular malformation was so severe as to cause death in intractable left heart failure at 17 months. Case 2 had in addition coarctation of the aorta, a large patent ductus, and a ventricular septal defect: the pulmonary artery overrode the septal defect arising chiefly from the left-sided or anatomic "right" ventricle. Despite these multiple defects he survived to 9 years of age. Embryologically, the defect is thought to be due to a rightward outgrowth of the caudal part of the ventricular loop, leading to a heart tube bent with its convexity toward the left instead of the right. The anatomic left ventricle thus occupied the right part of the pericardial cavity, and, consequently, the anatomic right ventricle was displaced to the left. The cranial part of the ventricular loop, in its descent, caused an abnormal counterclockwise rotation of the truncus in that the aorta came to lie on the left and anteriorly ("corrected transposition"). In both cases also the left atroventricular valve, (which had to take part in the migration characteristic of the right atroven-

tricular valve in a normal heart) became displaced in an Ebstein-type malformation.

Acknowledgment

We gratefully acknowledge and wish to express our appreciation to Dr. Catherine A. Neill for her help and advice in preparation of this manuscript.

References

Corrected Transposition of the Great Vessels with Ebstein Malformation of the Left Atrioventricular Valve: An Embryologic Analysis and Two Case Reports
ARENTE DEKKER, ALI MEHRIZI and AVINASH S. VENGSAKAR

Circulation. 1965;31:119-126
doi: 10.1161/01.CIR.31.1.119

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1965 American Heart Association, Inc. All rights reserved.
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:
http://circ.ahajournals.org/content/31/1/119.citation

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/