A Syndrome Featuring Defects of the Heart, Sternum, Diaphragm, and Anterior Abdominal Wall

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Three patients featuring a syndrome of defects of the heart, sternum, diaphragm, and anterior abdominal wall are presented. The striking similarity of the anomalies manifested by the 3 cases posed a question whether or not a recognized syndrome previously existed. In order to determine this, a search was made to find other such cases, and an attempt was made to establish a common embryologic pathogenesis. Review of the literature as well as extensive personal communication was carried out. Embryology of the involved organs was considered in order to determine a specific phase of defective development.

Three patients with congenital defects involving the heart, diaphragm, lower sternum, and anterior abdominal wall have been recently studied at the University of California at Los Angeles. The features that characterize these patients are (1) malrotation of the heart with dextroposition, (2) intracardiac anomalies including ventricular septal defect, (3) deficient lower sternum, (4) anterior diaphragmatic defect, and (5) midline abdominal defect with diastasis recti and umbilical hernia. These unusual but strikingly similar features suggested a specific syndrome.

Case Reports

Case 1. M.M. was admitted, at age 11 months to the U.C.L.A. Hospital. The pregnancy was complicated by ingestion of quinine and by minimal vaginal bleeding at 6 weeks' gestation. At 1 day of age, a 3 by 3 cm. omphalocele was repaired at another hospital without incident. Repeated respiratory infections marked the infancy period, requiring hospitalization 6 times. At 4 months of age, cyanosis was first noted during crying by the mother. A heart murmur was first detected by the family physician at 5 months of age. Weight gain was slow, but motor and social development were normal. The family history was unremarkable.

Physical examination showed an underdeveloped alert Caucasian infant with mild tachypnea but in no acute distress. The blood pressure was 70 mm. Hg in the upper and lower extremities by the simultaneous flush technic. The pulse was 120 per minute, and the respirations were 30 per minute. The height was 69 cm. and the weight 6.3 Kg., which placed the patient in the seventy-eighth percentile on the Wetzel grid. The mandible was somewhat underdeveloped. Circumoral cyanosis occurred with crying. There was no clubbing of the digits. Bilateral costal flaring and midline chest prominence were present. The lower sternum was deficient, with a vestigial unilateral xiphoïd process palpable to the left of the midline cleft extending to the fifth rib. Cardiac pulsations and a protuberance were visible extending 3 cm. below the apex of the sternal cleft as shown in figure 1. A 4-cm. diastasis recti, covered by skin, extended to the repaired omphalocele. Examination of the heart revealed a sinus rhythm with a markedly accentuated and slightly split pulmonic second sound. Cardiac dullness was greater to the right of the sternum. A grade III rough systolic murmur not associated with a thrill was present low at the right sternal border. Femoral pulsations were full. The electrocardiogram was abnormal, showing right-axis deviation, upright P waves, and inverted T waves in leads I and II and a prominent Q wave in lead I. There was no conduction delay. The T waves were upright in the conventional unipolar precordial leads, and the voltage of all waves was normal.

As shown in figure 2, roentgenograms demonstrated an unusual cardiac configuration with dextroposition, plethoric lung fields, and a deficiency of the lower sternum and of the anterior diaphragm. (The lead marker identifies the apex of the sternal cleft.) Cardiac catheterization was performed under rectal basal anesthesia. The unusual position of the catheter in the right and in the left ventricles..
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is shown in figure 3. The right ventricular systolic pressure equaled the left ventricular systolic pressure of 100 mm. Hg. A large left-to-right as well as a small right-to-left interventricular shunt was demonstrated.

Selective angioeardiography from the right ventricle showed the right ventricle to be at the far right anterior heart border and somewhat superior to its usual position as shown in figure 2. The pulmonary outflow tract crossed from the right to the left side of the heart superiorly and anteriorly. The aorta descended on the left. Definitive surgery was deferred due to the likelihood of a markedly deficient ventricular septum which was deemed not repairable by existing technics. When seen last at 16 months of age, the patient was doing well and had been free of infection for 4 months.

Case 2. D.H. was admitted to the U.C.L.A. Hospital at 22 months of age for right heart catheterization. He was adopted at 8 days of age, and a heart murmur was noted at that time. Nothing was known of the family history or gestational period. Growth and development were normal. The only recognized cardiac symptom was mild exertional dyspnea. Physical examination revealed a well nourished, active 22-month-old Caucasian boy in no distress. The blood pressure was 80 mm. Hg in the upper and 90 mm. Hg in the lower extremities by the simultaneous flush technic. The pulse was 92 per minute and the respirations were 24 per minute. Slight nailbed cyanosis associated with mild clubbing was present. The anterior chest bulged in the midline and there was bilateral costal flaring. The lower sternum was deficient and there was a rudimentary unilaterial xiphoid process palpable along the right costal margin near the apex of the sternal cleft. Extending 3 cm. below the deficient sternum could be seen a pulsating mass beneath the skin covering a 4-em. rectus separation as shown in figure 4. A 2-em. umbilical hernia was present. The cardiac dullness was greater to the right than to the left of the sternum. A grade IV harsh systolic murmur associated with a thrill was heard best low along the right sternal border. The pulmonic second sound was quiet.

The electrocardiogram showed inversion of T waves and upright P waves in leads I and II. A prominent Q wave was present in lead I. The P wave in lead II was 3 mm. Axis deviation was right. No conduction delay was present. T waves were upright from V₁ through V₆. The hemoglobin was 15.2 Gm. per cent and the red blood cell count 5.2 million per mm.³ Roentgenograms demonstrated dextroposition and an unusual configuration of the heart as shown in figure 5. The pulmonary vascularity was unremarkable.

Cardiac catheterization was performed under rectal basal anesthesia. The unusual position of the right and left ventricles with the catheter in them is similar to that shown in figure 3. The systolic pressure in each ventricle was 105 mm. Hg. The right atrial pressure was elevated to 23/7 mm. Hg. A bidirectional interventricular shunt was present. Cardiac irritability prohibited attempts to enter the pulmonary artery. Selective angiography was performed from the right ventricle as shown in figure 5. The right ventricle was at the anterior right heart border with the pulmonary artery crossing anteriorly and superiorly to the left border of the heart. An infundibular pulmonary stenosis was demonstrated as was a right-to-left interventricular shunt with subsequent filling of a left-sided aorta. Definitive surgical repair was deferred pending progression of polycythemia or symptomatology.

Case 3. W.E. was first admitted to the U.C.L.A. Hospital at 5 months of age for treatment of a severe respiratory infection. He was born following a normal full-term pregnancy. At 1 month of age a heart murmur was heard by the family physician, and at 4 months of age a pulsating mass was noted in the epigastrium. Tachypnea and slow weight gain were apparent but motor development was normal.

He was readmitted at 11 months of age for heart catheterization. Physical examination on admission showed a healthy appearing noneyanotic Negro infant. The blood pressure was 90 mm. Hg in the upper and 80 mm. Hg in the lower extremities by the simultaneous flush technic. The chest bulged at the anterior midline and mild costal flaring was present bilaterally. The xiphoid process was absent. A 2.5-em. diastasis recti extended to the umbilical hernia, which was 1 cm. in diameter. A mass beneath the skin could be seen and

Fig. 1. Case 1, M.M., age 11 months. The pulsating cardiac mass can be seen in the epigastrium below the left lower sternum. Costal flaring and a repaired omphalocele are demonstrated.
Fig. 2. Case 1, M.M. Top. Dextroposition of the heart and plethoric fields. Marker, apex of the sternal cleft. Bottom. Selective angiocardiogram from the right ventricle shows the right ventricle to be rotated to the far right anterior heart border with the pulmonary artery crossing to the left superiorly and anteriorly.

palpated to extend as a fingerlike projection one half the distance to the umbilicus. A distinct but synchronous pulsating mass was palpable just beneath the defective sternum as shown in figure 6. Cardiac dullness was predominantly on the right side. The pulmonic second sound was accentuated. A grade IV harsh systolic murmur associated with a thrill was heard best at the right lower sternal border. A loud to-and-fro systolic and diastolic murmur was prominent over the epigastric mass.

The electrocardiogram was abnormal showing upright P and inverted T waves in leads I and II. A prominent Q wave was present in lead I. There was no conduction delay. Axis deviation was right. T waves were upright in V1 through V6. The precordial QRS voltage was unremarkable.

The roentgenograms showed dextroposition of the heart with mild cardiomegaly and plethoric lung fields (fig. 7). There was evidence of an anterior diaphragmatic hernia. Cardiac catheterization was performed under rectal basal anesthesia. The bizarre position taken by the catheter in the right ventricle was similar to that shown in figure 3. The pulmonary artery and right ventricular pressure was elevated to 72 mm. Hg systolic. A large left to right interventricular shunt was found.

Selective angiography from the right ventricle
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![Images of heart images with labels RV and LV]

Fig. 3. Case 1, showing the unusual position of the right and left ventricles with a catheter in each.

demonstrated cardiac rotation with the right ventricle further to the right than usual and at the anterior right heart border. The pulmonary artery crossed anteriorly and superiorly to the left side (fig. 7). The suspected ventricular diverticulum was not outlined by the angiogram.

At 13 months of age, surgery was performed upon the patient. A sagittal exposure was made through a median sternotomy. A 3-cm. semilunar midline anterior diaphragmatic defect gave passage for a 3.5-cm. long diverticulum of the left ventricle covered by a membrane, presumably pericardium (fig. 8). The actual position of the heart was as suggested from the angiocardiogram. A prominent sagittal sulcus separated the right and left ventricles in the sagittal plane with the right ventricle somewhat superior to the left. The atria were in their usual positions. A right ventricular cardiomyotomy exposed an interventricular septal defect, 1 cm. in diameter, in the membranous portion a few millimeters below the aortic valve. Primary closure of the defect was made using interrupted silk sutures. Following this the diverticulum from the left ventricle was amputated at the base. This unusual tubular structure originated from the left ventricle as a thin-walled muscular stalk with an internal diameter of about 2 mm. The stalk ballooned out in the form of a sae at the distal portion and was covered by a membrane. A few ligamentous strands connected this structure to the liver capsule. Repair of the anterior diaphragmatic defect was incorporated in the closure of the thoracotomy as was approximation of the rectus muscles at the midline. Postoperative recovery was uneventful. When last seen, at 15 months of age, the patient was doing well.

**DISCUSSION**

Remarkably consistent features of the cases seen by us are the ventral abdominal wall defects and the unusual positional relationship of the heart within the thorax. This position of the heart can best be described as a 90° rotation on the longitudinal axis, so that the right ventricle comes to lie farther to the right than it normally does, and a rotation on the dorsoventral axis, so that the right ventricle comes to lie somewhat superior to its usual position.

Another feature common to these cases is that the electrocardiograms show upright P waves and inverted T waves in leads I and II; a prominent Q wave in lead I and upright T waves in V₁ through V₆. This is not typical of dextrocardia but suggests rotation of the ventricles with the atria in the usual position. Each of the patients had an interventricular septal defect; in one it was associated with
infundibular pulmonary stenosis and in another with a diverticulum of the left ventricle. The sternal defect varied from a rudimentary xiphoid process to a cleft lower sternum. The anterior median diaphragmatic defect and deficient lower sternum permitted cardiac impulses to be seen and felt in the epigastrium beneath the skin covering the diastasis recti.

The combination of anomalies presented by us has been in essence previously reported and probably erroneously categorized as a subgroup of ectopia cordis.\textsuperscript{1,2} Ectopia cordis was first described by Haller in 1706.\textsuperscript{3} Todd\textsuperscript{4} in 1836 classified the disease into 3 types: cervical, thoracic, and abdominal. In the thoracic type, a cleft sternum is present; a cleft sternum is not always associated with ectopia cordis. Grieg\textsuperscript{5} in 1926 reported 20 cases with varying degrees of sternal clefs which did not have ectopia cordis. Only one of his cases had intracardiac anomalies. Grieg\textsuperscript{5}
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and others\(^6,7\) have presented cases of ectopia cordis of the cervical, thoracic, and abdominal variety. A diaphragmatic hernia with a normal sternum and an abdominal heart characterized the abdominal type.

Byron\(^1\) in 1942 summarized 142 cases from the literature and added a fourth category called thoracoabdominal ectopia cordis, which manifested a defective sternum plus abdominal involvement.

Major\(^2\) in 1953 reviewed all the cases that could be classified thoracoabdominal ectopia cordis according to Byron’s terminology. The characteristics of this group were (1) partial absence or cleft of the sternum, (2) diaphragmatic defect, (3) midline abdominal defect with diastasis recti and omphalocele. A total of 15 cases was presented. Twelve died before 4 months of age. Two have had their epigastric defects successfully repaired and are living. Little mention was given specific cardiac position and function. These 15 cases probably represent the same syndrome as do our patients.

Cantrell, Haller, and Ravitch\(^8\) recently collected 5 cases similar to ours. All 5 had ventricular septal defects; in 2 there was associated pulmonary stenosis, and in 2 there was associated a diverticulum of the left ventricle.

It is our contention that this syndrome should not be classified as ectopia cordis. Maude Abbott\(^9\) defined ectopia cordis as “a displacement so that the heart passes out of the thorax and comes to be either upon the outer surface of the body or in the abdominal cavity.” The principal characteristic feature of our cases is the dextroposition and rotation of the heart within the thoracic cage.

The syndrome of dextroversion of the heart not associated with ventral abdominal wall defects was recently reviewed by Grant.\(^10\) This syndrome included many cases previously reported as isolated dextrocardia. Typically the heart was rotated so that the right ventricle came to lie farther to the right than usual “as in turning the pages of a book 90\(°\),” and appeared in dextroposition. The positions of the right ventricle and pulmonary artery as shown by angiography were iden-

![Fig. 6. Case 3, W.E., age 11 months. The diverticulum from the left ventricle is noted as a mid-epigastric pulsating mass. Costal flaring and an umbilical hernia are apparent.](http://circ.ahajournals.org/)

tical to the cases described here. Intracardiac anomalies including interventricular septal defect were usually present. We have studied 3 such patients in whom the heart lay in this position, 1 with tetralogy, and 2 with interventricular septal defects, without any evidence of abdominal wall anomalies.

**Embryology**

In considering the embryology, as with most of the congenital defects, the end result is known and something of the steps by which they were arrived at, but virtually nothing is known about the actual causative factors. The problem can be approached by considering briefly the development of the organs involved.\(^11-13\)

The cardiopericardial primordium begins as a paired zone of thickened mesoderm near the cephalic end of the embryo and with the formation of the head fold, and the lateral body folds, the pericardial cavity is swung beneath the pharynx. The splanchnic mesoderm forming the ventral part of the anterior intestinal portal also forms the caudal wall of the pericardial cavity. According to Patton\(^11\) this shelf of tissue is the transverse septum.

Thus the pericardial cavity is surrounded from at least the third week of development, by a thin but complete thoracic wall, consisting of a simple layer of ectoderm and a layer of somatic mesoderm. Into this thin wall the
sclerotome, the myotome, and the dermatome migrate, thickening it. This thickening progresses until the masses meet and fuse in the ventral midline. This fusion begins cephalically and progresses caudally toward the umbilicus, being essentially complete by the eighth week. Subsequently the cartilage anlagen of the sternum differentiate and fuse in the same cephalocaudal direction. The ventral edge of the myotomes of the lumbar segments differentiate into the rectus columns, forming the rectus abdominis muscles.

The endodermal cells of the developing liver grow out into the transverse septum, leaving a layer of mesoderm on its cephalic surface which subsequently differentiates into the "central tendon" of the diaphragm. Somite muscle from cervical segments 3-4-5 comes to lie within the lateral part of the diaphragm, most of which part has arisen from the pleuroperitoneal folds.

There is some reason to believe that some of the lateral part of the diaphragm is derived from the lateral body wall. If this proc-
ess of contribution to the diaphragm from the body wall also involves the ventral part (which seems likely, although there is no proof of this in the literature), then the ventral midline part of the diaphragm could be expected to be abnormally weak, as was the adjacent part of the body wall itself. This makes plausible a caudal outpouching of the weakened membranous part of the diaphragm in the midline at a point where it is least reinforced by the liver, i.e., ventrally. Into this pouch a diverticulum of the ventricle could project.

The organs just considered all have an intimate final relationship to each other. To the lower sternum or xiphoid process attach the anterior leaf (septum transversum) of the diaphragm, the linea alba, and medial fibers of the rectus abdominis muscle. By about 8 weeks these structures normally are united and fused in the midline. The causative factor for failure of normal fusion is speculative.

Since the skin was intact and presumably normal in the ventral midline, it is probable that there was no early defect in the lateral body folds and in the isolation of the pericardial cavity, such as occurs in cases when the heart is exposed on the surface of the chest.

It seems that the basic defect in these 3 cases was a failure of the mesoderm of the body wall to complete its migration to meet and fuse solidly in the ventral midline. This would account for the failure to fuse of the seleratome (cleft sternum and xiphoid process) and of the myotome (diastasis recti). This general failure also explains the presence of the omphalocoeles, or umbilical hernias.

The positional relationship of the heart is an interesting consideration. It suggests embryonic arrest with failure of complete rotation and bending to the left. The interventricular septum membranaceum is formed by the union of 3 parts: the descending conus ridge, the endocardial cushions, and the ascending ventricular septum. The conus and truncus ridge divides the outlet of the heart equally into the pulmonary artery and aorta by means of spiral torsion. The union of these 3 structures to form the intact ventricular septum occurs at about the eighth week and is dependent upon precise positional timing. Failure of complete rotation of the heart to the left, which normally occurs by the seventh week, could influence such a union.

A common gestational time can be presumed for the occurrence of the defects described but no causative factor can be explained other than failure of the body wall mesoderm of complete migration and fusion in ventral midline.

One can expect to find variation in cases of this type. Whether the same basic pathogenesis, differing only in degree, is responsible for mere dextroversion of the heart in one case and complete ectopia cordis in another is conjecture. Suffice it to say that the cases herein reported are sufficiently distinct to be considered a syndrome.
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SUMMARY

Three patients are reported who manifested unusual but strikingly similar features. These include (1) cardiac malrotation with dextroposition, (2) intracardiac defects including ventricular septal defect, (3) deficient lower sternum, (4) anterior diaphragmatic defect, and (5) midline abdominal defect with diastasis recti and umbilical hernia. The midline deficiency permitted cardiac impulses to be seen and palpated in the epigastrium.

The rotational position of the heart was demonstrated in each by selective angiography and electrocardiography. One case was operated upon and complete surgical repair of the defects, including amputation of a diverticulum from the left ventricle, was successful.

Review of the literature showed cases resembling ours to have been previously classified as a rare subgroup of ectopia cordis. This is probably erroneous classification, and these patients should be considered as comprising a distinct syndrome. Consideration is given to possible embryologic pathogenesis.

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SUMMARION IN INTERLINGUA

Es reportate le casos de tres patientes con unusual sed frappantemente simile caracteristicas pathologic. Isto include (1) malrotation cardiae con dexteroposition, (2) defectos intracardia incluse un defecto ventriculo-septal, (3) deficiencia del sterno inferior, (4) defecto antero-diaphragmatic, e (5) defecto centro-abdominal con diastasis de recto e hernia umbilical. Le defecto centro-abdominal permiteva vider le impulsos cardiae e palpar los in le epigastrio.

Le position rotational del corde essee demonstrate in le tres casos per selective angiographia e electrocardiographia. In un del casos, un intervention chirurgic essee effectuate pro reparar omne le defectos. Le operation succedeva, incluse le ablation de un diverticulo in le ventricle sinistre.

Un revista del litteratura resultava in le constatation que casos simile a illos del presente reporto essee classate in le passato como un rar sub-grupp de ectopia del corde. Isto es probabilemente erronee. Iste patientes deberea plusosto esser considerate como representante un syndrome distincte. Es considerate le possibilitate de un pathogenese embryologic.

REFERENCES

3. Haller: Quoted by Blatt and Zeldes.
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