Congenital Cardiac Disease Associated with Polysplenia

A Developmental Complex of Bilateral “Left-Sidedness”

By James H. Moller, M.D., Ahmad Nakib, M.D., Ray C. Anderson, M.D., Ph.D., and Jesse E. Edwards, M.D.

SUMMARY

The well-recognized association of congenital cardiac disease with asplenia has been termed “bilateral right-sidedness” or dextro-isomerism, since the spleen is absent, the liver is symmetrical, and each lung has three lobes and an epiarterial bronchus. In a study of pathological material from 12 patients with congenital cardiac disease associated with multiple spleens (as contrasted to accessory spleen), we found a definite tendency for the symmetrical development of organs but with a tendency for bilateral left-sidedness or levo-isomerism.

The abnormalities assumed one of three forms as follows: (1) absence of a normal right-sided structure, (2) bilateral organs, each with the structure of a left-sided organ, or (3) excessive tissue of a left-sided organ. Thus, in polysplenia we observed a tendency for (1) absence of the hepatic segment of the inferior vena cava and absence of the gallbladder, (2) two lobes in each lung with hyparterial bronchi, and (3) multiple spleens. Other noncardiac abnormalities were partial or complete abdominal heterotaxia and partial malrotation of the bowel. The cardiac malformations included dextrocardia, bilateral superior venae cavae, anomalous pulmonary venous connection with malposition of the atrial septum, and defects in the atrial septum and in the ventricular septum.

Our study suggests that the developmental complex of multiple spleens is closely related to the asplenic syndrome, with the important difference being left-sided symmetry rather than right-sided symmetry.

Additional Indexing Words:

Vena cava
Multiple spleens
Atrial septal defect
Absent spleen
Pulmonary veins
Disorder of body symmetry

Splenetic anomalies are commonly associated with anomalies of the cardiovascular system and of other organ systems. This phenomenon, as it relates to asplenia, is now commonly recognized.1-3 In contrast, the association of anomalies with polysplenia has received less attention, and to our knowledge only 19 such cases have been reported.4-14 It is the purpose of this report to describe our pathological observations in 12 cases in which congenital cardiovascular disease was associated with polysplenia.*

It is also our intention to contrast the anomalies associated with polysplenia, on the one hand, and those associated with asplenia, on the other. In each there is a tendency for “isomerism” or symmetry of body structure.

*Cases 6 and 12 of present report have been previously described.14, 15
In asplenia there is a tendency for bilateral "right-sidedness," while in polysplenia there is a trend toward bilateral "left-sidedness." Features of the latter phenomenon include the tendency for the presence of two lobes in each lung, absence of the hepatic segment of the inferior vena cava, and absence of the gallbladder.

As used in this report the term "polysplenia" refers to the state in which the bulk of splenic tissue is divided into two and often more nearly equal-sized splenic masses. This is contrasted to accessory spleen, in which, in addition to a normal-sized spleen, one or more small spleens are present.

From our 12 necropsied cases of polysplenia associated with congenital cardiac disease, it became apparent that when polysplenia is present in association with congenital cardiovascular malformations, the latter tend to be predictable in nature, and the extracardiac organs exhibit characteristic structure.

We shall describe the essential cardiac and visceral malformations observed in our cases of polysplenia according to three subjects as follows: (1) abnormalities of situs, (2) cardiovascular malformations, and (3) noncardiovascular malformations or variations. Where pertinent, comparison will be made with published accounts on polysplenia.

Observations

Among the 12 patients with polysplenia, six were males and six females. The youngest patient died on the day of birth and the oldest patient when 10 years old. Only four of the 12 patients survived the first year of life.

Abnormalities of Situs

Among the 12 cases, abnormalities of the situs of the heart and abdominal organs were frequently observed. Therefore, we divided the cases into three groups according to the relationships of cardiac structures and the position of the major portion of the liver and of the stomach. Certain arbitrary decisions were made in classifying the cases into one of these groups, since partial malrotation of the bowel and hepatic abnormalities were revealed in a number of cases.

The liver tended to be symmetrical but one lobe usually was somewhat larger than the other. For example, in situs solitus under normal conditions the left lobe is distinctly smaller than the right and displays a sharp lower edge. In the cases of polysplenia the lobe which would be anticipated as the smaller tended to be the smaller one, but the difference in size between the two lobes was less distinct than under normal conditions. Also, the lower edge of the smaller lobe was somewhat rounded.

Although the degree of malrotation of the bowel was variable, the relationship between the cardiac structures and the major lobe of the liver was easily determined. Therefore, the following system of classification based principally on the cardiac, hepatic, and gastric positions appeared the easiest to follow.

If the arterial atrium and stomach were on the left side and the venous atrium and the major lobe of the liver were on the right side, situs solitus was considered to be present (fig. 1a). In situs inversus, the arterial atrium and stomach were on the right side, while the venous atrium lay on the left side, as did the major lobe of the liver (fig. 1b). In both situs solitus and situs inversus the cardiac apex is generally located on the side opposite the major lobe of the liver, but deviations from this occur. The position of the cardiac apex, however, was of itself not considered in designating the situs of the organs in a given case. Furthermore, these states are considered concordant since the relative positions of the heart, liver, and stomach are either normal or the mirror-image of normal. If there were deviations from the relationships basic to determination of situs, the cases were considered to display discordant relationships of the organs and the term mixed situs was applied. Mixed situs was represented in our cases by certain characteristics. In one the major lobe of the liver and arterial atrium were located on the same side (fig. 1c). Another pattern designated as mixed situs was that in which the major lobe of the liver and the stomach were on the same side (fig. 1d).

Situs solitus was present in four cases, of
which one revealed dextroversion (right-sided apex) without ventricular inversion (fig. 1a, insert). In five other cases situs inversus was present, and in one of these the levoversion (left-sided apex) without ventricular inversion (other than that of situs inversus) was present (fig. 1b, insert). Three cases were classified as displaying mixed situs and demonstrated two types of discordance between the organs. In two of the cases of mixed situs, the liver and stomach were located as in situs inversus, but the heart was of the situs solitus variety (fig. 1c). Both of the cases were associated with continuity of the inferior vena cava with the azygos venous system. The third case displaying mixed situs was basically of situs solitus configuration, but the stomach was located on the right side (fig. 1d).

In seven of the 12 cases of polysplenia the cardiac apex was on the left side and in five the apex was on the right side.

Information regarding the relationships and attachments of the mesentery of the small bowel and colon was available in 10 of the 12 cases. Among six of the 10 cases an abnormal mesenteric attachment was observed. The abnormalities varied from the cecum not being retroperitoneal in position to complete malrotation of the bowel. In the latter instances the cecum and ascending colon had mesenteric attachments which permitted considerable mobility of the bowel. In two instances, the malrotation became complicated by intestinal obstruction which required operative relief.

Cardiovascular Malformations

The most consistently occurring malformations of the cardiovascular system involved the pulmonary veins, the venae cavae, and the atrial septum (table 1). Ventricular septal defect, either isolated or as a part of persistent common atrioventricular canal, also was common, as it occurred in nine cases.

Systemic Veins

Abnormalities of the systemic venous system were frequent. In seven of the 12 cases, the hepatic portion of the inferior vena cava was absent, and the abdominal inferior vena cava was continuous with the azygos venous system (so-called interruption of the inferior vena cava). In six of these the inferior vena cava joined the azygos vein while in the seventh case, the hemiazygos vein received the inferior vena cava. In each case the azygos or hemiazygos vein joined the homolateral superior vena cava.

Bilateral superior venae cavae were present in six of the 12 cases, four being cases with interruption of the inferior vena cava, and one of these was the case in which the inferior vena cava joined the hemiazygos vein. In four of these six cases the bilateral superior venae cavae were associated with the developmental complex described by Raghib and co-workers, in which (1) the coronary sinus is absent, (2) each superior vena cava joins its homolateral atrium directly, and (3) an atrial septal defect is present. Connection of the persistent superior vena cava to the left atrium with an intact atrial septum was present in the fifth case. In the remaining case of bilateral superior venae cavae, the persistent left superior vena cava connected with the coronary sinus.

Pulmonary Veins

In 10 of the 12 cases, anomalous pulmonary venous connection existed, six being of the partial variety and four of the total. In each case the anomalous pulmonary venous connection was to the venous atrium. In no case was there anomalous pulmonary venous connection to a systemic vein.

Among the six cases of partial anomalous connection, the form of the anomalous connection was similar. The two pulmonary veins of the lung on the side of the venous atrium (left lung in situs inversus) joined the venous atrium directly (fig. 2). In these cases, the pulmonary veins appeared to connect in a normal location with the posterior atrial wall. The basis for the anomalous termination of pulmonary veins seemed to result from the malposition of the atrial septum toward the arterial atrium. This malposition has two effects: (1) that two pulmonary veins join the
Diagrams of abnormalities of situs with polysplenia. Definition of abbreviations as follows:
S.V.C. = superior vena cava; I.V.C. = inferior vena cava; C.H.V. = common hepatic vein; P.V.
(Continued on p. 793.)

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Venous atrium, and (2) that the volume of the arterial atrium is compromised.

In three of the four cases of total anomalous pulmonary venous connection, the four individual pulmonary veins joined the venous atrium directly, and in each the atrial septum was significantly malpositioned toward the arterial atrium. In the fourth case, the pulmonary veins formed a confluence posterior to the venous atrium, and the confluence, in turn, connected with the venous atrium through a single ostium.

**Atrial Septum**

Several types of abnormalities were noted in the atrial septum. The first, as indicated, was the tendency of the atrial septum to be malpositioned toward the arterial atrium. Secondly, in several cases there was an absence of the fossa ovalis with the only interatrial opening appearing to be ostium II of septum primum (fig. 3).

In 10 of the 12 cases, defects in the atrial septum were present. Among seven of these the atrial septal defect was either in the region of the fossa ovalis or represented by an interatrial ostium II with absence of a fossa ovalis. In three of these seven there was also a defect in the lowermost part of the atrial septum (persistent interatrial ostium primum). In an additional three cases there was a defect in the latter portion, yielding six cases with a defect in the lowermost part of the atrial septum. In four of these six the defect was part of classical persistent common atrioventricular canal with its associated valvular clefts. In the other two cases in both of which the atrial septal defect was of the ostium primum type, no valvular clefts were associated. In one of the four cases with classical persistent common atrioventricular canal, the atrial septum was so rudimentary as to allow a designation of "single atrium."

**Ventricular Septum**

In nine of the 12 cases reviewed, the ventricular septum was defective. In five of these the defect was of the isolated variety, while in the remaining four the ventricular septal...
Table 1
Cardiovascular Malformations in Twelve Cases of Polysplenia Reported*

<table>
<thead>
<tr>
<th>Case</th>
<th>Position of Cardiac Apex</th>
<th>Associated Cardiovascular Malformations</th>
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<tr>
<th>Situs Inversus</th>
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<tr>
<td>5</td>
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<td>6</td>
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<tr>
<td>7</td>
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<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
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</table>

Mixed Situs

| 10   |       |      |                      |                   |                |              |                  |                  | Double Outlet Rt. Ventricle |
| 12   |       |      |                      |                   |                |              |                  |                  | Subaortic Atresia |

*Entire shading indicates condition present. Partial shading indicates partial anomalous pulmonary venous connection. Anomal. Pul. Vein = anomalous pulmonary venous connection; "Absent I.V.C." = absence of hepatic segment of inferior vena cava with azygos (or hemiazygos) continuation; Bilat. S.V.C. = bilateral superior venae cavae; Vent. Septal Defect = isolated ventricular septal defect. In cases 10 and 11, liver was on left; stomach on right. In case 12, liver was on right; stomach on right.

defect was a component of the aforementioned cases of persistent common atrioventricular canal.

Other Abnormalities

In three cases, the great arterial vessels were abnormally related. Origin of both great vessels from the right ventricle was present in two of these and, in the third, complete transposition of the great vessels was present. Subaortic obstruction existed in two cases. In one the anterior leaflet of the mitral valve was fused to the ventricular septum, resulting in subaortic atresia; this case has been reported previously. In the second case of subaortic obstruction, stenosis resulted from
anomalous chordal attachments of the anterior leaflet of the mitral valve to the hypertrophied ventricular septum.

In contrast to asplenia in which pulmonary stenosis is almost universally present, among our 12 cases of polysplenia only a single case...
Noncardiovascular Anomalies

In eight cases gross specimens of the lungs were available for review. In seven each lung had the fundamental structure of a left lung. In these seven cases, each lung had two lobes (fig. 4). The main stem bronchus to each lung was hyparterial, in that the homolateral pulmonary artery passed over the main stem bronchus and then proceeded behind the bronchus of the upper lobe to descend to the lower lobe (fig. 5). In addition, in each of these cases the distance between the carina and the first division of the major bronchus was identical in both lungs.

In the eighth case, the right lung exhibited rudimentary division into three lobes, and a bronchus suis was present in this lung. The right main stem bronchus was epiarterial. The left lung was normal, and the left main stem bronchus was hyparterial.

The number of multiple spleens varied from two to nine. They were located near the greater curvature of the stomach. The splenic masses were of relatively equal size, and the combined weight was normal (fig. 6).

In a single case the gallbladder was absent (fig. 7).

Comment

A large volume of literature has been accumulated describing the various features of the asplenic syndrome. In contrast, little has

Figure 5

Diagrammatic representation of characteristic relationship between major bronchi and pulmonary arteries in polysplenia. Bilateral hyparterial bronchi.

Figure 6

Case 10. Multiple spleens. Six splenic masses located along splenic artery.

Figure 7

Case 9. Inferior surface of liver. Absence of gallbladder. Both lobes are nearly equal in size.
appeared concerning the cardiovascular anomalies and other malformations associated with the polysplenic state. In most of the reports of cardiac disease associated with polysplenia, the emphasis has been on the nature of the cardiovascular anomalies, and the splenic abnormality has been mentioned only as an incidental necropsy finding. It is, therefore, difficult in reviewing the literature to discover all the cases of polysplenia.

The 17 cases of polysplenia reported from other institutions in general exhibit the same types of cardiovascular abnormalities as we have observed in our cases. Except for one case of Ivemark, in each of the other 16 cases reported in the literature cardiac abnormalities were present which allowed recognition of a tendency for (1) cardiac malposition, (2) interruption of inferior vena cava withazygos continuation, (3) partial or total anomalous pulmonary venous connection to the venous atrium, (4) bilateral superior venae cavae, and (5) defects in the atrial and ventricular septa. The cases described in the literature also exhibited frequent visceral malformations including (1) partial or total abdominal heterotaxy, (2) abnormality of pulmonary lobulation, and (3) symmetrical liver. In one of the cases reported by McLoughlin and associates the gallbladder was absent also, a condition also observed in one of our cases. From the experience with the literature and with our material, it appears that the malformations associated with polysplenia represent a developmental complex. As in the asplenic syndrome certain predictable cardiac and visceral abnormalities are present in polysplenia.

Comparison of the form of the visceral malformations present in these two syndromes discloses certain distinct differences (table 2). In asplenia, the frequent occurrence of three lobes in each lung, symmetrical liver, and absent spleen has suggested to some authors that this developmental complex represents a tendency for duplication of the normal right-sided structures. It is cited that the spleen is the only unilateral mesenchymal organ, and since it is a left-sided structure, its absence is part of "bilateral right-sidedness." The organs in the left side of the body exhibit the appearance of the normal right-

<table>
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<th>Table 2</th>
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**Comparison of Features of Asplenia and Polysplenia**

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Features associated with asplenia</th>
<th>Features associated with polysplenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>Corrected transposition of great vessels with ventricular septal defect or single ventricle</td>
<td>Continuity of inferior vena cava with azygos or hemiazygos vein</td>
</tr>
<tr>
<td></td>
<td>Pulmonary atresia or stenosis</td>
<td>Anomalous pulmonary venous connection to venous atrium</td>
</tr>
<tr>
<td></td>
<td>Common atrium</td>
<td>Atrial septal defect or common atrium</td>
</tr>
<tr>
<td></td>
<td>Bilateral superior venae cavae</td>
<td>Ventricular septal defect</td>
</tr>
<tr>
<td></td>
<td>Total anomalous pulmonary venous connection</td>
<td>Bilateral superior venae cavae</td>
</tr>
<tr>
<td></td>
<td>Malposition</td>
<td>Malposition</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Three lobes—each lung</td>
<td>Two lobes—each lung</td>
</tr>
<tr>
<td></td>
<td>Bilateral hyparterial bronchi</td>
<td>Bilateral hyparterial bronchi</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Heterotaxy</td>
<td>Heterotaxy</td>
</tr>
<tr>
<td></td>
<td>Complete</td>
<td>Complete</td>
</tr>
<tr>
<td></td>
<td>Situs inversus</td>
<td>Situs inversus</td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>Partial</td>
</tr>
<tr>
<td></td>
<td>Horizontal liver</td>
<td>Horizontal liver</td>
</tr>
<tr>
<td></td>
<td>Malrotation of bowel</td>
<td>Malrotation of bowel</td>
</tr>
<tr>
<td></td>
<td>Duodenum—common mesentery</td>
<td>Absent gallbladder</td>
</tr>
<tr>
<td></td>
<td>Midline gallbladder</td>
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</tr>
</tbody>
</table>

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sided structures, hence three lobes in the left lung and a symmetrical liver.

In contrast to the tendency for duplication of right-sided structures in the asplenic syndrome are the features of the complex of polysplenia. In the latter there appears to be a tendency for duplication of left-sided structures, with an absence of normal right-sided structures. The evidence to support this belief is the following. The first is the presence of polysplenia. The second is the frequent phenomenon that each lung has but two lobes and has the structure of a left lung. Seven of our eight cases of polysplenia in which the lungs were available for review revealed this anatomic relationship. Brandt and Liebow12 were the first to describe this feature of the lungs in a case of polysplenia. These authors emphasized the importance of the relationships between the bronchi and arterial branches in identifying whether the structure is that of a right or a left lung. The third feature favoring a concept of bilateral “left-sidedness” is absence of the gallbladder, as occurred in one of our cases and one described in the literature.9 The fourth is the frequent infrahepatic interruption of the inferior vena cava. This portion of the inferior vena cava normally develops from a right-sided venous structure.

Because of these features, it appears logical to consider that the polysplenic syndrome represents bilateral left-sidedness or levo-isomerism, the opposite form of isomerism from the asplenic developmental complex.

There are, on the other hand, basic similarities between cases with multiple spleens and those with asplenia as indicated by Ivemark, who found more variability of the cardiac malformations in the former group than in the latter. Campbell and Deuchar17 recently discussed the embryological implications of the malformations associated with asplenia and noted that some of their cases with cardiovascular features of the asplenic syndrome had multiple small spleens. The implications of these observations are important. The asplenic syndrome and the polysplenic syndrome are closely related development complexes in that each represents a defect occurring early in embryogenesis, which results in the lack of development of the normal body asymmetry. Furthermore, the types of cardiovascular and noncardiovascular malformations may appear similar. There is, however, one important difference between these two. The asplenic syndrome generally is associated with the tendency for right-sided symmetry, and polysplenia with the trend toward left-sided symmetry.

The cardiovascular and splenic abnormalities of these two developmental complexes have received considerable emphasis because significant cardiovascular malformations are present in the majority of cases. Abnormalities of these two organ systems are not invariably present, however. As indicated by Ivemark’s one case of polysplenia without cardiac disease, cardiovascular malformations need not be uniformly present. Ivemark also suggested that the absence of the spleen is not always associated with other features of the asplenic syndrome. This is illustrated by a recently reported case with the typical cardiovascular malformations of asplenia and with three lobes in each lung in which an accessory spleen was present.18 It is, therefore, probably possible to have each of these syndromes with a normal spleen.

The manifestations of these two developmental complexes are, therefore, variable and are represented by a spectrum of abnormalities with a varying number of structures showing symmetrical development.

The tendency for symmetrical organ structure may involve only one organ system, for example, the lungs. Therefore, it would appear advisable to classify these developmental complexes in a more inclusive fashion, namely, disorders of body symmetry with tendencies to either dextro-isomerism or levo-isomerism and with the extent of symmetry and organ involvement being defined.

Since the cardiac malformations associated with polysplenia follow a relatively uniform pattern, it would be helpful to the clinician to be able to recognize the polysplenia as a basis for anticipating the cardiovascular mal
formations that might be present in a given case. The asplenic syndrome can be readily recognized by finding Howell-Jolly bodies in a peripheral blood smear. We know of no easy clinical means of identifying polysplenia. The finding of absence of the hepatic segment of the inferior vena cava should suggest this possibility, but it appears that, other than angiographic or radioactive isotopic visualization of the splenic structures, there are no definite means of identifying the presence of polysplenia short of surgical exploration or necropsy.

An important clinical difference between polysplenia and asplenia relates to cyanosis. In asplenia, wherein pulmonary stenosis and defects of the ventricular septum are common, cyanosis and diminished pulmonary blood flow are usually present. In polysplenia, considering the tendency for absence of pulmonary stenosis and for the presence of septal defects, acyanosis with increased pulmonary blood flow forms the usual clinical pattern.

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