The Cardiac Conduction System in Situs Ambiguous

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SUMMARY The cardiac specialized conduction tissue was studied by serial sectioning in 13 cases of situs ambiguous. In four cases of right isomerism, we found paired sinus nodes in relation to a crista terminalis, and in each case a sling of conduction tissue between two atrioventricular nodes was present regardless of the ventricular morphology or cardiac position. In the cases with left isomerism, the sinus node was hypoplastic and abnormally located. We saw two types of atrioventricular conduction systems. In the three cases in which the morphologically right ventricle lay to the left of the morphologically left ventricle (presumed d-loop), a single atrioventricular bundle arose from a normally located atrioventricular node. In the five cases in which the morphologically right ventricle lay to the left of the morphologically left ventricle (presumed l-loop) and in the one case with a univentricular heart, paired atrioventricular nodes were present, linked or potentially linked by a sling of conduction tissue.

FAILURE OF LATERIALIZATION of thoracic and abdominal viscera into the pattern of either situs solitus or situs inversus results in the symmetrical visceral configuration with duplication of either left- or right-sided structures termed situs ambiguous.¹ This frequently results in major malformations in the cardiovascular system. In situs ambiguous with right isomerism, duplication of right-sided structures, such as the crista terminalis, is associated with duplication of the sinus node.² In the left isomorphic form, where the crista terminalis is absent, atrial depolarization is known to be abnormal as judged from the surface ECG.³ The sinus node has been reported to be abnormally located in two cases studied by Bharati and Lev,⁴ one with multiple spleens and the other with a single bilobed spleen.

The atrioventricular conduction system has not been studied extensively in hearts with situs ambiguous. We have previously observed a sling of ventricular conduction tissue connecting paired atrioventricular...
nodes in one case with left isomerism; Bharati and Lev\(^4\) have also described slings in their cases with polysplenia and a bilobed spleen.

To provide further information on the disposition of conducting tissue in situs ambiguous and its relation to the ECG, we studied 13 cases by serial sectioning techniques, four with right isomerism and nine with left isomerism.

**Materials and Methods**

We studied hearts from the pathological collections at the Royal Liverpool Children's Hospital and the Cardiothoracic Institute, Brompton Hospital, London. The gross morphological features of the specimens were photographed. We observed lung lobulation, and determined the pulmonary artery to bronchial relationship by dissection. When the abdominal viscera had not been preserved, we obtained the presence, number and location of the spleens from the autopsy report.

After gross study, tissue blocks were prepared for histological examination. In all cases the block comprised both atria, including the superior vena caval atrial junction, the atrial septum, the atrioventricular valve in its entirety and the base of the ventricular mass, including part of the ventricular septum, when present. In 11 cases we could accomplish this in a single tissue block. In the other two cases, however, two tissue blocks were necessary because of the size of the specimens. The blocks were prepared by embedding in paraffin wax and subsequently sectioned at 10 \(\mu\) thick. Each section was retained according to our usual practice, and initially each fiftieth section was mounted and stained using Masson's trichrome technique. Additional sections were mounted and stained from areas of particular interest. An electrocardiographic record was studied in each case.

**Results**

The principal morphological features and histological findings are summarized in Table 1. On the basis of the bronchial anatomy and lung morphology, the 13 specimens are divided into two groups.

In nine cases, left-sided symmetry or isomerism

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*Accessory atrioventricular connection identified.

†Anterior atrioventricular node in left lateral position.

‡Left bundle branch in rudimentary chamber.

Abbreviations: D = dextrocardia; Le = levocardia; RSVC = right superior vena cava; LSVC = left superior vena cava; MRV = morphologically right ventricle; MLV = morphologically left ventricle; UVH = univentricular heart; LBB = left bundle branch; R = right; L = left; + = present; node and bundle present but disconnected.
(polysplenia syndrome) was present. Eight of these cases had bilateral bilobed lungs with bilateral hyparterial bronchi; but in case 9, although both main bronchi were hyparterial, the right lung was trilobed. Multiple spleens were present in eight cases, and case 7 had a single bilobed spleen on the right side of the abdomen.

In four cases, isomerism of morphologically right-sided structures was present (asplenia syndrome). All four specimens had bilateral trilobed lungs, with bilateral eparterial bronchi. Three cases were associated with asplenia, but case 13 had a single, normally positioned spleen.

Left Isomerism (Nine Cases)

Gross Features

Each heart had anomalies of systemic venous drainage. Bilateral superior venae cavae were present in four cases. In seven cases the hepatic segment of the inferior vena cava was absent, and the venous return continued via an azygos system to either right or left superior vena cava. Only in cases 6 and 7 was an inferior vena cava present, draining to the left-sided atrium in case 6 and the right-sided atrium in case 7. In all cases the pulmonary venous return was characteristic, the right and left pulmonary veins entering the right- and left-sided atria or the right and left sides of a common atrium, respectively.

In five of the nine cases, two atria were present, and a common atrium occurred in the remaining cases. In all cases the atrial morphology showed evidence of left atrial isomerism; both atrial appendages had the morphological characteristics of the normal left atrial appendage. The coronary sinus was present only in cases 1 and 2, entering the right-sided atrium in both cases.

![Image](http://circ.ahajournals.org/)

Figure 1. The hypoplastic sinus node in the right lateral wall of the atrium in case 1. SAN = sinus node; RA Wall = right atrial wall.

We found a common atrioventricular valve in three cases. Mitral and tricuspid valves were recognized in the remaining cases, although the anterior leaflet of the mitral valve of case 4 was cleft. Two ventricles were present in eight cases; case 9 had the morphology of a univentricular heart of right ventricular type, with a rudimentary chamber of left ventricular type. A ventricular septal defect was present in seven of the eight cases with two ventricles, the ventricular septum being intact only in case 4. In five cases the morphologically right ventricle lay to the left of the morphologically left ventricle. In three cases it was to the right; the remaining case was the univentricular heart.

Double outlet of the morphologically right ventricle was present in cases 2, 3, 6, 7 and 8. In cases 1 and 9 pulmonary atresia occurred, the aorta arising from the morphologically right ventricle of case 1 and from the main ventricular chamber of the univentricular heart (case 9). In cases 4 and 5, two great arteries were present arising from separate ventricles. The aorta arose from the morphologically left ventricle of case 4 and the morphologically right ventricle of case 5.

Histological Findings

A sinus node was identified on the right lateral wall of the atrium related to the junction of the right-sided atrial appendage with the atrium in five cases. In two cases the sinus node was identified on the left lateral wall of the atrium and in a further two cases the sinus node could not be identified. In all the hearts in which a sinus node was recognized, the node was abnormally small (fig. 1).

All the hearts in this group had a posteriorly situated atrioventricular node, which was the only node in the three cases in which the morphologically right ventricle lay to the right of the morphologically left ventricle (fig. 2). In the five cases in which the morphologically right ventricle was left-sided and in the univentricular heart, a second atrioventricular node was present in the anterior part of the atrial septum. In these cases with two atrioventricular nodes, there was a well-defined sling of specialized conduction tissue on the inferior rim of the ventricular septal defect (figs. 2 and 3). In two cases (cases 3 and 6) the sling failed to connect with either atrioventricular node. The bundle branches arose from the sling, although only a single left bundle branch was identified in case 3. The anatomy of the bundle branches was compatible with the morphology of the ventricle to which they were related. In case 2 a lateral accessory atrioventricular connection was identified in relation to the annulus of the mitral valve (fig. 4).

Right Isomerism (Four Cases)

Gross Features

Total anomalous pulmonary venous return was present in all four cases; it was supracardiac in cases 12 and 13 and infradiaphragmatic in cases 10 and 11. We saw considerable variation in the site of systemic venous return (table 1). The sites of systemic venous
return could not be identified in case 12, but all other cases had an inferior vena cava which entered the left side of the common atrium in cases 10 and 11 and the right-sided atrium in case 13. The coronary sinus was absent in all four cases.

Evidence of right atrial isomerism was present in all cases, both atrial appendages having the morphology of the normal right atrial appendage. A well-developed crista terminalis was present bilaterally in each case. All four cases had a common atrioventricular valve. In two cases the ventricular morphology was that of a univentricular heart of indeterminate type without a rudimentary chamber. Two ventricles were present in the remaining two cases, the morphological right ventricle being right-sided in case 12 and left-sided in case 10. In both cases a ventricular septal defect was present.

Pulmonary atresia was present in cases 10 and 11 the aorta arising from the morphologically right ventricle in case 10. In cases 12 and 13 the ventriculo-atrial connection was double outlet, both great arteries arising from the morphologically right ventricle in case 12.

**Histological Findings**

All four hearts had two well-developed sinus nodes, each related to a crista terminalis (fig. 5). In those cases with bilateral superior venae cavae, the nodes were normally related to the junction of the superior cavae and the atra.

All four hearts had two atrioventricular nodes. The posterior node was constant in position and related to tendon of Todaro (fig. 6A). In the hearts with two ventricles, the second node was anterior in position, but in the two univentricular hearts the second node was located at the left lateral atrioventricular sulcus (fig. 6D). In all four hearts we identified a sling of specialized conducting tissue either on the inferior rim of the ventricular septal defect (fig. 2) or on a prominent trabeculation within the ventricular chamber of the univentricular hearts (figs. 2 and 6). In three of the hearts, the sling made contact with both atrioventricular nodes but in case 12 the sling failed to contact the anterior node. The bundle branches were represented

**FIGURE 2. Illustration of the distribution of atrioventricular conducting tissue in situ ambiguous according to ventricular morphology and relationships.** LV = morphologically left ventricle; RV = morphologically right ventricle; "RV" = univentricular heart with main chambers of right ventricular type; RC"LV" = rudimentary chamber of left ventricular type; Indet. = univentricular heart of indeterminate type.

**FIGURE 3. Morphologically left ventricle (right-sided) and right-sided atrium of case 7.** The position of the anterior and posterior atrioventricular nodes and the relationship of the sling of conducting tissue to the ventricular septal defect is indicated. Ant Node = anterior atrioventricular node; Post Node = posterior atrioventricular node; VSD = ventricular septal defect; LBB = left bundle branch; MLV = morphologically left ventricle.
by a solitary fascicle of conducting tissue which arose from the sling in the univentricular hearts. In case 10, normal right and left bundle branches were present in the morphologically appropriate ventricles but in case 12 only the left bundle branch was present.

Electrocardiographic Findings

An ECG was available in all cases. In the cases with left isomerism, the frontal P-wave vector lay within the range $+30^\circ$ to $-105^\circ$; the degree of leftward deviation from normal was most marked in the two cases with left sided sinus nodes (table 1). Complete atrioventricular block was present in cases 3 and 6. In these cases, both atrioventricular nodes failed to make contact with the atrioventricular bundles. Rightward deviation of the frontal P-wave vector occurred in three of the four cases with right isomerism.

Discussion

Our histological study has shown a high degree of uniformity in the disposition of the conduction system in situs ambiguus. Thus, in cases of left isomerism, the sinus node, when identifiable, was abnormally located in the lateral wall of the atrium. In five cases it was

FIGURE 4. A) Photomicrograph of case 2 showing an accessory atrioventricular connection close to the epicardial surface of the heart skirting the fibrous annulus of the mitral valve. B) The scalar electrocardiograph of case 2 showing type A Wolff-Parkinson-White Syndrome. Acc Conn = accessory connection.

FIGURE 5. Photomicrograph of case 11 at the junction of the superior vena cavae with the common atrium. High-power views of the boxed areas show well-developed sinus nodes each related to an artery. Right SAN = right sinus node; Left SAN = left sinus node; R-SVC-At = junction of right superior vena cava and atrium; L-SVC-At = junction of left superior vena cava and atrium; CT = crista terminalis.
FIGURE 6. The atrioventricular conduction tissue in case 11. A) The posterior atrioventricular node (Post AVN) gives rise to a penetrating bundle which continues as a sling; B) The sling near its midpoint lying on the left posterolateral ventricular wall; C) The anterolateral part of the sling; D) The anterior atrioventricular node (Ant. AVN) lying close to the left atrioventricular sulcus. AS = atrial septum; PVW = posterior ventricular wall; ALVW = anterolateral ventricular wall; Ant. Sling = anterior portion of sling; Mid sling = middle portion of sling; Post sling = posterior portion of sling.
right-sided and in two cases, left-sided. The atrioventricular conduction system was arranged in “normal” fashion when two ventricles were present and the morphologically right ventricle was right-sided. However, when the morphologically right ventricle was left-sided or in the presence of a univentricular heart, a sling\(^4,6\) of conduction tissue connected or potentially connected paired atrioventricular nodes. Cases of right isomerism had two sinus nodes situated in relation to a crista terminalis. All cases in this group had slings of ventricular conduction tissue, regardless of the ventricular morphology or relationships.

The findings regarding the sinus node are consistent with previous reports. Van Mierop et al.\(^8\) described the paired sinus nodes which exist in right isomerism, while Bharati and Lev\(^3\) described abnormally located sinus nodes in two cases which, from their description, had features of left isomerism. In both these latter cases, and in our cases, the sinus node was variably hypoplastic and in two of our cases, it was not identified at all. These observations correlate well with the present and previous electrocardiographic findings.\(^3\) The superiorly oriented frontal P-wave vector seen in left isomerism has been interpreted as indicating the presence of a low atrial pacemaker.\(^6\) Our findings provide anatomic evidence which confirms this interpretation. Similarly, the normal or rightward orientation of the P wave seen in our cases of right isomerism is consistent with activation of the atrium from a sinus node situated in relation to the superior end of a crista terminalis, close to the junction with the superior vena cava, when present.

The findings of a sling of ventricular conduction tissue in the majority of our cases is of considerable interest. The first sling was described by Mönckeberg\(^7\) in a case of atrioventricular discordance with double outlet right ventricle. Since then, slings have been encountered in patients with double outlet right ventricle in situs inversus with atrioventricular concordance,\(^8\) atrioventricular discordance,\(^4,9\) and in cases of left isomerism.\(^4,6\) Our present study shows that in patients with left isomerism, slings occur only when the morphologically right ventricle is to the left of the morphologically left ventricle (presumed l-looping\(^10\)) or when a univentricular heart of right ventricular type is present. In contrast, slings were found in all hearts with right isomerism, although the sling was incomplete in the heart with presumed d-looping.\(^10\) The slings in the two univentricular hearts of indeterminate morphology were particularly interesting, since the anterior node was left-sided and lateral (figs. 2 and 6) and the sling itself lay in the parietal wall of the ventricle. This confirms our earlier suggestion\(^11\) that atrioventricular connections are possible at any point around the atrioventricular junction of those univentricular hearts without rudimentary chambers. The heart that had ventricular preexcitation (case 2) did not have a sling, but an accessory atrioventricular connection was identified in the anticipated left posterior position,\(^12\) coursing through epicardial fat and skirting the fibrous annulus of the mitral valve. The cases with slings did not exhibit preexcitation. We have speculated that a sling might be responsible for preexcitation,\(^8\) but without having studied the remainder of the atrioventricular junction to exclude other pathways. The presence of a sling clearly provides a possible reentrant circuit, but whether the sling can function in this way depends on the electrophysiologic characteristics, which have not been determined.

Our investigation has demonstrated a consistent pattern in the disposition of conduction tissues in situs ambiguous. The findings show that the disposition of conducting tissue correlates with ventricular morphology and relationships rather than with cardiac position, exactly the same disposition of conducting tissue being present in similar hearts, regardless of whether they were positioned in the right hemithorax (dextrocardia), or the left hemithorax (levocardia). However, some questions have not been answered, particularly concerning the distribution of atrioventricular conduction tissues in situs ambiguous with univentricular hearts of left ventricular type, since it is difficult, theoretically, to envisage a sling in a heart with this ventricular morphology.

Acknowledgment

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