CLINICOPATHOLOGIC CORRELATIONS

De Subitaneis Mortibus

XX. Cardiac Electrical Instability in the Presence of a Left Superior Vena Cava

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SUMMARY Abnormalities of cardiac rhythm have been reported by others in patients with a persistent left superior vena cava. We present the histological findings from postmortem examination of the cardiac conduction system of two such patients. The first patient was a schoolboy who died suddenly and unexpectedly. His sinus node was abnormally small, his A-V node contained numerous venous lacunae and was stretched out beneath the enlarged coronary sinus, both A-V node and His bundle were dispersed in the central fibrous body in a fetal pattern, and isolated fragments of A-V nodal tissue were connected to the myocardium at the crest of the interventricular septum. The second patient complained of palpitations many months prior to surgical correction of an interventricular septal defect; his post-operative course included multiple arrhythmias and he died suddenly on the 16th postoperative day. Although his sinus node was histologically normal, the nutrient artery contained a polypoid fibromuscular mass virtually occluding its lumen; his A-V node and His bundle were also dispersed in the central fibrous body in the fetal pattern, and the A-V node contained numerous venous lacunae as well as being histologically disorganized in its cytological pattern. These anatomical findings may indicate a basis for various forms of cardiac electrical instability, and deserve consideration in the future evaluation of any patient found to have a persistent left superior vena cava, but particularly if there is clinical evidence suggesting an arrhythmia or conduction disturbance.

IN THE RABBIT and a number of other mammals there is normally a left superior vena cava present in adult life, but this is not true in man. During fetal development of the human heart, the left superior cardinal vein is normally incorporated into the formation of the coronary sinus and the only visible remnant of it which persists is the oblique vein of Marshall. When a left superior vena cava is present in the postnatal human heart, it is not only associated with considerable enlargement of the coronary sinus but may also be accompanied by a variety of other congenital cardiac anomalies.

Ontogenetic development of the sinus node, atrioventricular (A-V) node and His bundle may be significantly influenced by what happens to the right and left superior cardinal veins of the human embryo. If the sinus node and the A-V node are originally located at the junctions of the right and left superior cardinal veins (respectively) with the sinus venous, then the later migration and regressive obliteration of the left superior cardinal vein will determine the final location and perhaps the histological organization of the A-V node. The sinus node in normal development simply remains at the junction of the right superior vena cava and the right atrium. It can then be seen how persistence of a left superior vena cava or abnormalities of the right superior vena cava may alter the eventual location and possibly the histological organization of both the sinus node and the A-V junctional structures (A-V node and His bundle).

A number of observers have reported examples of cardiac electrical instability associated with persistence of a left superior vena cava. We were recently presented with the opportunity to study the heart of a boy who died suddenly and unexpectedly, and in whom the only gross anatomical abnormality of the heart concerned the venae cavae. Because there were a number of unusual findings in his cardiac conduction system, we are here reporting those observations and comparing them to changes also found in the cardiac conduction system of another case of persistent left superior vena cava.

Case Reports

Case 1

A thirteen-year-old boy was attending the prize distributions at his school, following which a gymnastic display was presented for the parents. He was one of a team of boys who were climbing up bars, swinging on a rope to other bars and then walking on a parallel bar about three feet above the ground. When he was on the parallel bar, he fell off onto the wooden floor and lay there face down and motionless. His doctor was in the audience and quickly went to his assistance. When he turned the boy over, he noticed that his pupils were dilated. No pulse could be detected. Artificial respiration was given and the boy made an occasional attempt to breathe but at no stage could his pulse be felt. He was conveyed to hospital by ambulance where further attempts were made to resuscitate him but he failed to respond.

He had always been a healthy boy and more athletic than many. About three or four years previously his cousin, a young man of about 20 years, dropped dead at home, and 15 years ago another cousin dropped dead coming home from school.
At postmortem examination there were no remarkable abnormalities except in the heart. There was no recognizable right superior vena cava, the crista terminalis of the right atrium was absent, and the region of the sinus intercavatum was irregularly trabeculated instead of having its normally smooth endocardial surface. A normal inferior vena cava was present. The ostium of the coronary sinus was larger than normal and led directly into a left superior vena cava (fig. 1) which coursed across the lateral wall of the left atrium exactly in the usual location of the oblique vein of Marshall. The left superior vena cava did not drain into the left atrium. The coronary sinus received the normal veins of the left ventricle. Ventricular sinus received the normal veins of the left ventricle. The right coronary crossed the crux to supply the A-V node; it also gave rise to the sinus node artery. After crossing the crux of the heart the right coronary artery terminated along the obtuse margin of the left ventricle, but just before turning from the atrioventricular sulcus down over the ventricular epicardium, it provided a distinct atrial branch which coursed up along the margin of the left superior vena cava as it passed over the surface of the left atrium. This atrio caval junction and the artery it contained were especially examined for the possibility of a "left sinus node" being present there.

Eleven blocks of tissue were cut from the region of attachment between the left superior vena cava with left atrium, eleven others cut from the approximate location of a crista terminalis which could not be found, and ten were cut from the junction of interatrial and interventricular septum. Each of these blocks was about 2 mm in thickness, and five to ten slides were screened from each block to determine the local histology. Because of certain abnormalities found in the A-V junctional region, selected blocks were then cut serially in 8 micron sections and every tenth of these mounted, so that 389 slides of A-V node and His bundle were examined. In searching for a normal right sinus node or an abnormally present left sinus node, 65 and 72 slides were examined for those purposes.

In only two of the eleven right atrial blocks was there any recognizable sinus node tissue (fig. 2), whereas normally over half of such blocks should have contained sinus node. There was sinus node present in a region no longer than 3 mm in maximal dimension, making this total mass of nodal tissue less than one-third that which is normally present in human hearts at this age. All of the other regions where sinus node should have been did contain sinus node artery but there was no periartrial node as would normally be expected. None of the blocks from the left atrium contained any nodal tissue.

Fragments of A-V nodal tissue were strewed out directly beneath the ostium of the large coronary sinus, from whence they continued forward in an irregular outline until they connected with the His bundle. Within the A-V node there was an exceptionally large number of venous profiles (figs. 3 and 4). Near the A-V node there were numerous isolated fragments of A-V nodal tissue lying within the central fibrous body, and some fragments were undergoing resorption (figs. 5 and 6). As the His bundle was being formed by the A-V node, there was an island of detached A-V nodal tissue atop the crest of the interventricular septum; this

![Figure 1](http://circ.ahajournals.org/content/circulation/54/4/690/F1.large.jpg)

**Figure 1.** In this photograph of the left superior vena cava (LSVC) of case 1, a woven cord passes from its cut end above the left atrium through the ostium of the coronary sinus via which the LSVC drained into the right atrium. LV = left ventricle.

![Figure 2](http://circ.ahajournals.org/content/circulation/54/4/690/F2.large.jpg)

**Figure 2.** The sinus node of case 1 was poorly organized and less than one-third the expected overall size for this age. These photomicrographs illustrate the midportion of what sinus node tissue was present. The two arrows in A indicate the region of sinus node, but its margins are less distinct than normal. Cells from the midportion of this section are seen at higher magnification in B. Unless otherwise indicated, all sections were stained with the Goldner trichrome method, and magnifications are indicated with reference bars.
The A-V node of case I contained large venous lacunae, one being marked with an asterisk in A. There are artifactual cracks in the central fibrous body (CFB) and some of these interrupt other venous profiles. A nodule of A-V nodal tissue lies near the bottom of the marked vein. The narrowed A-V node artery of case I is shown in B.

Case 2

A sixteen-year-old boy had long complained of his heart pounding. When a large ventricular septal defect was diagnosed, surgical correction was advised and then performed. He also had a persistent left superior vena cava, and only a fibrous remnant of the right superior vena cava. His postoperative course was stormy, characterized in part by long periods of supraventricular tachycardia (170/min) and bouts of atrial fibrillation. On the sixteenth postoperative day he suddenly became cyanotic and apneic. During resuscitative efforts an electrocardiogram showed varying patterns of A-V dissociation, atrial flutter and nodal tachycardia. Resuscitation was not successful and he died in that episode.

Details of this case, including the surgical procedure and certain findings at postmortem examination have been...
published. Additional unpublished observations are to be provided here for comparison with case 1. The large left superior vena cava continued as the coronary sinus to drain into the right atrium, but it did not receive left ventricular venous drainage. On the contrary, many thebesian ostia (1 to 2 mm diameter) were present in the normally smooth left atrial endocardium, giving it an appearance as if riddled with buckshot. Although similar thebesian ostia may have been present in the left ventricular endocardium, special studies required to detect them within the normally numerous endocardial trabeculae were not conducted. Selected sections at 1 mm intervals along the junction of left superior vena caval wall and left atrium failed to reveal any sinus node tissue.

In the area where a right superior vena cava should have been located there was an atretic cord. However, a rudimentary crista terminalis could be identified lying between the sinus intercavum and the normally trabeculated lateral half of the right atrium. This area of crista terminalis was excised in toto and serially sectioned at 8 microns to search for a sinus node; 5720 sections were cut, with every 20th section stained and examined. A fully formed and histologically normal sinus node was present surrounding a centrally placed artery (fig. 9). Within the central portion of the sinus node, however, there was a polypoid fibromuscular projec-

![Figure 5](image1.png)

**Figure 5.** Some of the isolated fragments of A-V nodal tissue of case 1 are boxed within the central fibrous body in A, and are seen to lie near the base of the mitral valve (MV). Arrow indicates the A-V node as it is becoming His bundle; RA marks the cavity of the right atrium. The boxed area is shown at higher magnification in B, where the resorptive degeneration of these fragments is apparent.

![Figure 6](image2.png)

**Figure 6.** Other examples of resorptive degeneration of fragments of A-V nodal tissue within the central fibrous body of case 1 are shown here at two magnifications. Some of the fragments in B were adjacent to the main body of the A-V node.

tion from the endothelial surface of the sinus node artery into its lumen, virtually occluding this vessel (figs. 9B and 10). There was no thrombosis around the protrusion.

To study the A-V node and His bundle eight blocks, each about 2 mm thick, were cut perpendicular to the junction of interatrial and interventricular septa; screening sections (minimum of ten) from each block were then used to determine the need for additional sections, a total of 325 eventually being stained and examined from the A-V junction. As in the first case, the A-V node appeared in some fragments just beneath the ostium of the very large coronary sinus, and then extended anteriorly in a stretched-out fashion until it formed the His bundle. Also as in the first case, there were excessively numerous venous lacunae within the A-V node (figs. 11 and 12), and isolated islands of A-V nodal tissue were dispersed in a fetal pattern throughout the central fibrous body, with some of these islands undergoing resorptive degeneration while other better preserved isolated fragments of A-V node were connected to the ventricular cells at the crest of the interventricular septum (fig. 13). Both the A-V node and the His bundle (figs. 14 and 15) exhibited multiple compartimentations by abnormally bulky collagen septa. Within the midportion of the A-V node, the histological organization of slender transitional cells was disarrayed (figs. 11 and 12), as if the normal architec-
Figure 7. Small groups of A-V nodal transitional cells (open arrow in A, upper half of C) were present at the crest of the interventricular septum and continuous with it. They were separated from the A-V node (black arrow in A, shown in more detail in B) by the central fibrous body. One can compare the size of A-V nodal transitional cells and of working ventricular myocardial cells in C, where most of those in the upper half are A-V node and those in the lower half are septal myocardium. C is a higher magnification of the area indicated with the open arrow in A. Magnification in B and C is the same.

Discussion

Electrical instability of the heart is sometimes observed in patients who have a persistent left superior vena cava, and the two cases reported here illustrate some of the consequences to be anticipated because of unstable cardiac rhythm or conduction. Furthermore, in both cases there were a number of histopathological abnormalities in the centers of cardiac impulse formation and conduction which may have contributed to functional disturbances of the heart beat. These findings suggest certain questions which may be considered for prospective studies in future cases of persistent left superior vena cava, even in the presence of apparently normal cardiac rhythm.

While the younger boy (case 1) died suddenly and unexpectedly, we have no information about his electrocardiogram or even any clinical observations about his cardiac rhythm, except that no pulse could be detected a very short time after he collapsed. Whether this terminal episode represented ventricular fibrillation or cardiac standstill or complete A-V block with no ventricular escape, the information that two of his relatives had also died suddenly and unexpectedly suggests that the disturbance, whatever its nature, may have been heritable. Histological features of his cardiac conduction system which may be especially important are the poorly formed and very small sinus node, fetal dispersion of the A-V node and His bundle within the central fibrous body, the small diameter of the His bundle and the narrowing of the A-V node artery. Both of the latter features have previously been observed in association with sudden unexpected death. Fetal dispersion of A-V junctional tissues is often associated with formation of loops and other insulated “short circuiting” connections in these crucially important structures and could lead either to the development of re-entrant tachycardias or ectopic automatic rhythms; the latter may particularly occur in the isolated fragments of A-V nodal tissue which were in direct continuity with the crest of the interventricular septum (figs. 7 and 13), a situation theoretically highly conducive to the
formation of a parasystolic focus. The thin His bundle could fail to conduct under a variety of circumstances, and if no automatic rhythm emerged distal to that location (as experimental evidence in the dog infers may be the case,\textsuperscript{18, 19} then the heart might cease beating. Finally, the narrowed A-V node artery may have contributed to maldevelopment of the His bundle, or could have led to intermittent ischemia, as would be expected based on both anatomic studies of vascular supply in man\textsuperscript{15, 20} and postmortem correlative studies in sudden death.\textsuperscript{17}

Many of these same considerations could apply in the second case. Although the sinus node was normally formed in case 2, its nutrient artery contained a polypoid mass within its lumen. This unique lesion may have intermittently impaired flow within this important vessel. An important negative finding in both cases was the absence of any sinus node tissue in the vicinity of the left superior vena cava, even when the right superior vena cava was not completely normal. This may be explained by the later development of atresia of the right superior vena cava after the normal full development of a sinus node, or it may mean that whatever factors determined the final normal location of the human sinus node would still be operative, even when the right superior vena cava is rudimentary. It may also mean that the right atrio caval junction being the site of the normal sinus node is coincidence and not a functionally or ontogenetically dependent relationship.

In both cases the numerous thebesian venous profiles scattered throughout the body of the A-V node were conspicuous. There may be two reasons for this: 1) the need for extra venous drainage routes when the normal cardiac venous drainage was not properly formed (particularly the circumstance in case 2), and 2) perhaps the persistence of accessory venous channels was simply another part of the failure of the left superior vena cava to regress as would normally occur. In both cases the left superior vena cava drained entirely through the coronary sinus, as is usually the case, and the consequently very large ostium of the coronary sinus effectively displaced the A-V node anteriorly. It is possible that the abnormal persistent fetal dispersion of A-V node and His bundle within the central fibrous body\textsuperscript{6, 14} represents simply another manifestation of a primitive state of fibroblast behavior within this region, so that failure of normal maturation of the A-V junctional tissues was but one more expression of the same anatomical immaturity represented by persistence of the left superior vena cava. If such immaturity is also associated with maldevelopment of adrenergic neural input into the A-V node and His bundle, a
FIGURE 11. The A-V node of case 2 also contained an excessive number of venous profiles, five of which are marked with asterisks in A. A portion of A is shown at higher magnification in B to demonstrate the erratic cytological organization of the A-V nodal transitional cells.

FIGURE 12. Histological disarray of the A-V node (AVN) of case 2 is further illustrated here, and the unusual number of veins is again apparent in A. This section is about 2 mm from the one in figure 11.
matter which we were not able to determine anatomically in the two present cases, this too may have impaired the facility with which A-V junctional escape rhythms could emerge if the sinus node defaulted its normal pacemaker function, since in experimental animals it has been demonstrated that A-V junctional escape rhythm is crucially dependent on normal adrenergic neural input.21

All these correlative comments are speculative, but they

**Figure 13.** An island of A-V nodal cells separated from the A-V node but attached to the crest of the interventricular septum is indicated with a black arrow in A and B. The two sections in A and B are 40 microns apart, and they are about 150 microns anterior to the one in figure 12.

**Figure 14.** As the A-V node of case 2 veered centrally to form the His bundle, it was widely compartmented by collagen and exhibited a fetal pattern of dispersion within the central fibrous body. The orientation of these histological sections on the slide is the reverse of ones shown for case 1 in figures 3–5. A and B are two different magnifications of the same section, which was about 2 mm anterior to the ones in figure 13. TV = tricuspid valve.
fit reasonably well with the clinical circumstances such as are known. They may be of some value in helping to understand electrical instability of the heart which has been reported by others in describing the clinical course of patients with left superior venae cavae. The histological abnormalities in both cases suggest that function of the sinus node, A-V node and His bundle should be evaluated in any patient having a left superior vena cava, but particularly if there are clinical or electrocardiographic findings indicative of any form of electrical instability of the heart.

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