CLINICOPATHOLOGIC CORRELATIONS

De Subitaneis Mortibus

XI. Young Girl With Palpitations

By THOMAS N. JAMES, M.D., RALPH J. MARILLEY, JR., M.D., AND HENRY J. L. MARRIOTT, M.D.

SUMMARY
A seventeen-year-old girl in apparent good health was found dead in bed one morning. Two clinical features of note were multiple premature beats present in her electrocardiograms for several years, and a tall thin habitus without stigmata of Marfan's syndrome. At necropsy examination the heart was grossly normal. At its margin abutting the central fibrous body the ativoventricular (A-V) node exhibited numerous fronds and outcroppings, some forming loop connections from one part of A-V node to another. Groups of A-V nodal cells detached from the A-V node were also found connected to the crest of the interventricular septum. There were large connections directly from the His bundle to the crest of the interventricular septum (Mahaim fibers). The A-V node artery was moderately narrowed but patent. The possible significance of these findings in the pathogenesis of re-entrant arrhythmias or ectopic automaticity is discussed.

Additional Indexing Words:
Loop connections, A-V node  Resorptive degeneration of A-V node  Mahaim fibers

NEWSPAPERS often carry stories of sudden unexpected death of young people. There is a special poignant sadness about life plucked in full bloom. The human interest of such stories is usually heightened by a sense of mystery due to the lack of a suitable explanation. When the death remains unexplained even after a careful forensic pathological examination, then a lethal failure of cardiac rhythm becomes a prime consideration. Disorders of the rhythm of the heart need not be related to anatomical changes, but in fact there are structural abnormalities in the cardiac conduction system of patients dying suddenly and unexpectedly. The examinations necessary to discover these changes are unfortunately not a part of the routine necropsy, although it has recently been pleaded that such study should become a mandatory procedure in the case of any death which is sudden and unexpected.1

In the present case death was sudden and unex-
pected, although this girl had been examined on several previous occasions because of palpitations. Some of the postmortem anatomical findings in her cardiac conduction system will be discussed relative to the clinical events.

Case Report
A seventeen-year-old girl who had gone to sleep in apparent good health was found dead in bed by her father the next morning. She had been active in sports in school and had no recent complaints. As a younger girl she had several bouts of arthralgia but no specific cause was found; both rheumatic fever and rheumatoid arthritis were considered and appropriately excluded. Several examiners had commented on her tall thin habitus and long thin fingers and toes. Two had specifically raised the question of a frustrated form of Marfan's syndrome, although none of the other stigmata was present.

At the age of fifteen, during an examination for one of the bouts of arthralgia, she was found to have multiple premature beats. These diminished in number only slightly during exercise. Quinidine, procaine amide and diphenylhydantoin sodium were prescribed at various times and had no significant effect on the cardiac irregularity. Her physical activity and general health were excellent until the time of death. There was no history of syncope or any form of loss of consciousness. One year prior to death she fell during gymnastic exercises and fractured her nose, but this was considered a simple accident rather than syncope.

One sister and one brother have a seizure disorder of undetermined nature. The electrocardiogram of that brother, one of a second brother without seizures, and of both
parents were unremarkable. The sister with seizures and two other siblings lived some distance away and their cardiac status is unknown. There was no family history of deafness.

Except for being tall (68 inches) and thin (weight varying from 110 to 125 pounds), and having frequent premature beats, the subject of this study was entirely normal on careful physical examination. There was in particular no hypertension, cardiac murmur or abnormal cardiac sounds.

Her premature beats varied in their frequency, their QRS configuration, and in their relationship to the basic sinus rhythm (figs. 1 and 2). When the premature beats continued in series or runs, their cycle length varied but most were associated with retrograde conduction to the atria. After a run of premature beats, there was a pause terminated by sinus escape; no examples of atioventricular (A-V) junctional escape beats were recorded. No close coupling intervals or R on T phenomenon were recorded. In figure 1 there are runs of right ventricular premature beats with occasional fusion beats. In figure 2 there are frequent isolated right ventricular extrasystoles and also numerous examples of aberrant ventricular conduction when the resuming sinus cycle is preceded by the longer post-ectopic cycle. The aberrant beats suggested abnormal conduction to both right and left ventricles (fig. 2). The Q-T interval of sinus beats was normal.

At necropsy examination there were no abnormalities outside the heart. The heart was small and of normal appearance and configuration, weighing 270 grams. The cardiac valves, septa of the heart, and all the major coronary arteries were normal. The aorta was normal. Both the sinus node artery and the A-V node artery originated from the right coronary artery and were grossly normal. The region of the sinus node was removed as one block and cut into 2 mm slices perpendicular to the crista terminalis; a series of 12 such slices was embedded in paraffin for sectioning. The region of the A-V node and His bundle was cut perpendicular to the junction of atrial and ventricular septa, and 9 slices were embedded in series. Samples of the left and right ventricular myocardium were additionally examined. All sections were cut eight microns thick and routinely prepared with the Goldner trichrome stain.

The sinus node was normal in size and location but contained rather more collagen than is usual in the human heart (fig. 3). The sinus node artery and the nerves of the region were normal.

The A-V node was normal in location and size. Its nutrient artery was narrowed about 40% proximal to entry into the node but the lumen was patent; beyond the A-V node, where this same artery curved down into the ventricular septum, it was markedly narrowed (fig. 4). Along the surface of the A-V node which normally lies on the central fibrous body, there were many fronds and outcroppings of A-V nodal cells protruding into the adjacent collagen (figs. 5–7). Some of these formed distinct loops connecting one portion of the A-V node with a more distal portion (figs. 5 and 8). There were also isolated pockets of A-V nodal cells deeply placed within the central fibrous body, but which had no connection with either the A-V node, the interatrial septum or the interventricular septum.

The His bundle had slightly more dense collagen partitions than is normal, and there were occasional small foci of abnormal fat within the His bundle. At one point the His bundle was directly connected to the crest of the interventricular septum by Mahaim fibers (fig. 9). In addition, there were numerous clusters of both A-V nodal and His bundle type cells directly connected to the crest of the interven-

Figure 1

The electrocardiogram here was recorded about two years prior to sudden death. The multiple premature beats tend to be uniform in configuration in each lead. Retrograde conduction to the atria is present. The coupling interval is long, in some places (e.g., last beats in aV, V, and V,) resulting in fusion complexes.

Figure 2

This electrocardiogram is from an examination six months before death and now contains two types of anomalous beats: right ventricular extrasystoles of similar configuration to those in figure 1 (examples indicated by black dots); and aberrantly conducted sinus beats (some indicated by open circles).
tricular septum but not connected to either the A-V node or His bundle (fig. 10). The origins and proximal course of the right and left bundle branches were normal.

Discussion

Palpitations and swooning maidens are recurring subjects in classic literature and drama, the ending in some being sudden death. However, neither in the world of imagination nor in the one in which we live has there been much success in genuinely explaining such dramatic tragedies. The present case offers a number of substantive objective observations which lend themselves to logical analysis, and thereby to some plausible hypotheses as to how disturbances in her cardiac rhythm occurred. Despite this opportunity, it will be seen that accounting for the differences between innocuous palpitations and lethal electrical instability of the heart ultimately remains conjectural.

There was little wrong with this girl’s sinus node. The small amount of excessive collagen might be compatible with a slight decrease in the volume of cells in the sinus node, but what the functional significance of this might be is uncertain. The sinus node artery and the connections between the node and adjacent right atrium were in particular normal. It may be assumed, at least from an anatomical standpoint, that the fault here was not one of failure of sinus rhythm.

What the focal narrowing of the A-V node artery proximal to the A-V node may mean is also uncertain. This type of lesion has been described in association with Marfan’s syndrome and sudden death, but in those two reports the degree of narrowing was greater than in the present case. Serial sections were made of the area of the A-V node artery in this heart, making it unlikely that any greater degree of focal narrowing was missed. The more marked narrowing of the A-V node artery after it had passed through the A-V node may have accounted for some focal ischemia in the crest of interventricular septum, but the area perfused did not include the conduction system. Whether focal ischemia of working myocardial cells could cause ectopic activity is to be considered but seems unlikely. Furthermore, there was no histological evidence of

**Figure 3**

There is slightly more collagen than usual for a human sinus node at this age, but the node is otherwise normal. The atrionodal margin is indicated with arrows in A, and B is enlarged from A. All histological sections were prepared with the Goldner trichrome stain, and magnifications are indicated with bars.

**Figure 4**

Cross sections of the A-V node artery are seen near its entry into the posterior margin of the A-V node (A), and after its curve down into the interventricular septum beyond the A-V node (B). The cells surrounding the artery in A are entirely A-V node; those surrounding the artery in B are all working myocardial cells of the septum.
Figure 5

Two different sections of A-V node (AVN) about 100 microns apart are shown at two magnifications. Loop connections of the A-V node are indicated with open arrows. An isolated island of A-V nodal cells (black arrow) is seen in B. CFB is the central fibrous body, IVS is the interventricular septum, RA is the chamber of the right atrium and LV is the chamber of the left ventricle.

Figure 6

Some branching fronds of A-V nodal cells are undergoing resorptive degeneration, as shown here and in figure 7. The A-V nodal cells coursing into the central fibrous body as indicated with long arrows in B ended in a blind pocket (on serial sections) but did form a continuum with the A-V node itself.

Figure 7

Two portions of figure 6B are seen here at higher magnification. Resorptive degeneration is indicated with an arrow in A, and is apparent adjacent to the fatty replacement seen in B.
Figure 8
Typical looping branches of the A-V node from two points about 400 microns apart are seen here. Virtually the complete loop (arrows) is seen in the sectioning plane in A, while completion of the loop was only apparent on examination of adjacent serial sections for B. An isolated fragment of A-V nodal cells is indicated with an open arrow in B.

Figure 9
Mahaim fiber connections from the His bundle (AVB) to the interventricular septum are seen at two magnifications of the same section. Most of the left bundle branch had already been provided at this point so that these His bundle cells except for their Mahaim connections became right bundle branch. Cells of the His bundle characteristically stain lighter than working myocardium of the septum.

Figure 10
Groups of A-V nodal cells were present detached from the A-V node and not attached to the interventricular septum (open arrow in A). At other points there were large groups of A-V nodal cells connected exclusively with the septum; the general line of junction between light staining A-V nodal cells and dark staining working myocardial cells is indicated with two arrows in B from one of several such examples.
septal ischemia, so that collateral circulation in that region may have sufficed for normal function.

There are three anatomical substrates which in this case may have accounted for multiple premature beats. One is the abundant examples of loop connections between one part of the A-V node and another, resembling in real biology exactly the type of schematic diagram often drawn to illustrate potential routes for A-V junctional re-entry (figs. 5 and 8). The second is the presence of numerous blind pockets of A-V nodal cells protruding into (or from) the central fibrous body and directly connected to a margin of the A-V node. Some of these pockets may have contained cells which periodically became active automatic centers. The third anatomical feature was the presence of direct connections to the crest of the interventricular septum from groups of specialized cells. Some of these were in the vicinity of the A-V node but not at the time of this examination connected to the node (they may have been in the past). Others were a direct connection from the His bundle itself, thus being characteristic Mahaim fibers (fig. 9).

Those cells in the heart specialized for its electrical function are all thought to be capable of automatic activity, although it has recently been questioned whether such automaticity can be considered stable for prolonged performance except in the sinus node and A-V junction.1,2 In the present case it may be deduced that at least transient ectopic automaticity may have been present. The anatomic basis for A-V junctional re-entry was even more impressive, however, particularly in and around the A-V node.

In the present case the anatomical changes in the A-V junction may be considered abnormal because of their quantitative rather than qualitative features. Many hearts of individuals dying of non-cardiac disease, not known to have had any form of cardiac electrical instability (although such negative information is usually grossly inadequate), have some histological irregularities at the margins of the A-V node. On the other hand, they seldom have the number of bypassing loop connections seen in the present case. Similarly, very small clusters or strands of specialized cells connected to the crest of the interventricular septum but not connected to the conduction system are not uncommon. But here again, the number and size of such examples in the present case was considerably greater than usual. Both the abnormal number of loops of A-V nodal cells in the central fibrous body and the clusters of specialized cells at the top of the septum are the type of fragmentation normally tidied up in the postnatal period, or during childhood and early adolescence, by the active anatomical molding and shaping normally ongoing in this crucial region.3,4 Some of this active resorption of A-V nodal cells is apparent in portions of this heart (figs. 6 and 7).

It may be concluded that several possible anatomical substrates were present in this heart which may have accounted for a variety of disturbances in cardiac rhythm. Why they should have been in the nature of multiple premature beats most of the time, but then become deranged to lethal instability at another time remains an unexplained puzzle. As has recently been emphasized by Pruitt,6 death from functional causes merits our interests. But in recognizing that reflexes gone awry or loss of the will to live may indeed contribute to death, we must also be aware that "absence of organic disease" may be more apparent than real. We see only what we seek.

References
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T N James, R J Marilley, Jr and H J Marriott

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