Anatomic Findings in a Case of Ventricular Pre-Excitation (WPW) Terminating in Complete Atrioventricular Block

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Ventricular pre-excitation (WPW syndrome) which becomes associated with atrioventricular block (A-V) sometime in its course is rare. The literature of this combination up to 1959 was reviewed by Moret and associates. Cases have been reported by Feldmann and Koch, Segers and associates, Coelho, Levine and Burge, Rodstein, Fox and associates, Scherf and associates, Pick and Katz, Zuckermann, Grant and associates, Le Damany and Gouffalt, Pick and Fisch, and Wolff. Recently we were able to follow such a case, with fatal outcome, clinically and in serial electrocardiograms, and had the opportunity of studying both A-V junctions and the conduction system by serial sections of the heart. To our knowledge this is the only case of WPW syndrome terminating in heart block so studied. Previously Levine and Burge had studied part of the right A-V groove by serial section, but not the conduction system in such a case. Correlation of electrocardiographic and anatomic findings led us to certain conclusions bearing on the anatomic background of the pre-excitation syndrome and some of its variations.

Report of Case

This 34-year-old white male was first admitted to Marion General Hospital on August 7, 1955, at age 32, because of generalized convulsions first experienced at age 16. In the interval he had shortness of breath, palpitations, and decreased tolerance for exercise. An electrocardiogram in 1952 (fig. 1) showed sinus arrhythmia at an average rate of 68 with premature supraventricular beats. All ventricular complexes had a pre-excitation contour (type B) with QRS prolonged to 0.16 second by a delta wave, corresponding secondary ST-T alterations, and a short P-R interval (0.08 second) in the sinus beats. An unusual feature was the prominent late R wave and inverted T wave in V1, suggesting an additional independent right ventricular conduction disorder.

On admission, his heart rate varied from 25 beats per minute before seizures to 72 beats per minute after seizures, and his blood pressure was 110/72 mm Hg. On August 8, one day after admission (fig. 1), an electrocardiogram showed, at a sinus rate of 75, a 2:1 A-V block with a P-R interval of 0.14 second in the conducted beats. Ventricular pre-excitation had disappeared and the ventricular complexes had a pattern of right bundle-branch block (QRS, 0.12 second) with left axis deviation to about −30°. He was discharged from the hospital on the following day. On August 15, in the doctor’s office, physical examination revealed no abnormal cardiac findings and x-ray showed a heart normal in size and configuration. In electrocardiograms on August 15 and 19 (fig. 1), the sinus rate had slowed to 53 and the ventricular complexes resembled the pre-excitation beats of 1952. However, the delta wave was now larger, the QRS more prolonged (0.18 second), and the secondary ST-T alterations more prominent, indicating

An atrial tachycardia at twice this rate, with irregular ventricular response, was ruled out by lead V1 and in a longer portion of lead I (not shown).

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that ventricular activation was affected to a greater extent by the pre-excitation forces.

He continued to have mild seizures in January and August 1956 and his other complaints were as previously stated. Electroencephalograms were borderline normal.

On January 5, 1957, the patient suddenly lost consciousness while at work. On arrival at the hospital his heart rate was 16 to 18 beats per minute. He had periods of apnea about every 20 minutes with generalized clonic and tonic convulsions lasting a few minutes. He regained consciousness only temporarily during the first 4 hours; after that he was conscious except for periods of Adams-Stokes attacks. On January 6, six hours after admission, the electrocardiogram (fig. 2) showed sinus tachycardia of 120 with complete A-V dissociation due to an advanced A-V block, the ventricles following a regular slow (22 per minute) supraventricular pacemaker without pre-excitation. The pacemaker origin was established by the similarity of the ventricular complexes with the normally conducted sinus beats on August 8, 1955 (fig. 1), but an ischemic type of T inversion was now present in leads II and III.
Figure 2

The terminal electrocardiograms (described in text).

The patient's heart rate was never above 32 beats per minute, and most of the time it was between 22 and 24 beats per minute. He received isoproterenol (Isuprel) sublingually every 2 hours, and an external pacemaker was used to combat recurrent periods of asystole. The electrocardiogram on January 8 (fig. 2) showed persistence of complete A-V dissociation, without alteration of atrial and ventricular rates, of the QRS duration, or of the ischemic T-wave configuration. However, the shape of the QRS complexes had changed to the configuration of a left bundle-branch block. By the fourth day, the Adams-Stokes attacks occurred more frequently, and the response to artificial stimuli by the pacemaker was unsatisfactory. The patient expired January 9, 1957, after 10 minutes of asystole.

Pathologic Examination

Only the heart was available for study. The heart was enlarged and weighed 504 g. The apex was formed by the left ventricle. The right atrium, the right ventricle, and the left atrium were normal in size but their walls were thickened. The left ventricle was considerably thickened but its size was normal. There was some thickening of the endocardium in the left ventricle at the base of the ventricular septum. The pulmonary orifice was enlarged. The anatomic diagnoses were hypertrophy of the heart (both atria and ventricles) and dilatation of the pulmonary trunk.

Microscopic Examination

Methods. The A-V rings were serially sectioned, the right at 10 μ and the left at 7 μ. All sections were retained on the right side, while every tenth section was retained on the left. Every fifth section was stained with Weigert-van Gieson stain and the remainder with hematoxylin and eosin. The S-A node.
was serially sectioned and every tenth section was retained. The approaches to the A-V node, the A-V node itself, the A-V bundle, and the bundle branches up to the region of the muscle of Lancisi were serially sectioned and all sections were retained. The remainder of the right and left bundles up to the moderator band were serially sectioned and every tenth section was retained. All sections from the conduction system were alternately stained with hematoxylin-eosin and Weigert-van Gieson stains. The remainder of the heart, that is, the atrial septum, the remainder of the ventricular septum, and the parietal walls of the atria and ventricles were divided into blocks and two sections were cut from each block. These were alternately stained with hematoxylin-eosin and Weigert-van Gieson stains. In this manner a total of 14,662 sections were examined.

Right A-V Ring. No bundle of Kent was found. The myocardium of the atrium showed vacuolar degeneration of the muscle cells with fibrosis while that of the ventricle adjacent to the A-V ring showed less extensive similar changes (fig. 3). This was present mostly adjacent to the epicardium and endocardium. Fibroelastosis and small fibroelastic scars were present throughout the atrium and ventricle in these regions. Focal infiltration of small numbers of mononuclear cells and neutrophils was present in the epicardial fat of the A-V ring and to a lesser extent in the atrium and ventricle.

Left A-V Ring. No bundle of Kent was found. The inflammatory and degenerative changes noted in the right A-V ring were seen here only to a mild degree.

Conduction System: S-A Node. There were no remarkable changes. Elastosis and focal infiltration of neutrophils were apparent in the approaches to S-A node.

Approaches to A-V Node. These approaches showed vacuolar degeneration of muscle cells with fibrosis and fatty infiltration (fig. 4). There was slight infiltration by mononuclear cells. The superior and inferior approaches were especially involved while the connections with the left atrium showed healthy myocardium in spots.

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**Figure 3**

Section through the right A-V annulus showing elastofibrosis of the atrial and ventricular myocardium in this region, with vacuolar degeneration of the myocardium. Weigert-van Gieson stain, × 21. A = atrial myocardium; V = ventricular myocardium; TV = tricuspid valve.
The atrial septal musculature at the approaches to the A-V node sent a large fasciculus into the central fibrous body. This fasciculus consisting of atrial muscle cells was equal to about one tenth of the cross section of the node. This tract made a fine connection with the beginning of the bundle of His just as the latter gave off the Mahaim tracts to the ventricular septum (figs. 4 to 6).

Fibrous Skeleton of the Heart. This skeleton was abnormally formed. The tricuspid annulus was connected only to the pars membranacea, but not to the central fibrous body (fig. 7).

A-V Node. The A-V node was a spherical structure lying at the base of the distal part of the atrial septum, adjacent to the mitral annulus but unrelated to the tricuspid annulus (figs. 5 and 7). On its right side it was covered by right ventricular septal musculature. At the beginning of its course it showed no changes. More distally, there was considerable fibrosis of its periphery. At its most distal portion, it lay within the central fibrous body but still had atrial communications. At this point it gave off a large group of Mahaim fibers to the septum.

A-V Bundle (Penetrating Portion). This bundle showed marked vacuolar degeneration of its muscle cells (fig. 8). Numerous large fasciculi of Mahaim fibers left the A-V bundle to enter the left side of the ventricular septum (fig. 8). These paraspecific fibers showed vacuolar degeneration.

A-V Bundle (Branching Portion). Many cells showed marked vacuolar degeneration, and there was fibrosis of the superior portion of the bundle. At the bifurcation there was
marked fibrosis of the A-V bundle with vacuolar degeneration of the cells (fig. 9).

*Left Bundle Branch (LBB).* The entire beginning of the left bundle branch extending into the anterior and posterior radiations showed marked vacuolization of the muscle cells lying in a sea of fibrosis (fig. 10). The Purkinje cells of the LBB peripherally, the Purkinje nets, and most of the terminal Purkinje cells showed marked vacuolization with pyknosis of nuclei in some cases (fig. 10 right).

*Right Bundle Branch (RBB).* The first part of the RBB showed marked fibrosis with replacement in its superior half and vacuolar degeneration of the cells of the lower half (fig. 11 upper). The second portion showed marked vacuolar degeneration. The third portion was completely replaced by fibroelastic and fat tissue (fig. 11 lower).

*atrial Septum Between Approaches to S-A and A-V Nodes.* Marked vacuolization of the muscle cells with marked fatty infiltration was present in this area. This was more apparent on the right side than on the left side. Hypertrophy of many muscle cells was present.

*Ventricular Septum.* Minimal fibrosis was present at the base. But more apicalward there was a fine diffuse fibroelastosis of the myocardium with a fine infiltration of mononuclear cells and neutrophils. Some of the arterioles showed acute degeneration with narrowing.

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**Figure 5**

Section through the approaches to the A-V node, the A-V node, and the central fibrous body showing the bypass tract in the central fibrous body. Weigert-van Gieson stain, × 18. A = atrial musculature; V = ventricular musculature; N = A-V node. Arrow points to the bypass tract.

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Section through the junctional area between the A-V node and bundle showing termination of the bypass tract in the A-V bundle. Weigert-van Gieson stain, × 23. N = A-V node; B = A-V bundle; V = ventricular musculature; C = central fibrous body. Arrow points to the bypass tract.

Right Atrium. There was a focal fibroelastosis of the myocardium, hypertrophy of cells, and a focal infiltration of mononuclear cells. This process was especially prominent beneath the epicardium.

Right Ventricle. Marked elastofibrosis was present throughout with small scars. This was accompanied by a fine infiltration of mononuclear and neutrophilic cells. As elsewhere, the process was seen to enter from the epicardium and endocardium.

Left Atrium. There was a marked vacuolization of muscle cells with marked fatty infiltration.

Left Ventricle. Diffuse fibroelastosis of the myocardium was present with small scars, but the process was not as intense as in the right ventricle.

Pathological Diagnoses
These are as follows:
1. Abnormal formation of the fibrous skeleton of the heart.
2. Severe degeneration and fibrosis of the conduction system.
3. Abnormal tract from atrial septum to A-V bundle.
4. Copious diffuse Mahaim communications from end of A-V node and from A-V bundle.
5. Vacuolar degeneration with fibrosis of the approaches to the A-V node, the A-V bundle, Mahaim fibers, the bifurcation, and the right and left bundle branches.

Discussion

Electrocardiograms
The records were interpreted in the light of
VENTRICULAR PRE-EXCITATION

Figure 7

Section through the central fibrous body showing its lack of junction with the tricuspid annulus. As stated in the text, the tricuspid valve did make attachment to the pars membranacea in later sections. C = central fibrous body; MV = mitral valve; TV = tricuspid valve; A = atrial musculature; V = ventricular musculature; N = A-V node.

recent detailed anatomic studies of the entire conduction system in cases of bundle-branch block\textsuperscript{16-18} as well as of cases of ventricular pre-excitation\textsuperscript{19-22} which lend support to the concept of an accessory anomalous muscular A-V connection as the explanation of the pre-excitation syndrome. Accordingly, a prediction of the anatomic findings, as noted above, was attempted, based on the following reasoning.

The orientation of pre-excitation forces in the precordial leads corresponding to type B\textsuperscript{23} suggested an A-V bypass inserting somewhere in the right ventricle. The similarity of premature and conducted sinus beats in the first record of 1952 was taken as evidence of an ectopic focus located proximally to the origin of the bypass. This focus could have been in the atria, or conceivably in the normal A-V junction, if the anomalous path were a branch of the junction.

Assumption of such a close proximity of normal and accessory A-V pathways appeared especially attractive in the explanation of the changes in degree of the intermittence and eventual disappearance of the pre-excitation with advancing A-V block. In this way it was feasible to attribute the 1955 and 1957 records (a) to a single lesion involving both available pathways to a varying and progressive extent, and (b) to reconstruct a probable sequence of events. During an initially incomplete A-V block, the normal A-V path could conceivably have functioned as long as the sinus rate was fast (8/8/55) while the alternate path became predominant after slowing of the sinus rate (8/19/55, figs. 1, 12, and 13). This would be possible if at one stage of the block the faster conducting path had the longer refractory period. However, if used by the sinus impulse, well ahead of the slow conducting normal path, it would produce more complete pre-excitation as reflected in the electrocardiogram by a larger delta wave and a more marked QRS prolongation and secondary ST-T alterations (8/19/55, fig. 1). Subsequently, as the pathological process in the A-V junction progressed, both pathways became permanently afunctional so that in 1957 the ventricles followed their own pacemaker (figs. 2, 12, and 14).

In addition to this blocking lesion in the A-V junction, anatomic alterations were postulated causing a bilateral interventricular conduction defect. The diagnosis of some conduction delay in the right bundle branch was based on the presence of a prominent late R wave in lead V\textsubscript{1} in all records except the last. The persistence of marked left axis deviation, on the other hand, suggested a partial left sided ventricular conduction block most likely in the anterior ramifications of the left bundle branch.\textsuperscript{24} At the time of the final record on January 8, 1957, these lesions appeared to have extended to the posterior ramifications (fig. 14) since the QRS configuration had changed to that of a left bundle-branch block.
Figure 8


With the implication of multiple bilateral bundle-branch lesions, the question arises whether progression over the years of such alterations may not have caused the complete A-V dissociation in 1957, without advancement of the A-V junctional lesion. In this instance, this possibility can be readily excluded since on January 6, 1957 (fig. 2) the automatic beats controlling the ventricles resembled closely the conducted sinus beats 2 years previously (August 8, 1955, fig. 1). This is an indication that: (1) the site of the ventricular pacemaker during A-V dissociation must have been above the bifurcation of the common bundle, and consequently, (2) the complete disruption of A-V conduction must have occurred proximal to this pacemaker, that is, somewhere within the boundaries of normal and accessory A-V junctional fibers.

The huge symmetrical T waves in the terminal electrocardiograms (fig. 2) suggested a recent ischemic alteration of the posterior (diaphragmatic) wall. However, signs of tissue destruction in the form of Q waves were absent. Since isolated T-wave alterations of this type may, in our experience, occur as a transient functional event after Stokes-Adams attacks, recent myocardial infarction was not included among the anticipated anatomic findings.

Pathological Findings

The basic anatomic plan of conduction in this patient was as follows (fig. 12): The S-A node was in normal position. The A-V node,
Figure 9
Section through bifurcation showing fibrosis and vacuolar degeneration. Weigert-van Gieson stain, × 25. LBB = left bundle branch; RBB = Right bundle branch.

Figure 10
Section through left bundle branch. Hematoxylin-eosin stain. (Left) Higher portion showing elastofibrosis with vacuolar degeneration, × 49. (Right) Peripheral Purkinje cells showing vacuolar degeneration, × 210. Arrows point to the left bundle branch.
however, was placed more centrally in the distal atrial septum, lying on, rather than to the right of, the central fibrous body (fig. 7). The latter was abnormally formed as will be discussed below. The A-V bundle, bundle branches, and peripheral Purkinje nets and cells were in normal position.

In addition to the above pathway, a tract proceeded from the atrial septal musculature, penetrated the central fibrous body, and
Figure 12

Diagrammatic sketches of the anatomic plan of conduction, and the recent and old pathological changes.

Figure 13

Correlation of anatomic and electrocardiographic findings in this figure and in figure 14. The assumed conduction pathways, effective on the days when the five electrocardiograms illustrated in figures 1 and 2 were taken, are superimposed on the diagrams of anatomic findings illustrated in figure 12.

terminated in the beginning of the penetrating portion of the A-V bundle (figs. 4 to 6). This tract thus bypassed the node. This was in addition to the normally present fibers connecting the atrial musculature to the end of the node called "bypass" fibers by James.29 In addition copious Mahaim fibers continually passed from the end of the A-V node and
Correlation of anatomic and electrocardiographic findings. See legend of figure 13 for details.

Throughout the extent of the A-V bundle to the posterior part of the summit of the muscular ventricular septum (fig. 8 left). These fibers were much more copious than those seen normally. Thus in addition to the main conduction pathway, an accessory anatomic pathway passed from the atrial septum through the A-V bundle to the posterior part of the ventricular septum. There were no bundles of Kent either in the junctional region of the septum or in the right and left parietal walls.

Upon these basic pathways older and more recent pathological changes were superimposed (fig. 11). The older change consisted of fibrosis. This involved the approaches to the A-V node (fig. 4), part of the periphery of the A-V node, and the A-V bundle (fig. 8 left), and this process became more marked at the bifurcation (fig. 9). It was even more marked in the anterior and posterior radiations of the left bundle branch (figs. 9 and 10 left), and the first part of the RBB (fig. 11 upper), and was maximal in the third part of the RBB (fig. 11 lower). This process was reinforced by fatty infiltration at the approaches to the A-V node (fig. 4), and elastosis and fatty infiltration of the third part of the RBB (fig. 11 lower). The more recent lesion consisted of marked swelling of the cells with vacuolar alteration (or degeneration?) of the cytoplasm (figs. 8 to 10). This was again seen in the locations described, but also involved the second part of the RBB.

Thus, a close correlation of the anatomic findings with the predicted ones becomes...
Ventricular Pre-excitation

The Nature of the Pathological Process

Two alternative explanations are possible for the elastofibrotic and vacuolar degenerative process occurring in the conduction system and in the myocardium. Either they are related fundamentally to the abnormal central fibrous body formed in this patient, or they are independent of it. If they are related to the abnormality of the central fibrous body, we may theorize as follows:

The poor formation of the central fibrous body is associated with a lack of union between the central fibrous body in our case and the tricuspid annulus, although connection had been made between the latter and the pars membranacea. The abnormal formation of the central fibrous body permitted large communications to persist between the atrial septum and ventricular septum, which connections ordinarily are reduced to small proportions, or are completely obliterated; hence, the perpetuation of a special bypass tract between the atrial septum and the A-V bundle, and of the copious paraseptal fibers of Mahaim which far exceed in quantity those normally present. At the same time the right ventricle was tenuously moored to the fibrous skeleton of the heart and hence a degenerative process set in within the conduction system and the myocardium of the atria and ventricles. In support of this thesis is the marked involvement of the myocardium of the right ventricle and the right A-V junction (fig. 3) as compared to the left ventricle and the left A-V junction. If there is no connection between the abnormal formation of the fibrous skeleton in the heart and the degenerative process, then we do not know the nature of the latter process. The amount of infiltration of inflammatory cells is insufficient to dignify this process as a myocarditis.

Conclusions Regarding Structural and Functional Anomalies in This Unusual Case of the Pre-excitation Syndrome

1. Correlation of the anatomic and electrocardiographic data would indicate that two discrete accessory A-V pathways were responsible for the two features of the pre-excitation pattern: a) an anomalous connection of the atria with the bundle of His, which, in bypassing the A-V node, caused the short P-R interval and b) copious Mahaim fibers that could conduct to activate the ventricles in an anomalous fashion and thus became responsible for the delta wave. The assumption of conduction through Mahaim fibers in this case is unavoidable in order to explain the pre-excitation in the absence of ordinary Kent fibers between atrium and free wall of the ventricles. This does not mean that Mahaim fibers in the normal heart, which are ordinarily relatively meager structures, are able to conduct. This possibility needs further investigation.

Conceivably, such a separation—although exceptional—of the two features considered pertinent for the diagnosis of the pre-excitation syndrome could point to a specific anatomic background for atypical or related cases characterized by: (1) a normal P wave, a short P-R but no, or only a diminutive, delta wave,50 (2) a delta wave with a normal or prolonged P-R interval9,13,31 and (3) a delta wave in ectopic beats originating in the A-V junction.2,23,32–34

Of course other cases may be present with this electrocardiographic background in which anatomically no abnormality in the fibrous skeleton may be present. In these cases, other types of bypass may be found anatomically.

The most distal connections of the atrium to the A-V node, called “bypass” fibers by James29 cannot be invoked as functionally bypassing the node in our case. For these are commonly found without electrocardiographic evidence of pre-excitation. The “A-V node bypass tract” present in our case is not found in normal hearts.

2. The data in this case might also be extrapolated to indicate that the anatomic base of cases of WPW syndrome terminating
in A-V block is the presence of an accessory tract adjacent to the main tract, accompanied by the progressive destruction of both tracts.

3. The anatomic data in this case also enlarge the concept of cardiac skeletal diseases, which in general may be associated with conduction disturbances. Our case may be considered as related to Ebstein’s disease in which the tricuspid annulus is also abnormally formed and in which WPW syndrome is relatively common. These might be considered congenital cardiac skeletal diseases. These diseases would be in contrast with sclerosis of the left side of the cardiac skeleton acquired with advancing age which may be associated with severe A-V block.

Summary

1. Electrocardiographic and detailed histological studies are presented of a case of ventricular pre-excitation with progressive A-V and intraventricular block terminating in complete A-V dissociation.

2. Whereas the demonstration of a tract which leads from the atrial septal musculature to the A-V bundle bypassing the A-V node explains the short P-R interval, the delta wave is accounted for by the demonstration of unusually copious Mahaim fibers from the A-V bundle to the posterior portion of the muscular ventricular septum.

3. Thus, this appears to be the first demonstration of Mahaim fibers responsible for A-V transmission in the pre-excitation syndrome.

4. The correlation of the data permitted reconstruction of anatomic changes preceding, and responsible for, the gradual progression of the atrioventricular and intraventricular conduction disorder.

5. On the basis of this correlation it would appear that the two characteristic criteria of ventricular pre-excitation, shortened P-R and the delta wave, may in some cases have a different anatomic background. A separation of these parameters permits an explanation of certain atypical and puzzling aspects encountered in the syndrome of ventricular pre-excitation and related conditions.

References


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