Inexcitable Right Ventricle and Bilateral Bundle Branch Block in Uhl’s Disease

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SUMMARY A 29-year-old female with Uhl’s anomaly developed complete atioventricular (A-V) block. His bundle studies revealed block distal to the His bundle recording site with narrow QRS complexes. Right ventricular capture could not be obtained and despite successful left ventricular epicardial pacing, the patient died. Autopsy revealed absence of myocardium in most areas of the right ventricle and the right side of the ventricular septum with a normal tricuspid valve. Conduction system examination revealed total destruction of both bundle branches. This is the first case where bilateral bundle branch block is shown to be present in Uhl’s anomaly. Narrow QRS complexes probably reflected the absence of right ventricular forces.

UHL’S DISEASE is characterized by partial or complete absence of the myocardium of the right ventricle and replacement by fibroelastic and adipose tissue, in the presence of a normal tricuspid and pulmonary valve. In previous cases the ventricular septum has been spared. The present study is the first reported case with both marked involvement of the ventricular septum and atioventricular (A-V) block. In addition, electrophysiologic studies correlated well with serial section findings in the conduction system.

Report of Case

The patient was a 29-year-old female admitted to Saint Francis Hospital, Lynwood, California on September 17, 1975 following a syncopal attack. The patient first became symptomatic nine years prior to admission during a pregnancy, at which time she noticed dyspnea on exertion and ankle edema. One year prior to admission, her symptoms increased markedly with episodes of breathlessness on mild exertion, and weakness and diaphoresis associated with episodes of rapid heart rate. An X-ray taken at this time revealed cardiomegaly; cardiac catheterization revealed normal pulmonary artery pressure. The cardiac output was 2.5 L/min and the cardiac index was 1.25 L/min/m². Angiocardiography revealed moderate tricuspid regurgitation and
right heart enlargement. Ebstein's anomaly was suspected and the patient was advised to lose weight and reduce her physical activity.

Approximately two weeks prior to the present admission, the patient noted intermittent episodes of light headedness and near syncope. On the day of admission she collapsed, was diaphoretic and lost consciousness temporarily. Physical examination revealed an obese, weak, anxious woman. The pulse rate was 50 and the systolic blood pressure was 80. The skin was cool and moist. A few basal crepitant rales were heard in the chest. There were diminished heart sounds with no audible murmurs and no right ventricular lift. Routine laboratory results, including complete blood count and urinalysis, were within normal limits.

Electrocardiographic Analysis and Electrophysiologic Study

An electrocardiogram taken approximately 10 months before the patient's death revealed sinus rhythm, first degree A-V block (PR of 0.26 seconds), bialtrial enlargement, a narrow QRS with marked right axis deviation, poor R wave progression, and nonspecific ST-T wave changes (fig. 1). The electrocardiogram taken on the patient's terminal admission revealed complete A-V block with an atrial rate of 115/min and a ventricular escape rate of 47/min. The escape rhythm was characterized by narrow QRS complexes, similar in contour to previously conducted complexes shown on the electrocardiogram taken 10 months prior to admission (fig. 2).

His bundle electrograms were recorded utilizing previously described catheter techniques. There was complete A-V dissociation with an atrial rate of 100/min and a ventricular escape rate of 32/min with coupled premature ventricular contractions. These premature contractions were approximately 80 msec in duration. All atrial electrograms were followed by conducted His bundle potentials with a normal A-H interval of 84 msec. There was complete block distal to the His bundle recording site. There were no recordable high frequency potentials (split His bundle potentials) prior to escape complexes or to premature ventricular contractions (fig. 3).

Hospital Course

Initial management with atropine and isuprel caused frequent episodes of ventricular tachycardia. Temporary pacing was attempted via the femoral vein. Right ventricular capture could not be obtained despite extensive catheter manipulation. Because of the inability to achieve transvenous pacing, a thoracotomy was performed for insertion of a pacemaker. Capture could not be obtained at three separate right ventricular epicardial sites. Adequate capture was finally obtained utilizing a left ventricular epicardial site. Following successful left ventricular epicardial pacing, the patient temporarily improved.

Two days after surgery, she developed fever, hypotension and anuria. She died in shock three days after admission.

Post Mortem Examination

The autopsy was limited to the heart and lungs. The lungs showed pulmonary edema, chronic passive hyperemia, and small peripheral pulmonary emboli with an infarct of the right lower lobe.

Gross Examination

The heart was enlarged weighing 545 g. An epicardial pacemaker was present on the apical portion of the left ventricle. The right atrium was hypertrophied and enlarged.

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**Figure 1.** Electrocardiogram taken on 11-8-74. Note first degree A-V block, bialtrial enlargement, right axis deviation, narrow QRS.
The foramen ovale was closed. The tricuspid orifice was normal in size and the tricuspid valve was normally formed, with no evidence suggestive of Ebstein's disease (fig. 4).

The right ventricle was tremendously enlarged. Myocardium could not be recognized grossly in most areas and where it was seen it measured 1 mm in greatest thickness (fig. 5). The septal and parietal bands were flat and atrophied so that the outflow tract was not sharply demarcated from the inflow tract. The endocardium of the distal (downstream), septal, apical and anterior walls was covered with thrombus material. The remainder of the endocardium was considerably thickened and whitened. The amount of fat in the wall of the right ventricle was considerable both in the conus area and in the apical region. The pulmonary orifice was enlarged but the valve was normally formed.

The left atrium was hypertrophied and enlarged. The mitral orifice was normal in size and the valve was normally formed. The left ventricle was enlarged and its wall was thinner than normal. The ventricular septum was remarkable in that for a distance of 3 cm from the base of the aorta going toward the apex and 4 cm from the posterior to the anterior wall in this area, the entire septum was paper-thin.
and translucent (fig. 6). The aortic orifice was normal in size and its valve was normally formed. The coronary arteries showed no evidence of narrowing.

Microscopic Examination

Methods

The sino-atrial (SA) and A-V nodes and their approaches were serially sectioned and every 10th section was retained. The A-V bundle and the beginning of the bundle branches were likewise serially sectioned and every 5th section was retained. The remainder of the bundle branches up to the region of the moderator band was serially sectioned and every 10th section was retained. The atrial preferential pathways were likewise serially sectioned and every 40th section was retained. Consecutive sections were stained with hematoxylin-eosin, Weigert-van Gieson and Gomori-trichrome stains. Those parts of the aortic, mitral and tricuspid valves not included in the previous sections and their adjacent atrium and ventricle, and the pulmonic valve and its adjacent right ventricle were cut into blocks and five sections were cut from each block and stained with hematoxylin-eosin, Weigert-van Gieson, Gomori-trichrome, Alcian blue and Periodic acid-Schiff stains. The remainder of the heart was cut into blocks and three sections were taken from each block and stained with hematoxylin-eosin, Weigert-van Gieson, Gomori-trichrome stains. In this manner 1562 sections were studied. This method of study, somewhat modified, has previously been reported.17, 18

Findings in the Conduction System

SA node. This showed chronic epicarditis, moderate mononuclear cell infiltration in the node, and moderate hemorrhage.

Approaches to SA node. There was a considerable amount of mononuclear cell infiltration. A recent thrombus was present in the right atrial appendage. Some myocardial cells showed large bizarre nuclei.

Atrial preferential pathways. A moderate infiltration of mononuclear cells with focal necrosis of myocardial cells

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Findings in the Conduction System

SA node. This showed chronic epicarditis, moderate mononuclear cell infiltration in the node, and moderate hemorrhage.
with large bizarre nuclei were present. Acute venular and arteriolar degeneration with chronic panniculitis was seen.

_A-V node_. There was a slight amount of mononuclear cell infiltration.

**Figure 6.** Left ventricular view of the heart at outflow tract. _A_ = aorta, _S_ = area of marked thinning and transparency of muscular ventricular septum, _T_ = thrombus in wall of right ventricle.

_A-V node_. A moderate increase in young connective tissue and an infiltration with mononuclear cells was present. At the end of the node there was moderate elastosis and arteriosclerosis.

_A-V bundle, penetrating portion_. This showed a slight increase in connective tissue (fig. 7). The right bundle branch was given off early.

_A-V bundle, branching portion_. That part of the bundle which remained after the giving off of the right bundle branch is considered to be the branching bundle. The beginning of this part and a few fibers of the left bundle branch showed a moderate infiltration of mononuclear cells. Gradually this part of the bundle became markedly infiltrated with mononuclear cells in which only fragments of parenchymal cells could be recognized (fig. 8).

**Figure 7.** Photomicrograph of summit of ventricular septum. Hematoxylin-eosin stain × 30. _PB_ = penetrating portion of bundle of His, _TV_ = tricuspid valve. Note that the musculature of the right side of the septum is replaced by connective tissue, while the left side is relatively normal.

Left bundle branch (LBB). This was markedly replaced by inflammatory cells (fig. 9) with degenerative changes in the remaining cells.

Right bundle branch (RBB). As stated above the RBB was given off early and consisted in the beginning of its course of atrophic cells with marked mononuclear cell infiltration (fig. 10). Progressively the RBB was replaced by connective tissue. At the end of the first part the RBB was completely replaced by connective tissue.

_Pars membranacea_. This was markedly thickened by an increase in connective tissue, and fat tissue containing many vessels.

_Muscular ventricular septum_. The right side of the septum was completely replaced by connective tissue, fat tissue with a marked infiltration of mononuclear cells at its junction with the left side (fig. 7). Recent and organized mural thrombi with endocardial fibroelastosis were present on the right side. The summit was converted into a mass of granulation tissue in which scattered degenerated muscle and fat cells were present. In this mass, the small vessels and arterioles were thickened. Peripherally, scattered groups of Purkinje cells were present on the left side posteriorly. The anterior
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 PURKINJE CELLS showed acute degenerative changes with a slight infiltration of mononuclear cells.

RIGHT VENTRICLE. In most areas there was complete absence of muscle and replacement by fat and fibrous tissue (fig. 11). Marked endocardial fibroelastosis accompanied these changes. In areas where muscle was present, the nuclei of these muscle cells were enlarged, often bizarre, with degenerative changes in the cytoplasm, and there was an infiltration of mononuclear cells. Venules and arterioles also showed thickening and degenerative changes. Recent and organizing thrombi were present between muscle trabeculae or were included in fibroelastic masses extending to the epicardium. There was considerable epicarditis.

LEFT VENTRICLE. Although the myocardium in general was intact there were focal areas of replacement by fibrous and fat tissue, and focal areas of degeneration of muscle cells. This was accompanied by arteriolar and venular degeneration and intimal proliferation.

LEFT ATRIUM. The underlying myocardium was also involved in the chronic epicarditis.

RIGHT ATRIUM. The endocardium of the atrium adjacent to the myocardium showed an increase in mucopolysaccharides. Interdigitating endocardial channels with thrombus material were noted adjacent to the inferior leaflet of the tricuspid.

AORTA AND PULMONARY TRUNK. The vasa vasorum were thickened.

AORTIC VALVE. This was normal.

TRICUSPID VALVE. The tricuspid valve was at the anulus. There was no increase in mucopolysaccharides. PAS positive material was increased in the anulus.

PULMONARY VALVE. This was normal.

MITRAL VALVE. There was an increase in PAS positive material in the fibrosa and anulus.

DISCUSSION

In this paper, a case is considered to be Uhl's disease if there is partial or complete absence of myocardium in the

FIGURE 8. Photomicrograph showing distal portion of the branching bundle. Hematoxylin-eosin X 90. Note that the bundle is markedly infiltrated with mononuclear cells. The left side of the ventricular septum is similarly infiltrated. BB = branching portion of bundle of His, VS = ventricular septum.

FIGURE 9. Photomicrograph showing fibers of the left bundle branch which are a continuation of the branching bundle. Hematoxylin-eosin X 90. The parenchymal cells are degenerated and the whole structure is infiltrated with mononuclear cells, as is the left side of the ventricular septum. VS = ventricular septum. Arrows point to the left bundle branch.
right ventricle, with the tricuspid and pulmonic valves normally formed. Thus, we exclude cases of Ebstein’s disease, pulmonary atresia, or absence of the tricuspid valve, which may produce marked changes in the myocardium of the right ventricle resembling Uhl’s disease. In the literature, others have included some of these cases as variations of Uhl’s disease.19-22

The pathologic findings in UHL’s disease depend upon the age of the patient and the extent of involvement of the right ventricle. Thus, only a small part, or most of the right ventricle may be involved at any age. The absent myocardium is replaced by fat and fibrous or fibroelastic tissue. When seen in the younger age group, there may be no inflammatory reaction. When seen later in life there may be an inflammatory reaction with venular and arteriolar changes. This may be accompanied by degenerative changes in the remainder of the myocardium of the right ventricle and that of the right atrium and atrial septum as in our case. These changes may be looked upon as a reaction to the absence of myocardium with resultant distention of the chambers.

It is unusual to find necrosis and scars in the left ventricle with arteriolar and venular changes as seen in our case. The causes of these changes in the left ventricle are unknown. The focal necrosis and scars are not due to narrowing of the large coronary arteries, since the coronary arteries are normal in our case. Are they due to the arteriolar changes? If so, we would have to postulate that generalized arteriosclerosis of the myocardium with involvement not only of the right ventricle but also of the left ventricle may be a complication of Uhl’s disease.

To our knowledge, there have been no cases of involvement of the right side of the ventricular septum in Uhl’s disease. In our case the right side of the ventricular septum shows a diffuse absence of musculature with replacement by fat and fibrous tissue. A marked infiltration of mononuclear cells is present at the border with the remaining musculature of the left side of the septum. In the region of the summit of the ventricular septum this involvement of the septum is both on the right and left sides and the pars membranacea is markedly thickened with fibrous and adipose tissue.

These changes have resulted in secondary pathologic changes in the conduction system. The approaches to the A-V node and the short penetrating bundle are slightly to moderately involved with fibrosis, elastosis and arteriosclerosis. The RBB, which is given off early, shows marked inflammatory changes and is eventually completely replaced by connective tissue. The branching bundle, after giving off the RBB, progressively becomes more infiltrated with mononuclear cells with marked degeneration of the cells. The beginning of the LBB is completely replaced in an inflammatory and fibrotic summit of the ventricular septum. The peripheral Purkinje cells on the left side are clearly seen. No such cells are seen on the right side.

The above findings explain the clinical, electrocardio-
graphic and the His bundle recording data. The electrocardiogram taken 10 months before the patient's death revealed sinus rhythm, first degree A-V block, and a narrow QRS with marked right axis deviation and poor R wave progression. On her last admission she showed complete A-V dissociation. The QRS complexes of the ventricular escape rhythm were similar in contour to the conducted complexes in the previous electrocardiogram. The His bundle electrogram recorded during the patient's terminal admission showed A-V dissociation, with H potentials following P waves with a normal AH interval. This suggested a site of block distal to the His bundle recording site.

The presence of narrow QRS complexes usually suggests simultaneous activation of right and left ventricles via intact conducting bundle branches. However, the pathological findings revealed the right bundle branch to be totally and chronically destroyed. With the above knowledge of pathologic change, one can then speculate that right bundle branch block had been present ten months prior to death when narrow conducted QRS complexes had been recorded. If right bundle branch block had been present, the presence of narrow QRS complexes could have reflected left ventricular activation with absence of right ventricular forces because of the marked involvement secondary to Uhl's dis-

**Figure 11.** Photomicrograph of the wall of the right ventricle. Top) Weigert-van Gieson stain × 13.8. Note the absence of myocardium in this area. Bottom left) Weigert-van Gieson stain × 13.8. Section is taken at the tricuspid valve annulus. Bottom right) Hematoxylin-eosin stain × 45. This is one of the few areas where muscle was present in right ventricle. E = endocardium, F = fat tissue, TV = tricuspid valve, V = ventricle, A = atrium, P = pericardium, EP = epicardium, M = myocardium.
case. This hypothesis is supported by the presence of right ventricular endocardial and epicardial inexcitability with electrical stimulation, noted on the patient's terminal admission. The absence of septal forces and marked right axis deviation during conducted rhythm, could have reflected the marked septal involvement (Uhl's disease) and possibly additional left posterior fascicular block (since there was pathologic involvement of the left bundle branch system).

With the advanced pathologic findings demonstrated, it is difficult to speculate regarding the pattern of ventricular activation at that time.

Fixed P-R prolongation would have then reflected right bundle branch block with delayed conduction in the left bundle branch (first degree left bundle branch block). A His bundle electrogram was not recorded at that time. However, the terminal His bundle electrogram revealed a normal A-H (A-V nodal conduction time) supporting the above interpretation. Progression of incomplete to complete left bundle branch block (suggested by pathological findings) immediately prior to the last admission would result in complete bilateral bundle branch block (complete A-V block).

This is consistent with results of His bundle recordings which revealed a site of block distal to the His bundle recording site. The narrow QRS escape rhythm would then appear to be idioventricular, arising possibly from the posterior ventricular Purkinje network or left posterior fascicles (accounting for right axis deviation). The QRS was narrow in contour because of absent right ventricular forces as described above. Although the coupled ventricular premature contractions appear widened when compared to the "idioventricular rhythm", these were only 80 msec in duration. This observation is also consistent with the absence of right ventricular participation in these premature systoles, which could reflect left ventricular ectopy with fragmented conduction in the left ventricle. Although the electrophysiological findings are also consistent with a site of block in the His bundle (distal to the His bundle recording site), this seems unlikely considering the absence of split His potentials, and the pathological findings.

The clinical picture of this patient is of interest in the overall natural history of Uhl's disease. The great majority of cases reported in the literature were diagnosed at autopsy and many involve infants and children with rapid deterioration of their cardiac status early in life. Another group survived into adulthood with a relatively benign course during early life followed by an insidious onset of low output symptoms terminating in arrhythmia or cardiac surgery. Occasionally Uhl's disease has been reported as an incidental autopsy finding. Here the absence of right ventricular muscle was partial and not hemodynamically significant. Only rarely has Uhl's disease been diagnosed clinically.

If Uhl's disease is due to an embryological variant, then this variant is unknown. Uhl originally explained the abnormality as due to a deficiency in the formation of the myocardial mantle on the right cardiogenic field before it joins the left to form the ventricular portion of the heart tube. This would place the abnormality at the 4-9 somite stage of the normal development of the heart. While this is possible, it is unlikely. According to Pernkopf and Wirtinger the normal definitive right ventricle is formed only after the formation of the bulboventricular loop and after the absorption of the bulbus with the shift of the atrial canal to the right. Thus the right ventricle is formed from a portion of proamplulla (descending limb of the bulboventricular loop), most of the metaamplulla (proximal part of the ascending limb of the loop), and a portion of the bulbus (distal part of the ascending limb of the loop). It is conceivable that absence of the musculature of the right ventricle may occur due to faulty union of these components. We do not know whether the anomalies "isolated aneurysmal enlargement of the right atrium," or "absence of the musculature of the left ventricle" are related to Uhl's disease.

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