Idiopathic Hypertrophic Subaortic Stenosis with Split His Bundle Potentials
Electrophysiologic and Pathologic Correlations

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SUMMARY A 25-year-old white female had idiopathic hypertrophic subaortic stenosis proved by catheterization. The ECG revealed left bundle branch block. Electrophysiologic studies revealed normal PA and AH intervals, but the HV interval was prolonged (70 msec). The width of the His spike was 20 msec. A clear, reproducible split His potential was demonstrated with the atrial extrastimulus technique. Because the patient was symptomatic, a permanent pacemaker was inserted. One week later the patient died suddenly.

Autopsy revealed an enlarged heart with a markedly thickened and sigmoid ventricular septum and a small and coarsely trabeculated lumen. Histologically the common bundle was situated on the right side of the septum. It was intact at its origin, but showed fibrotic changes more distally. The beginning of the left bundle branch was markedly disrupted as it traversed the septum. The right bundle branch was moderately fibrosed.

There was excellent correlation between the electrocardiographic and electrophysiologic findings and the findings in the conduction system. The cause of the sudden death was related either to the outflow obstruction or to an arrhythmia, or both.

IDIOPATHIC hypertrophic subaortic stenosis (IHSS) is frequently associated with arrhythmias and occasionally with atrioventricular (AV) block. However, there have been few electrophysiologic studies in these patients, and only one case of correlative electrophysiologic and pathologic studies of the conduction system in IHSS has been reported.

A patient with IHSS underwent both electrophysiologic and pathologic studies. The latter included extensive examination of the conduction system. We believe this study contributes to the understanding of the genesis of arrhythmias in IHSS.

Case Report

The patient was a 25-year-old white female who had a 4-year history of chest pain, dyspnea and near-syncopal spells. The ECG showed nonspecific ST-T abnormalities. (She was included in a report of a group of patients with His bundle disease.) Cardiac catheterization performed in 1970 when she was 19 years old revealed a 10-mm Hg left ventricular outflow tract gradient at rest, which increased to 60 mm Hg with an isoproterenol infusion and to 105 mm Hg with postextrasystolic beats. Her condition was diagnosed as IHSS.

She was seen in the medical outpatient clinic in July 1975 because of recurrent dyspnea and anginal chest pain. She had no history of dizziness or syncope. Physical examination findings were compatible with the diagnosis of IHSS. The ECG showed a left bundle branch block pattern. In March 1976, she complained of dizzy and near-syncopal spells but no true syncope. Chest pains and dyspnea continued, but she was taking no medications. She consented to undergo an investigational intracardiac electrophysiologic study.

With insertion of a tripolar catheter in the right ventricle, transient 3:1 AV block occurred. However, the catheter was not well positioned and the level of the block could not be shown clearly. The catheter was repositioned and the AV block disappeared. It was assumed at the time of the study that AV block was the result of trauma to the right bundle by the catheter. With return of sinus rhythm her PA and AH intervals were normal. The HV interval was 70 msec (normal < 55 msec). The width of the His spike was 20 msec (normal values not established). There was no evidence of sinoatrial (SA) or AV nodal disease with atrial pacing or with the atrial extrastimulus evaluation. The HV interval did not change during atrial overdrive pacing. Atrial extrastimuli produced a clear and reproducible split His potential when the spontaneous sinus cycle length was 700 msec and when the AV interval was 250 msec and the H1H2 interval was 350 msec (fig. 1). The HH' interval with the premature beat was 100 msec. The H1V1 interval was 72 msec, essentially the same as the baseline HV interval. Because the patient's symptoms could have been
caused by transient bradyarrhythmias and because at that time the clinical significance of a split His potential was not known, but considered ominous by some, a permanent pacemaker was inserted. A week later the patient died suddenly. Permission for a limited autopsy involving examination of the heart was granted. The endocardial pacemaker electrode was in a good position and pacemaker generator function was normal.

Gross Examination of the Heart

The heart was enlarged, weighing 408 g. The right atrium and ventricle were normal in size and thickness. The left atrium and ventricle were hypertrophied and enlarged. The mitral valve, although normally formed, showed markedly increased hemodynamic change (i.e., thickening due to altered hemodynamics, such as increased pressure or flow). The chordal attachments of the tricuspid valve assumed an abnormal pattern. The semilunar valves were normal.

The architecture of the left ventricle was distinctly abnormal (fig. 2). The septal surface was sigmoid with a bulge in its midportion. It was coarsely trabeculated, with large longitudinal trabeculae proceeding from apex to base. At the top of the septum there was a 1.2-cm indentation surrounded by thickened endocardium. The parietal wall was also covered by thickened trabeculae with numerous areas of thickened endocardium. The lumen of the left ventricle was relatively restricted. The coronary circulation was normal, with no atherosclerotic changes.

Microscopic Examination of the Conduction System

Methods

The SA node and its approaches, the AV node and its approaches, the AV bundle and the bundle branches up to the region of the moderator band were serially sectioned and every tenth section was retained. The atrial preferential pathways were serially sectioned and every fortieth section was retained. Consecutive sections of the SA and AV nodes and the AV bundle and the beginning of the bundle branches were stained with hematoxylin-eosin, Weigert-van Gieson and Gomori trichrome stains. The atrial preferential pathways and the remainder of the bundle branches were alternately stained with hematoxylin-eosin and Weigert-van Gieson stains. The remainder of the heart was cut into blocks and two sections were

Figure 1. Tracings from the surface electrocardiographic leads I, II, III and V	extsubscript{1} and two His bundle electrogram leads (HBE) are shown. At a spontaneous sinus cycle length of 700 msec, a single His potential was recorded (first and third beats) and the H	extsubscript{1}V	extsubscript{1} interval was prolonged to 70 msec. During evaluation using an atrial extrasinusul (s), a split His potential (H	extsubscript{2}H	extsubscript{2}) was observed at a A	extsubscript{1}S interval of 250 msec (shown here) and a H	extsubscript{1}H	extsubscript{2} interval of 380 msec. The H	extsubscript{2}H	extsubscript{2} interval was 100 msec. This finding was repeated. The H	extsubscript{1}V	extsubscript{1} interval was 72 msec, almost the same as the baseline H	extsubscript{1}V	extsubscript{1} interval. With earlier atrial extrasin stimuli on subsequent testing, the effective refractory period of the atrium was reached.

Figure 2. View of the outflow tract of the left ventricle. LV = left ventricle; Ao = aorta.
FINDINGS

SA node: This was in normal position. An occasional cell showed acute degeneration.

Approaches to SA node: Some large arterioles were thickened and narrowed. There was a slight infiltration of mononuclear cells in the myocardium and epicardium.

Atrial preferential pathways: These showed no changes.

Approaches to the AV node: The myocardial cells were markedly swollen. There was moderate thickening and narrowing of the ramus septi fibrosi.

AV node: The AV node was flattened in a vertical direction (fig. 3), but showed no other abnormalities.

AV bundle, penetrating portion: This was also flattened in a vertical direction. In its initial portion, it was normal. Then it showed moderate fibrosis that varied from level to level, becoming more intense distally (fig. 4).

AV bundle, branching portion: This showed moderate fibrosis that varied at different levels (fig. 5A). Some arteriolosclerosis was also present. The bundle remained on the right side of the pars membranacea. The left bundle branch was given off from the left upper pole of the bundle.

Left bundle branch: The left bundle branch went over a bulge on the summit of the septum to get to the left side (figs. 5A and B). Fibrosis was present at the junction of the branching bundle and left bundle branch. The beginning of the left bundle branch revealed marked fibrosis with a marked infiltration of neutrophils and mononuclear cells, as it lay beneath a large area of fibroelastosis. More peripherally, only
fragments of left bundle branch were present, with scattered cells in the Purkinje nets (fig. 6).

Right bundle branch: In the first part there was moderate fibrosis. The second and third parts were normal.

Central fibrous body: It was thick and abnormally formed. There was an abnormally large projection from the eustachian valve and a thick prong extended to the tricuspid valve (fig. 3). The arterioles were markedly thickened.

Summit and midportion of the ventricular septum: The architecture was markedly altered by the thick trabeculations on the left side, producing projections and indentations (figs. 3 and 7). The large and small arterioles were markedly thickened and narrowed. New and old connective tissue scars were in evidence. Marked endocardial fibroelastosis was present on the left side. There was an immense increase in tissue spaces. Areas of “disarray” were in evidence in the midportion of the septum (fig. 8).

Mitrval valve: The fibrosa was markedly thickened.

The ventricularis showed marked fibroelastosis with “coral reefing.” There was also focal fibroelastosis of the atrialis.

Left ventricle: The anterior and posterior walls showed the heavy trabeculation seen grossly. Arteriolosclerosis was present with slight narrowing. Moderate fibrosis was present in the inferior wall. The thickness of the anterior and posterior walls and the septum below the crista were measured with and without the trabeculations. With trabeculations, they each measured 2.4 cm; without trabeculations, the septum measured 1.8 cm and the anterior and posterior walls each measured 1.4 cm.

Right ventricle: There was no arteriolosclerosis. There was an organizing thrombus in the inferior wall where the catheter had been.

Discussion

IHSS is usually described as showing asymmetrical septal hypertrophy with disarray of fibers in the septum seen by light and electron microscopy.\textsuperscript{26-38}
The specificity of the criteria for the diagnosis of this condition pathologically are in question. Asymmetric septal hypertrophy has been seen in hearts with other types of pathology, and architectural disarray has been seen in normal and in pathologically altered hearts. According to Maron et al., there is greater disarray in IHSS compared with normal and other types of pathologic hearts. Our case is of interest in that the abnormal architecture of the left side of the septum and an abnormal parietal left ventricular wall were grossly visible. In addition, there were many areas of disarray histologically.

Patients with IHSS have a predisposition to both tachyarrhythmias and bradyarrhythmias. These include auricular fibrillation, left bundle branch block and other types of fascicular block, and various degrees of AV block. When our patient was first seen and IHSS was diagnosed, only ST-T abnormalities with no arrhythmias were present. Five years later she had left bundle branch block.

The electrophysiologic studies performed 1 week before death showed a split His potential in response to atrial extrastimuli. There was no evidence of SA abnormalities and no clinical or electrophysiologic evidence of AV nodal disease.

The mechanism of the split His potentials with the atrial extrastimulus technique remains in doubt. Because the split His potentials were present only with this technique and with a certain cycle length, their genesis may have a functional component. In view of the spotty areas of fibrosis in the penetrating and branching portions of the AV bundle, it appears that under certain functional conditions, separate parts of the bundle could produce separate potentials. It is also conceivable that under certain functional conditions the second His potential may represent a reentrant phenomenon.

The conduction system in patients with IHSS has been pathologically evaluated. Ferris, studying the AV node and His bundle in four cases, found marked disorganization of the AV node with an increase in connective tissue as well as hypertrophy of some of the His bundle fibers in one patient. In the second case, he found fatty infiltration of the AV node with a normal His bundle. In the third he saw marked narrowing of the ramus septi fibrosi with some fatty infiltration of the node. In the fourth case, he found slight fibrosis of the AV node and bundle. In a pathologic evaluation of 22 patients with asymmetric hypertrophy of the heart and sudden death, James and Marshall noted increased fibrosis of the SA node in 12 and a conspicuous fetal pattern of the AV node and bundle in 13; fibrosis and fatty infiltration of the AV node and His bundle were present in some, and the ramus septi fibrosi was thickened and narrowed in many.

Electrophysiologic studies have been performed in patients with IHSS, but the split His potential has not been previously described. Ingham et al. evaluated 13 patients and found normal PA and AH intervals in all. The HV interval was prolonged in 83% of these patients and the atrial refractory period was prolonged in 25%. Dual nodal responses were found in seven of these 13 patients.

However, we have been able to find only one report in which electrophysiologic findings were correlated with pathologic findings of the conduction system. The patient evaluated in that study had documented AV block and His bundle recordings revealed first-degree infra-Hisian block, progressing to 2:1 block and then to complete supraventricular block. The pathologic studies of the conduction system revealed moderate fibrosis of the SA node, fibrosis of the approaches to the SA node with arteriolar sclerosis, marked fatty infiltration of the approaches to the AV node, fatty infiltration, vacuolar degeneration and necrosis of the penetrating portion of the bundle, and marked fibrosis of the right bundle branch.

We hypothesize as follows as to the causes of the pathology of the conduction system in our case. The congenitally abnormal architecture of the left side of the septum produced a secondarily abnormal central
FIGURE 7. Arteriolosclerosis (arrows) in abnormal ventricular septum. F = fibroelastosis; VS = muscular ventricular septum; PM = pars membranacea. Hematoxylin-eosin stain; magnification × 22.

FIGURE 8. Ventricular septum showing "disarray." Hematoxylin-eosin stain; magnification × 45.
fibrous body, flattening the AV node and bundle and displaced the bundle to the right side. The abnormal septum resulted in arteriolosclerosis, which has been found in many cases of IHSS. Thus, ischemia may have accentuated fibrosis of the bundle and bundle branches. The left bundle branch was probably traumatized as it went over the hump of the septum into the markedly trabeculated left side of the septum.

Thus, in IHSS, not only is the ventricular septum abnormal, but the central fibrous body either primarily or secondarily also shares in the abnormality. This may lead to thickening and narrowing of the ramus septi fibrosi and arteriolosclerosis of the summit of the ventricular septum. The conduction system is thereby altered. There may be disorganization and fibrosis of the AV node or bundle of His. The left bundle branch may be impaired by mechanical factors created by hypertrophy of the ventricular septum, and both bundle branches may show fibrosis due to ischemia. The cause of the changes in the SA node found by James and Marshall and Garrilcescu et al. is not clear.

The split His potential, the unexplained symptoms and the development of high-degree AV block were the basis for insertion of a permanent pacemaker in our patient. When this decision was made, a split His bundle was considered a potential harbinger of complete AV block. Subsequent reports suggest that a pacemaker is not required in patients with a demonstrated split His potential unless symptomatic bradycardhythmias are present.

Sudden death, which frequently occurs in IHSS, may be a result of either tachyarrhythmias or bradyarrhythmias related to an abnormally formed or developed conduction system or secondary to pathologic changes in the conduction system. Because our patient was protected from the effects of a bradycardhythmia by a pacemaker that was recently inserted and functioning normally, sudden death could have been due to tachyarrhythmia or left ventricular outflow obstruction.

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