Histopathologic Studies of the Conduction System in Marked Left-Axis Deviation

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The histopathologic changes of the left ventricular (LV) conduction system were studied in 11 autopsy cases with marked left-axis deviation (LAD). In all cases the LV conduction system was fanlike and spread broadly over the left septal surface. However, the sizes and sites of the histopathologic lesions varied. In 2 cases the lesions were small and localized at the initial portion of the LV conduction system, whereas in 9 cases the lesions were located more peripherally and were more extensive, especially in 2 cases in which the lesions were mainly localized in the apical third of the LV conduction system. These differences in the sizes of lesions were believed to be due to the anatomic structure of the conduction system. At the initial portion of the LV conduction system, cells were oriented longitudinally with collagen partitions, which presumably resulted in functionally longitudinal dissociation. The variability in the lesions in these patients may explain why prognosis in terms of development of complete heart block is not always poor in patients with LAD and right bundle branch block.

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The concept of trifascicular block and hemiblock[1,2] is popular among clinicians. However, there are still differences of opinion regarding the morphologic characteristics of the left ventricular (LV) conduction systems[3–8] and considerable numbers of studies indicate that the LV conduction system is fanlike and that the anatomic structure of the LV conduction system is very complex. James et al[5,9,10] found that at least in the proximal portions of the LV conduction system, the cells are oriented longitudinally and are separated by collagen fibers, suggesting longitudinal functional dissociation in this portion, as reported in the His bundle.[11] Therefore, in the present study, based on the detailed anatomy of the conduction system, we examined the histologic lesions in 11 cases of marked left-axis deviation (LAD) on the electrocardiogram.

Methods

Eleven hearts from subjects (10 men, 1 woman) 32 to 79 years old (mean 69) showing LAD on electrocardiograms were studied. The following criteria were used for recognition of marked LAD: (1) Deviation of the mean QRS axis in the frontal plane to the left of −45° or more. (2) Ventricular complexes qR in leads I and aVL, and rS pattern in leads II, III and aVF. One case was associated with myocardial infarction, 2 with systemic hypertension and 1 with aortic valvular disease. Electrocardiograms of these patients are shown in Figure 1.

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All hearts were studied by serial sectioning of the septum. A single specimen of tissue containing the ventricular septum was removed from each heart and was separated into 4 to 12 blocks. The anterior margin of the specimen was cut through the base of the LV anterior papillary muscle and the posterior margin through the base of the LV posterior papillary muscle. For serial sectioning, the plane of cutting was as recommended by Demoulin and Kulbertus[3] (parallel to the atrioventricular [AV] ring) in 7 cases and as recommended by Lev[12] (perpendicular to the AV ring) in the others. Sections 5 μ thick were prepared and every 15th section was stained with Masson's trichrome stain and examined histologically. When necessary, judging by examination of initially selected samples, intervening sections were later stained and examined. The anatomy of the LV conduction system in each of the 11 hearts was reconstructed after examination of serial microscopic sections. The LV conduction system was studied in detail as far distally as it was distinguishable. The cell type and anatomic structure was studied in each portion of the LV conduction system. The lesions of conduction fibers were expressed semiquantitatively as: + = 30 to 40% loss, ++ = 40 to 60% loss, and +++ = more than 60% loss of the conduction fibers. Pathologic findings were superimposed on the reconstructed LV conduction system and correlated with electrocardiographic findings.

Results

The hearts weighed 180 to 500 g (mean 338); 8 hearts weighed more than 300 g. One case showed subendocardial infarction distributed in the anteroseptal and lateral walls. Four cases showed coronary stenosis of 50 to 75% in at least 2 main coronary arteries. Fibrosis of the summit of the ventricular septum was remarkable in 4 cases. Histologic changes of the AV node were found, but were not significant.

TABLE I Histopathologic Findings in the Conduction Systems of 12 Cases with Marked Left-Axis Deviation

Case	His Bundle	RBB	Left Ventricular Conduction System						HW (g)
			Ant.	Mid.	Post.	Basal	Middle	Apical	
1	...	Fi+	Fi++	Fa+++	Fa+	Fi+++	Fa++	...	300
2	...	...	Fi++	Fi+	...	...	Fi++	...	350
3	...	Fi+	Fi++	Fi++	...	...	Fi++	...	180
4	...	...	H+++	H+++	...	...	...	H+++	380
5	...	...	Fi+	Fi++	...	...	Fi+	Fi++	400
6	...	...	Fi++	Fi++	...	Fi++	Fi++	...	240
7	...	...	Fi++	Fi++	...	...	Fi++	...	250
8	Ca+	...	Fi++	...	...	Fi+	Fi++	...	500
9	...	Fi++	Fi++	...	...	Fi++	...	...	340
10	...	...	Fi++	Fi++	...	...	Fi++	...	430
11	...	...	Fi++	Fi++	...	...	Fi++	...	350

Ant., Mid., Post = anterior, midseptal and posterior portion; Basal, Middle, Apical = basal, middle and apical thirds of the left ventricular conduction system; Ca = calcification; Fa = fatty metamorphosis; Fi = fibrosis; H = hemorrhage; HW = heart weight; RBB = right bundle branch.

The distribution of the LV conduction system varied markedly from heart to heart. The LV conduction system was not divided simply into 2 discrete fascicles and was a fanlike structure in all cases. The reconstructed LV conduction system superimposed on the excised heart is shown in Figure 2. There is no division for 7 mm from the origin (main portion of the left bundle branch). The anterior radiation coursed to the anterior papillary muscle with complex interconnections with other fibers. The rest of the conduction fibers (posterior radiation) fans out over the entire midseptal area and to the posterior papillary muscle. It was usually difficult to determine the cells that marked the anterior and posterior radiations. Therefore, we arbitrarily divided the anterior to posterior axis of the LV conduction system into anterior, midseptal and posterior portions.

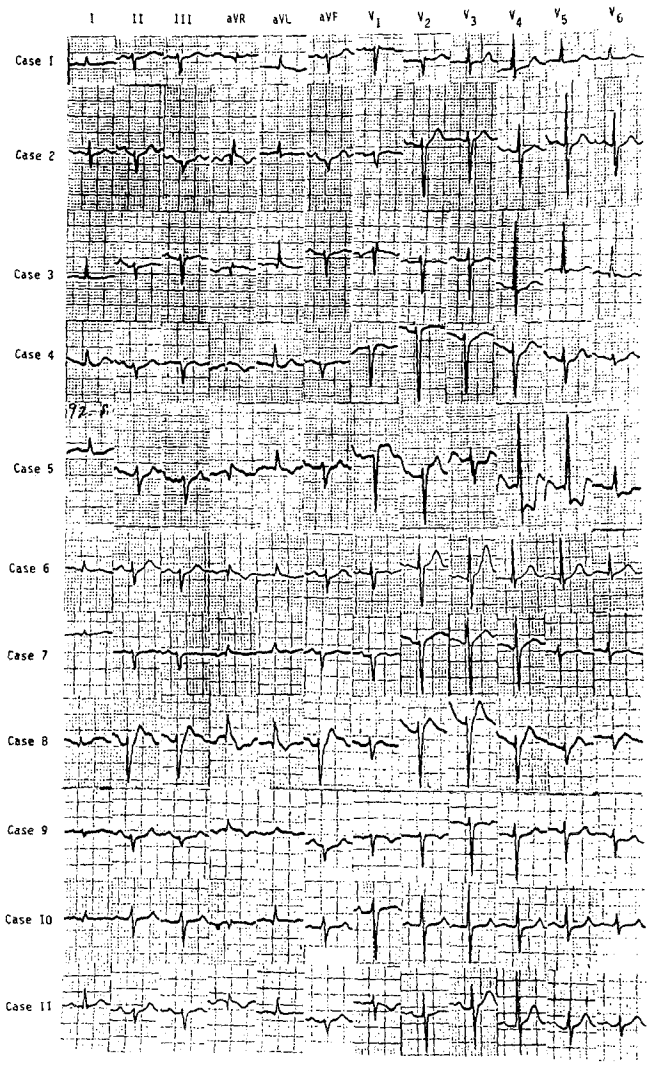

FIGURE 1. Standard 12-lead electrocardiogram from 11 patients with left-axis deviation.

Histologic examination showed that the basal third of the LV conduction system had more slender fibers than those in the working muscles. At this area, the fibers were arrayed in organized parallel strands (Fig. 2a). These strands were separated by collagen partitions, which were oriented longitudinally. During the course of the conduction system down the intraventricular septum, the cells gradually became larger and stained paler. In the region a few millimeters to 20 mm from the origin, the cells of the conduction system were gradually replaced by large, vacuolated Purkinje cells (middle third, Fig. 2b). More distally, the Purkinje cells formed an interlacing network (apical third; Fig. 2c). The LV conduction system could be reconstructed with confidence for a length of 9 to 44 mm, but beyond this portion, the cells became smaller and the left septal surface was relatively diffusely covered by conduction fibers.

The morphologic characteristics of reconstructed LV conduction systems with superimposed histopathologic lesions in the 11 cases are shown in Figure 3. Table I is a summary of the pathologic findings in these cases. The lesions of the LV conduction system were located between the anterior and midseptal portions. With respect to their anatomic structure and pathogenesis, the locations of these lesions in the LV conduction system could be separated into the basal, middle and apical thirds (Fig. 2).

In 4 hearts the basal third of the LV conductior system was damaged, especially close to the bifurca

tion, where immediately after branching the conducting fibers were replaced by loose connective tissue between the fibrous tissue of the summit of the intraventricular septum and the left septal endocardium. Two of these hearts showed the small lesions mainly at this area. Lesions of the middle third of the AV conduction system were found in 9 hearts. Five cases (nos. 2, 3, 7, 10 and 11) showed the lesions mainly at this area, and these lesions were more extensive than those in the 2 cases with lesions in the basal third (nos. 8 and 9). Histologically, fibrosis and fatty metamorphosis were observed. In 2 cases the lesions were localized in the apical third. In these cases pathologic lesions were extensive and also involved the working muscle. In 1 case (no. 4), the conduction fibers were affected by hemorrhagic fibrinous endocarditis (case 5). In another case, fibrous displacement of the conducting fibers was found in association with subendocardial infarction.

Discussion

There is some controversy concerning the histopathologic lesions underlying the electrocardiographic pattern of LAD.[3,6,13,14] Moreover, recent studies have shown that the anatomic structure of the LV conduction system is very complex.[5,10] At the basal third of the LV conduction system, the fibers are oriented longitudinally and are separated by collagen fibers. In this portion, conduction in the direction parallel to the fibers is much more rapid than that in the direction perpendicular to their long axis. The structure of the conduction system in this region is similar to that of the His bundle and the fibers are probably functionally dissociated longitudinally.

Within 10 to 20 mm from the origin of the LV conduction system, the large classic Purkinje cells start to appear (middle third). We considered this portion the left bundle branch-Purkinje network junction, although we could not delineate the junction clearly. Within 20 to 40 mm from the origin, the small bundle cells are replaced by the Purkinje cells. Massing and James[5] delineated the LV conduction system with confidence for a distance of 24 to 41 mm in 10 hearts and defined this portion as the left bundle branch-Purkinje network junction. In our study the definition of the junction was based on the cell type, i.e., small bundle branch cells and the large classic Purkinje cells, so the discrepancy in our location of the junction was simply due to a difference of the definition: The morphologic characteristics and histologic structures of the corresponding portions in our studies and those of Massing

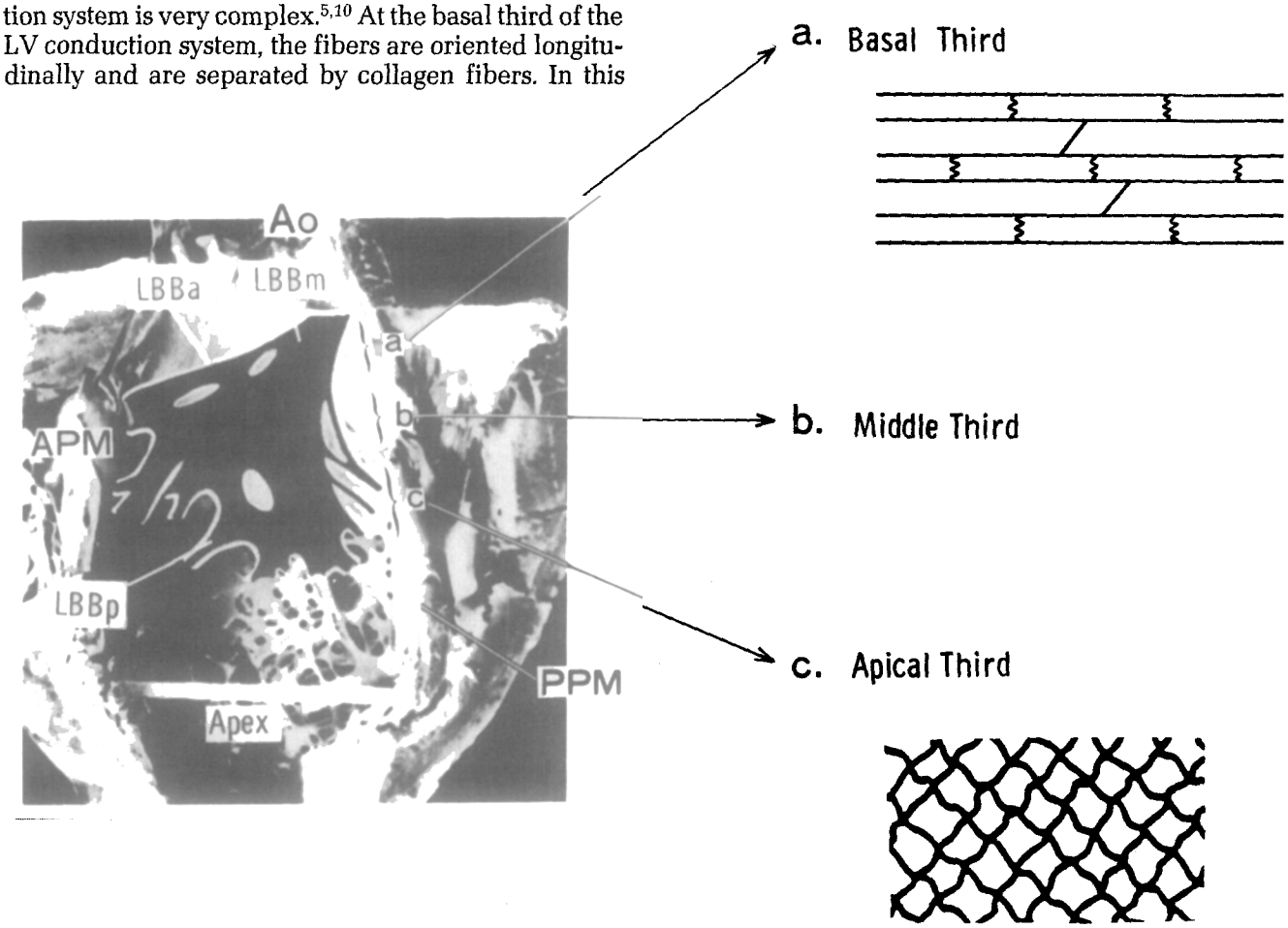

FIGURE 2. Reconstructed left ventricular conduction system superimposed on the excised heart. The left ventricular (LV) conduction system is superimposed on the excised heart. The anterior radiation of the left bundle branch (LBBa) courses to the anterior papillary muscle (APM). Several posterior fibers (posterior radiation, LBBp) originate from the main portion of the left bundle branch (LBBm) and widely covered the midseptal area. *Right*, schematic of the histologic findings. At the basal third of the LV conduction system (a), the fibers are oriented longitudinally with separation of the collagen fibers. At the middle third (b), Purkinje cells start to appear. The apical third of the LV conduction system was covered by the Purkinje fibers (c). Ao = aorta; PPM = posterior papillary muscle.

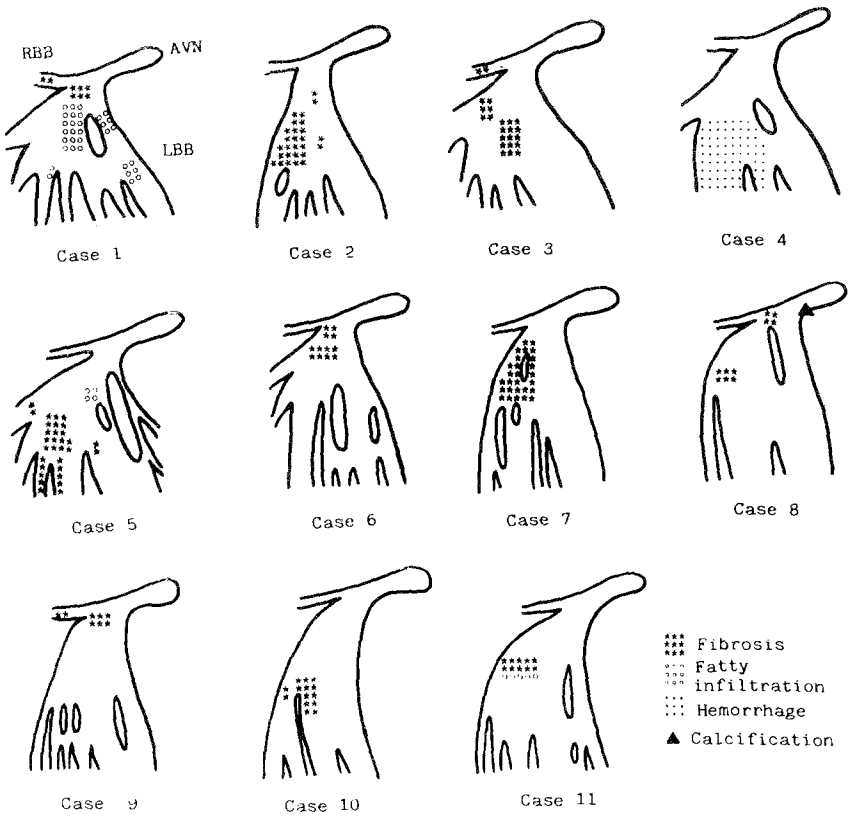

FIGURE 3. Histopathologic lesions in 11 cases with left-axis deviation. AVN = atrioventricular node; RBB = right bundle branch.

and James were identical. Because of the abundant connections of the Purkinje network, small lesions in the peripheral conduction system are unlikely to produce significant delay in ventricular activation.

In hearts with left anterior hemiblock, Demoulin and Kulbertus[3] found that the histopathologic lesions were located peripherally and were not limited to the anterior division, but were widely distributed, also being present in midseptal or posterior divisions. Experimental studies on excised heart by Myerburg et al[16] and epicardial activation and electrocardiographic studies by Gallagher,[17] Inoue[18] and their co-workers also support the histologic findings of Demoulin and Kulbertus.[3]

Our results confirmed that at least some lesions can be found in the anterior portion of the conduction system in cases of marked LAD. Consistent with the studies of Demoulin and Kulbertus,[3] in 9 of our 11 cases, the lesions were widely distributed and were found in both the anterior and midseptal portions. However, in the other 2 cases, the lesions were small and were located in the basal third of the LV conduction system.

To explain this difference, we studied the relation between the sites and sizes of the lesions. In our studies, the basal third of the LV conduction system was involved in 4 cases. As a consequences of the anatomic partition of the collagen between longitudinally arranged fibers, small lesions in this region may interrupt or delay in later distribution of electrical impulses to the anterior septum or free wall. Consistent with this hypothesis, in cases 8 and 9, small focal lesions located in the basal third of the LV conduction system produced LAD in the electrocardiogram. The lesions of the middle third of the LV conduction system (cases 2, 3, 7, 10 and 11) were larger than in cases 8 and 10. In 2 hearts the lesions were found mainly in the apical third of the LV conduction system. In these cases the lesions were relatively extensive and severe, and also found in the myocardium.

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