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Morphologic Differential Diagnosis of Idiopathic Cardiomyopathies

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Summary. Scanning electron microscopic examination of the myocardium in cardiomyopathies is a valuable complementary method beside light and transmissionelectron microscopy for the differential diagnosis of this rare disease. In two cases of congestive cardiomyopathy no marked alterations of the myocardial architecture could be found whereas in one case of nonobstructive hypertrophic cardiomyopathy myocardial cell alterations and structure disorders could be demonstrated in an almost stereologic view. The pathogenesis of heart failure in this disease was clearly shown. Similar changes were not observed in hearts without cardiomyopathy or in other forms of cardiac hypertrophy.

Key words: Cardiomyopathy – Myocardium – Scanning electron microscopy.

Zusammenfassung. Rasterelektronenmikroskopische Befunde am Herzmuskel bei idiopathischer Kardiomyopathie können eine methodische Bereicherung der Differentialdiagnose dieses seltenen Krankheitsbildes darstellen: Bei zwei Fällen von kongestiver Kardiomyopathie ist die räumliche Architektur der Muskelzellen unverändert, bei einem Fall von nicht-obstruktiver hypertrophischer Kardiomyopathie werden sowohl die räumlichen Texturstörungen der Herzmuskelzellen als auch der Myofibrillen dargestellt. Die formale Pathogenese der Herzinsuffizienz wird hier mit Hilfe der Rasterelektronenmikroskopie plastisch herausgearbeitet.

Introduction

There have been relatively few attemps to study human heart muscle with the scanning electron microscope (SEM) (Buss et al., 1970; Poh et al., 1971;

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Sybers et al., 1973). Difficulty in preparing tissue without extensive artifactual distortion and postmortem alterations of cellular structures has made SEM-observations of human myocardium of limited practical value.

In previous light- and electron microscopic studies of the cardiomyopathies, which may be defined as heart muscle disorders of unknown cause and without coronary, endocardial or other systemic disease (Goodwin, 1970; Abelmann, 1974), structural disorders of the myofibers were observed (Knieriem et al., 1975; Loogen and Kuhn, 1975; Olsen, 1976). The present study presents Scanning electron microscopic observations of myofiber structure in different forms of cardiomyopathies compared with normal myocardium.

Materials and Methods

Hearts from autopsies were used for this study. Three had the usual clinical and morphological features of cardiomyopathy [1], one with non-obstructive hypertrophic cardiomyopathy and two with congestive cardiomyopathy. The others were non-myopathic myocardium with or without myocardial hypertrophy.

All hearts studied were first fixed in 10% formalin. Light- and electron microscopic examinations of the myocardium of the left ventricle, septum and right ventricle were made in the cardiomyopathy cases. For the SEM-observations parts of the ventricles and septum from each heart were trimmed to blocks of about 0.7 cm × 0.5 cm × 0.3 cm. By stripping the endocardial and subendocardial layer with fine tweezers the myocardial layer could be prepared for examination. The tissue blocks were washed in 0.1 M phosphate buffer, dehydrated through an ascending series of acetone and dried by the criticalpoint method.

The specimens were mounted on metal-stubs, coated with gold using a sputter coater (Polaron E 5000) and examined with Jeol SM 1 scanning electron microscope.

Results

Nonmyopathic myocardium always showed trabeculae of almost rounded muscle cells in parallel arrangement surrounded by a network of collagenous and reticular fibers (Figs. 1 and 2).

Capillary branches of the coronary vessels were in close relation with the muscle cells. Through the ruptured sarcolemm bundles of myofibrils, T-tubules and sometimes intercalated disks could be identified with the scanning electron microscope No irregularity was seen in the muscle cells of those hearts with or without myocardial hypertrophy.

All three hearts with cardiomyopathy showed, on the gross specimens, marked endocardial fibrosis of the left ventricle. In agreement with the light microscopic findings in the myocardium from the patient with nonobstructive hypertrophic cardiomyopathy, where complete disorientation, abnormal branching and severe hypertrophy of the muscle cells were observed (Fig. 3A), the SEM showed widened flattened and shortened muscle cells with abnormal branchings running in several directions instead of in parallel (Fig. 3B). Abnormal myofibril orientation already seen in the semi-thin sections could also be

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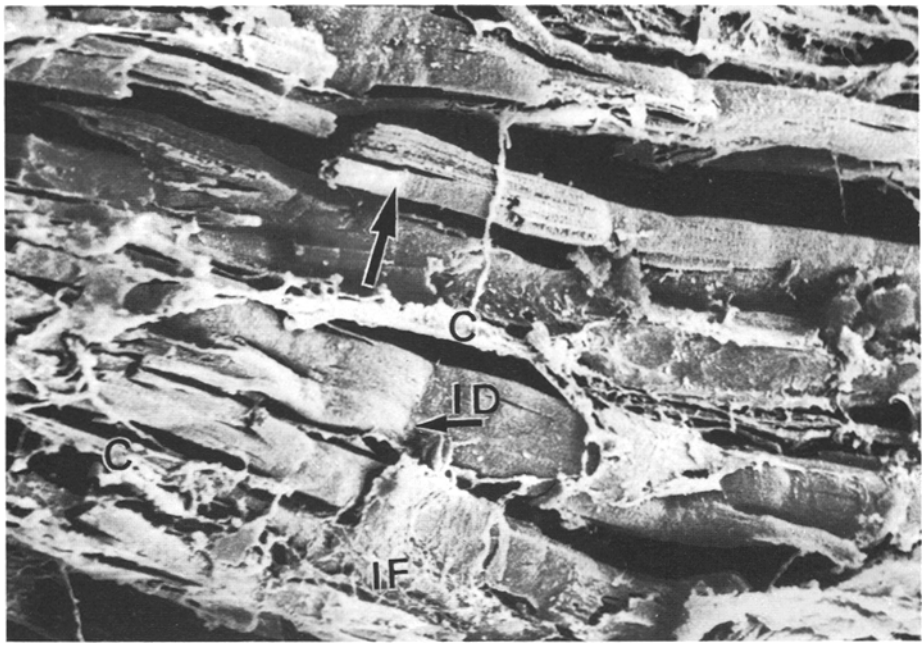

Fig. 1. SEM-view of myocardial cells in heart without cardiomyopathy. Note the parallel arrangement with almost circular cross sections of the muscle cells (arrow) with coronary capillaries (*C*) and reticular and collagenous interstitial fibers (*IF*). Intercalated disc (*ID*). ×1000

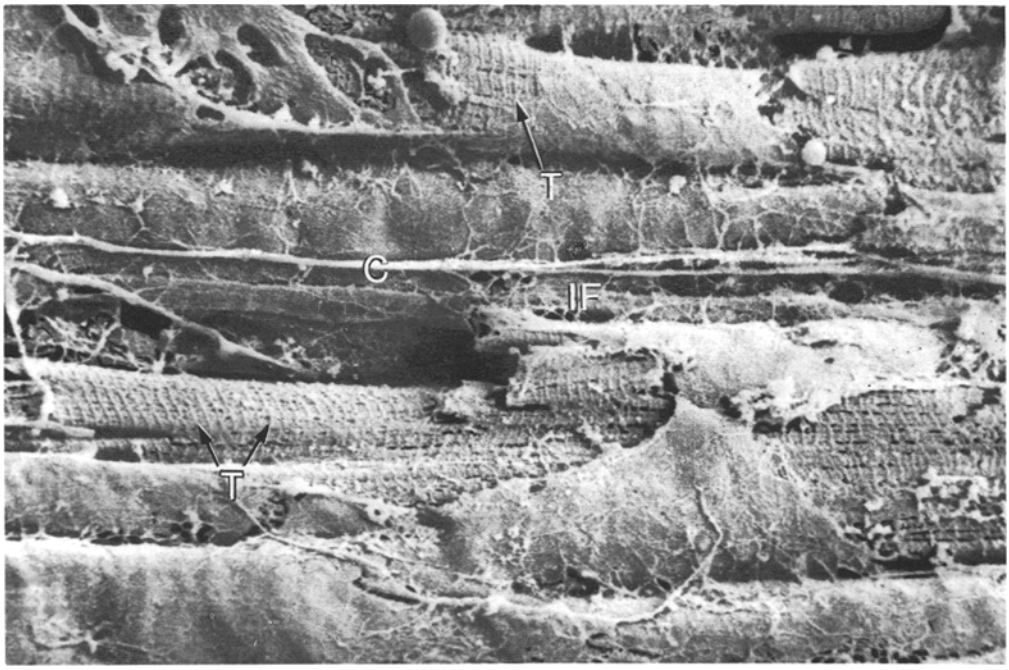

Fig. 2. Hypertrophied heart muscle cells (in aneurysma dissecans Erdheim-Gsell). No disorientation of the myocardial cells or of the myofibrils. Coronary capillaries (*C*) and interstitial fibers (*IF*) surrounding the muscle cells. T-tubules (*T*). ×3000

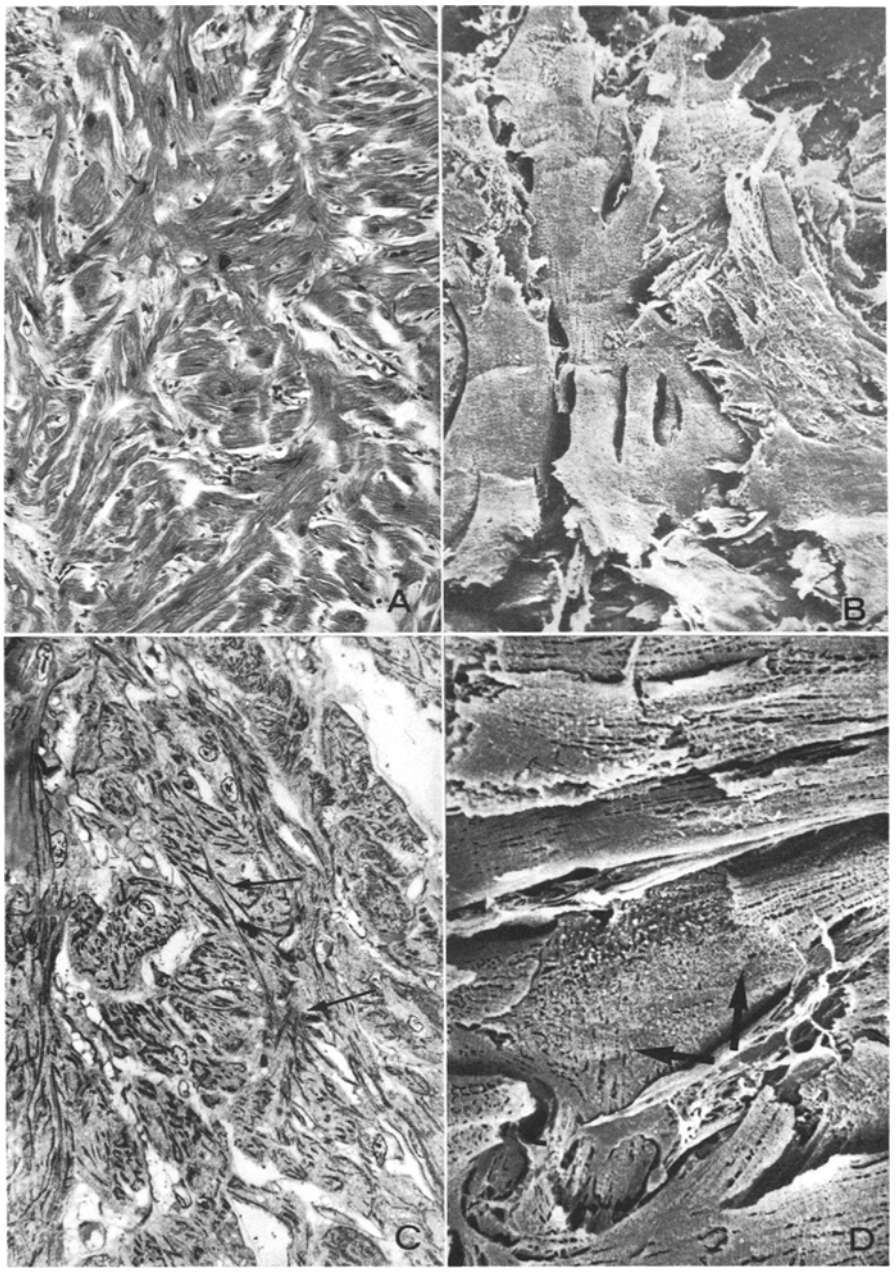

Fig. 3. A Abnormal branching and shortened heart muscle cells in non-obstructive cardiomyopathy. Left ventricle, HW, ×120. **B** SEM-view of the left ventricle in non-obstructive hypertrophic cardiomyopathy showing flattened and abnormal branching myocardial cells. ×450. **C** Random orientation of the myofibrils in the heart muscle cells (arrow). Non-obstructive hypertrophic cardiomyopathy. Semi-thin Section, Toluidine blue, ×300. **D** SEM-view of the disoriented myofibrils in non-obstructive cardiomyopathy (arrow). ×2000

Fig. 4. SEM. Pathological forms and random orientation of the myocardial cells in several layers of the myocardium. Non-obstructive hypertrophic cardiomyopathy. ×1500

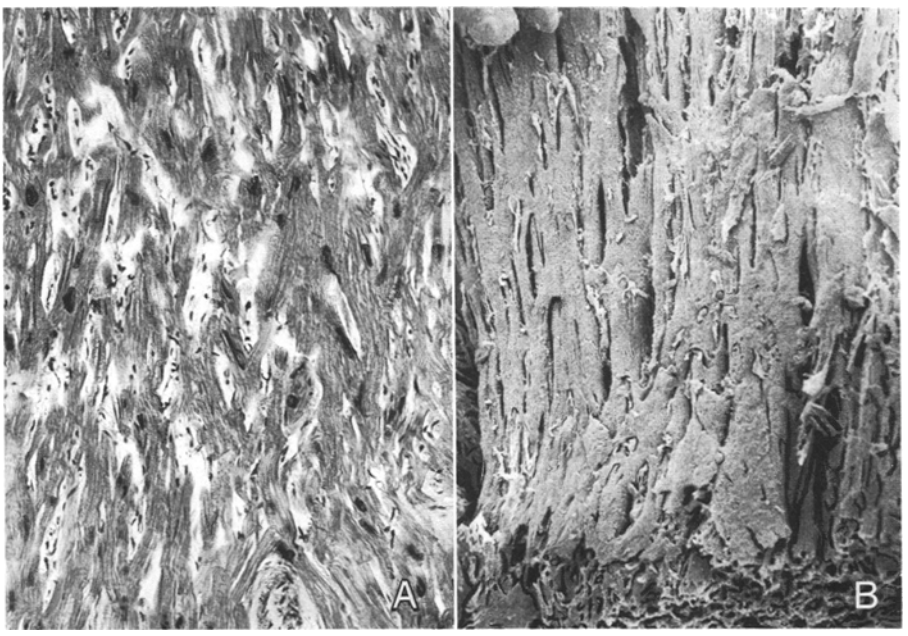

Fig. 5. A More oriented but still shortened and abnormal branched muscle cells of the right ventricle. Non-obstructive hypertrophic cardiomyopathy. HE, ×120. **B** SEM-view of the right ventricle in non-obstructive hypertrophic cardiomyopathy correspond to the light microscopic findings

observed with the SEM (Fig. 3C and D). The almost stereologic SEM-view showed that the abnormal arrangement was not limited to one myocardial plane but could also be found in the deeper parts of the myocardium (Fig. 4).

The features of "myocardial disorientation" were best demonstrated in the wall of the left ventricle and septum. In the wall of the right ventricle the muscle bundles ran in a more parallel direction (Fig. 5A and B).

The myocardium in congestive cardiomyopathy showed no marked abnormality of orientation of muscle cells and myofibrils. In the first patient with congestive cardiomyopathy long runs of attenuated muscle cells, alternating with wavy areas, were the most striking features seen with the light- and scanning electron microscope (Fig. 6A and B). The second patient with congestive cardiomyopathy showed slight hypertrophy of the wavy and longitudinally running muscle cells (Fig. 6C).

Discussion

Cardiomyopathies have been divided in three groups: congestive, hypertrophic (obstructive and non-obstructive) and obliterative cardiomyopathy (Goodwin, 1974; Loogen and Kuhn, 1975). These forms are "idiopathic" or "primary" in contrast to "secondary" forms (McKinney, 1974)

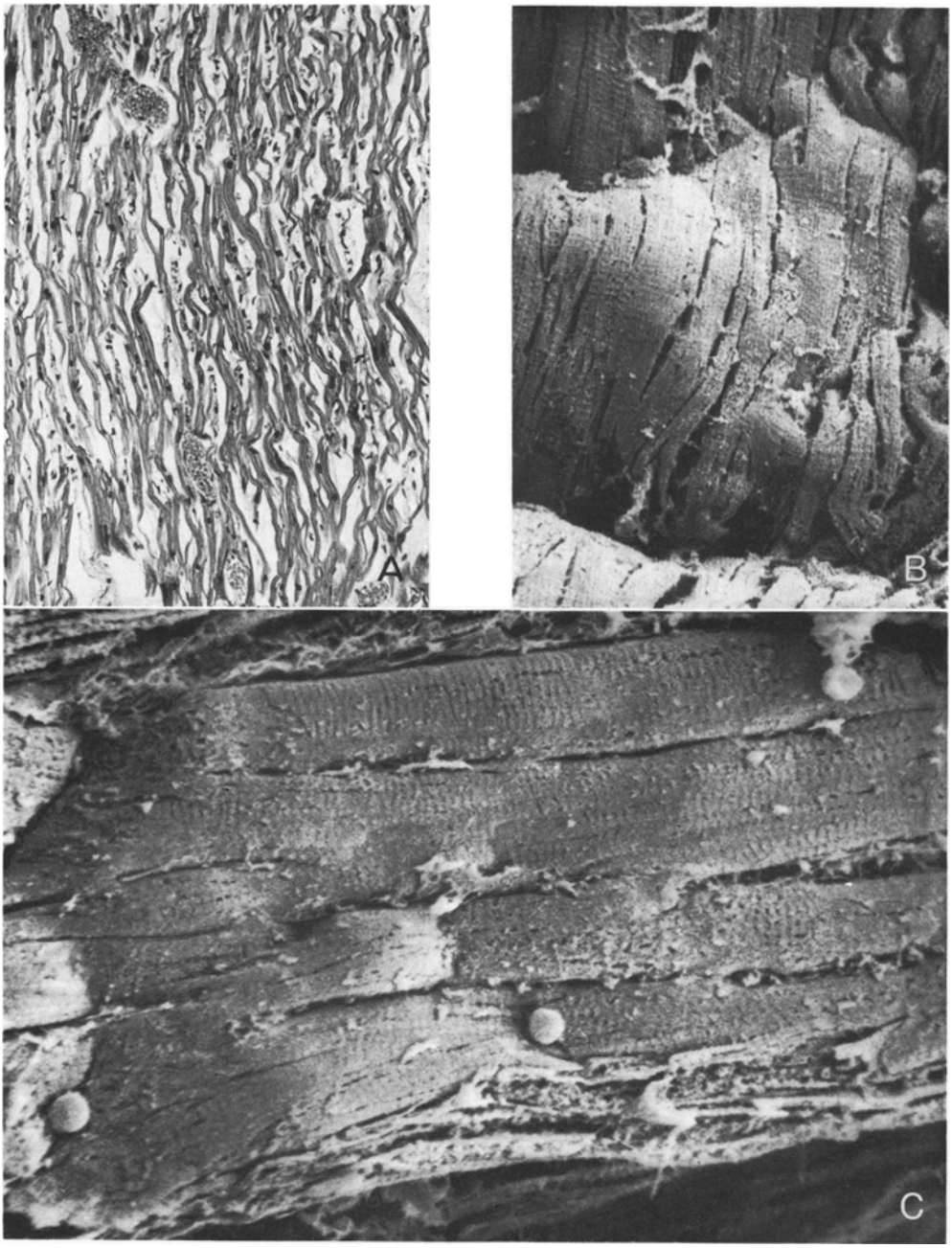

Fig. 6. A Slender wavy muscle cells in congestive cardiomyopathy. HE, ×120. **B** SEM-view of the muscle cells in congestive cardiomyopathy showing the wavy thin muscle cells. ×1000. **C** Congestive cardiomyopathy with slight hypertrophy of the wavy muscle cells. ×3000

With increased interest and knowledge of this disease greater efforts have been made to determine its etiological factors and pathogenesis. Doerr (1974) demonstrating cases with extreme increase of mitochondria proposed a congenital disorder combined with enzyme abnormalities as possible etiological factors. Auto-allergic etiology caused by antibodies against heart muscle sarcolemma (Sack et al., 1975) or viral infection (Doshi and Lodge, 1973) have been suggested by others.

The most significant SEM findings in this study concerned the distinct differences between myocardial structure in hypertrophic non-obstructive cardiomyopathy, in congestive cardiomyopathy or in other disease. The abnormal shape and disarrangement of the heart muscle cells in different layers of the myocardium seen in hypertrophic non-obstructive cardiomyopathy supports a congenital abnormality as a possible cause of this disease. No efficient force can be produced by such a group of diversely oriented cells. Ferrans et al. (1972) discussed whether this disorderly arrangement of muscle cells could be the stimulus to hypertrophy and random myofibrillar orientation in the cells. Such abnormal myofibrils have been observed in myocardial cells at the marginal zone of infarctions (Dusek et al., 1971), in embryonal myocardium (Manasek, 1970) and also in congestive cardiomyopathy (Olsen, 1974). Other ultrastructural changes discribed were non-specific and related to muscle cell hypertrophy (Van Noorden et al., 1971; Ferrans et al., 1972).

The main difference between the obstructive and non-obstructive cardiomyopathy is the distribution of these myocardial abnormalities. In the non-obstructive hypertrophic cardiomyopathy the abnormal architecture was distributed throughout both ventricles, septum and some areas of the left atrium (Moran et al., 1974; Knieriem, 1975). The SEM-observations showed that there were slight differences in severity of the abnormalities between various parts of the left and right ventricles of the same heart in non-obstructive cardiomyopathy. The slight alteration seen with the SEM in the myocardium of congestive cardiomyopathy hearts conformed with former light and electron microscopic findings. No abnormalities of the muscle cells could be observed, the main findings were hypertrophy, degenerative changes and fibrosis (Ferrans et al., 1974; Olsen, 1976).

This study demonstrates that in spite of some artifacts the SEM is a valuable complementary method beside light and transmission electron microscope for studying the myocardium, especially in diseases with structural myocardial disorders.

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