ENDOMYOCARDIAL BIOPSY IN IDIOPATHIC CARDIOMYOPATHY; WITH REFERENCE TO ITS NATURAL HISTORY

By Tadasu Takatsu

For the past seven years we have experienced ninety-four patients with idopathic cardiomyopathy, which refers to subacute or chronic myocardial disease of unknown cause, often associated with endocardial involvement. After routine clinical examinations including cardiac catheterization, endomyocardial biopsy of the right and/or left ventricle was performed by Sakakibara-Konno's bioptome in the majority of the cases to investigate morphological changes of the myocardium.

Sixty-six cases were male and twenty-eight were female. A familial appearance was observed only in four cases. The second and third decades seem to be included much frequently in the present series, and the majority of the cases revealed Class I and II.

After Prof. Goodwin's classification our cases were divided into two types, i.e. hypertrophic and congestive, considering cardiothoracic ratio in chest X-ray, left ventricular hypertrophy in electrocardiogram, left ventricular enddiastolic volume (LVEDV) and pressure (LVEDP) and ejection fraction, although a clear-cut classification was very difficult because of possible shift of the hypertrophic type to the congestive one. The hypertrophic type was observed much more frequently than the congestive one, where six cases of obstructive type were included in the former.

Among the symptoms on admission palpitation was most often encountered; dyspnea, chest pain, fainting, fatigue, arrhythmia, and edema were followed in that order. There were no great differences between the two types except for dyspnea and edema, which were more common in the congestive type.

With respect to the cardiothoracic ratio, about two thirds of the cases showed over 0.50, where the congestive type revealed an enlarged heart in much higher per cent than the hypertrophic one.

Among the electrocardiographic abnormalities left ventricular hypertrophy was observed most frequently; and it was noteworthy that A-V block, right bundle branch block, ventricular extrasystoles and pathological Q waves were found relatively often. Extrasytoles, pathological Q waves, abnormal P, atrial fibrillation and right bundle branch block were observed more frequently in the congestive type.

On phonocardiogram the 3rd and 4th sounds were detected in 54.3% and 38.3%, respectively, accompanied by mild systolic murmurs in about 80%. There seemed no differences between the two types.

Cardiac catheterization revealed decreased cardiac index in about one fourth of the total cases, elevation of enddiastolic pressure of the right and left ventricles in about one third, and prominent atrial kick in the right and left ventricular pressure tracings in about one third and a half, respectively. In the hypertrophic type prominent atrial kick was observed more frequently in the left ventricular pressure tracings than in the congestive type, whereas in the latter that was present more frequently in the right ventricular pressure tracings. These findings suggest that forceful contraction of the left atrium associated with decreased diastolic compliance of the left ventricle might become weak with progress of congestive heart failure.

Endomyocardial biopsy was performed in 42 cases of the hypertrophic type on the right ventricle and in 12 cases on the left ventricle, whereas in 23 cases of the congestive type on the right ventricle and in 10 cases on the left ventricle. By light microscopy the myocardial cells in general revealed hypertrophy, occasionally intermingled with atrophy, degenerative changes, i.e. deformity of nucleus, vacuolar degeneration, scarcity of myofibrils; and in some cases deposit of chemically unknown substances in the sarcoplasmic space; and excessive contraction. Mild to moderate fibrosis in the interstitium and mild thickening of the endocardial layer were also observed. Generally speaking, these features showed no great differences between the two types except for severe hypertrophy, i.e. marked increase in average diameter of the myocardial cells in cross section in the obstructive type and a tendency to fibrosis in the congestive type.

Electronmicroscopically, the myocardial cells showed scarcity of myofibrils, increase in number and destructed mitochondria, increased and dilated sarcoplasmic reticulum, abundant glycogen granules, and in some cases well developed Golgi apparatus, appearance of ergastoplasm, lysosomes, lipofuchsin pigment granules, lipid droplets, dehiscence of intercalated discs, and contraction bands. There were no significant differences between the two types, although these appearances varied markedly individually.

The morphological appearances of the heart found in cardiomyopathies were not specific to the disease because they were also observed in other heart diseases such as valvular disease, congenital heart disease and so forth. Therefore, endomyocardial biopsy might not be of value in this aspect. However, it gave a decisive basis on the diagnosis of endocardial fibroelastosis, amyloidosis and so on. For instance, a high school boy with no symptoms and normal heart in the chest X-ray and electrocardiogram was diagnosed by cardiac biopsy to have endocardial fibroelastosis.

Moreover, there was a case (22-year-old male) without symptoms whose prognosis was known to be poor by endomyocardial biopsy. His electrocardiogram revealed a pattern of bilateral bundle branch block. Biopsied specimens of both ventricles showed diffusely stained or granular substances of histochemically unknown nature filled in the sarcoplasmic space of myocardial fibers. The substances were fine fibrous structures electronmicroscopically, which revealed tubular appearance measuring 50 to 80 A in diameter. About a half year later there appeared recurrent Stokes-Adams attacks. Although he spent normal life with implanted electric pacemaker for further two years, he expired eventually because the myocardium became unresponsive to electric stimulation. At autopsy the peculiar deposits filled the whole sarcoplasmic space of all myocardial cells, which electronmicroscopically revealed many fine tubular structures besides fine fibrous ones found at the first biopsy.

With respect to the course of cardiomyopathy there were some differences between hypertrophic and congestive types. In the hypertrophic type the majority of cases were in Class I and II, in most of which the course was stable or improved with exception of one case with sudden cardiac death. On the other hand, Class II, III and IV yielded over 90% of the congestive type, and some cases became worse during the follow-up period, even with seven deaths.

One expired case of the hypertrophic type was a 14-year-old boy, who showed normal cardiac roentgenogram, nonspecific ST depression in the electrocardiogram, and elevation of enddiastolic pressure only in the right ventricle with normal cardiac index. The

The Third Division, Department of Internal Medicine, Osaka Medical College, Takatsuki, Osaka, Japan.

myocardial cells of the biopsied ventricle revealed moderate hypertrophy with very few degenerative changes. Nevertheless, he expired suddenly on a road a half year later.

Among the seven deaths of the congestive type five died suddenly, one of which was that with deposits of peculiar degenerative substances in the myocardial cells as described previously. The other four cases died unexpectedly on a road, during class at school or during watching television. In the remaining two cases congestive heart failure became refractory to the treatment. It is noteworthy that four of seven cases showed QS patterns in the electrocardiogram, and that the biopsied myocardium showed atrophic changes mixed with hypertrophy and interstitial fibrosis in many cases. One of them with sudden death is as follows:

A 16-year-old high school boy revealed features of congestive type with enlargement of the heart and QS in V_{1-3}, whereas the heart was normal in size two years previously and somewhat enlarged a year ago. By endomyocardial biopsy moderate hypertrophy with degenerative changes of the myocardial cells and slight to moderate fibrosis, but no changes in the endocardium were observed. Electronmicroscopical appearances of the myocardial cells were scarcity of myofibrils, mitochondriosis, dilatation of sarcoplasmic reticulum with ergastoplasms and so forth. The symptoms of Class III were improved to Class II, but he died suddenly during class at school one year later. At autopsy the heart weighed 815 g, both atriums dilated, and both ventricles, especially left ventricle hypertrophied. The thickness of the left ventricular wall was 2.0 to 2.5 cm and the septum with no special thickening of the upper part of the septum. The endocardium was markedly thickened in many areas, which was fibroelastosis histologically. The myocardium revealed marked fibrosis with invasion of elastic fibers from the endocardium. As these findings of the myocardium and endocardium were much advanced as compared to those at biopsy, there might be rapid progress of the disease for one year. At the same time it should be considered the fact that the biopsy could provide only a limited information of localized lesions.

Finally, it must be said that the biopsied cardiac specimens give a good material to investigate etiology of the disease by histochemical and immunological procedures. We maintain a viral-infection theory of the disease, on which Dr. Burch reported many papers. The immunofluorescent techniques were applied to determine viral antigens in the myocardium such as Coxsackie B, ECHO, adeno and so forth, but only one case showed positive reaction for adenovirus antigen. As the results were not coincident with those of Dr. Burch, experimental investigations in animals are now going on in order to determine the reliability of our immunofluorescent technique for detection of viral antigen in the myocardium.