An Epidemiologic and Histopathological Study of Sudden Cardiac Death
in Osaka Medical Examiner's Office

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From 1982 to 1986, 1230 sudden death cases were autopsied in Osaka Medical Examiner's Office. Among them, 810 cases were sudden cardiac deaths (SCD) including coronary heart disease (77%), cardiomyopathy (7%), valvular disease (3%). All SCD cases were dead within 24 hours of the appearance of the fatal symptoms, and most of them (72%) were considered instantaneous death. Many of the fatal symptoms began in bed (31%), at bath (17%), at toilet (8%), or at work (8%). Thirty-four percent of them were thought by themselves or by their families to be healthy before the death. Hypertension (38%), coronary heart disease (13%) and diabetes mellitus (11%) were the major past history recorded. Microscopic observation of the hearts of 200 cases autopsied in 1986 showed various cardiac lesions: hypertrophy, atrophy, degenerations of myocytes, cellular and fatty infiltrations of the interstitium. According to their cardiac lesions and degrees of severity of coronary sclerosis, patients who died suddenly were divided into 8 groups as follows: 1. myocardial infarction (41) 2. myocarditis (6) 3. hypertrophic cardiomyopathy (19) 4. chronic ischemia with severe coronary sclerosis (65) 5. chronic ischemia with moderate coronary sclerosis (27) 6. small vessel disease (18) 7. amyloidosis (1) 8. unknown (23). These results suggest that coronary heart disease and hypertension play an important role in SCD.

Sudden cardiac death (SCD) has been vigorously studied for a long time in various medical fields including forensic medicine, and has attracted a great deal of recent public attention. The cause and mechanisms of SCD must be clarified in order, if possible, to prevent it. First of all, investigation of the circumstances surrounding sudden death cases is necessary. However, such reports are relatively rare in Japan1,2 compared with foreign countries3-7. In this investigation, 1230 autopsy cases of SCD in Osaka Medical Examiner's Office over the last 5 years were epidemiologically investigated. To elucidate the mechanisms of SCD, microscopic observation was performed on the hearts of 200 sudden death patients autopsied in 1986.

METHODS

Among about a thousand autopsy cases per year in Osaka Medical Examiner's Office, 60-70%

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Japanese Circulation Journal Vol. 33, December 1989 1581

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in patients in which the interval between fatal symptoms and death was less than 24 hours. In addition, a microscopic examination was performed on 200 SCD cases autopsied in 1986, mainly using hematoxyline-eosin staining.

RESULTS

An epidemiologic study
There were 1230 sudden death cases which fit the above-mentioned criteria. Among them, the most commonly observed were SCD (810 cases) (66%) followed by diseases of the central nervous system (16%), the respiratory system (6%), the alimentary system (5%) and the vascular system (5%) (88% of which were the rupture of aorta). Other diseases (2%) were also seen.

Sex, age and cause of death
Among these SCD cases, 77% were identified as ischemic heart disease, 7% as cardiomyopathy, 3% as valvular disease, 2% as alcoholic cardiomyopathy, 2% as hypertensive heart disease, 1% as myocardiitis and 8% as other heart diseases. There were 601 males and 209 females, and SCDs were most commonly seen in people in their fifties (Fig. 1).

Time interval between fatal symptom and death
All of the SCD cases were dead within 24 hours of the onset of fatal symptoms: 86% were dead within one hour, and 72% were estimated as instantaneous death, namely clinical events occurring immediately before and during the acute terminal events.

Action at the onset of symptoms
The fatal symptoms began most commonly in bed (33%), not necessarily sleep. They began also in the bath (17%), at toilet (8%), at work

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Sudden cardiac deaths (200)

- Myocardial infarction (41)
  - Myocarditis (6)
  - Amyloidosis (1)
  - Hypertrophic Cardiomyopathy (19)
    - Coronary sclerosis (−) or (+) Small vessel disease (18)
      - Unknown (23)
    - " (++) (27)
    - " (+++) (65)

Fig. 2. Histopathological classification of 200 sudden cardiac deaths autopsied in 1986.

*Japanese Circulation Journal  Vol. 33, December 1989
(8%), during a meal (6%), while walking (5%), during leisure (4%) and at exercise (2%).

Past history and physical condition

Eighty-one percent of sudden cardiac deaths had past histories including lumbago, appendicitis and diseases seeming to have no relation to sudden death. As there were some cases having many past histories, 1 or 2 serious diseases were listed for each case. Hypertension was most commonly seen (38%), and ischemic heart disease (13%), diabetes mellitus (11%) and bronchial asthma (7%) were also observed. As for physical condition of the patients of SCD before death, 34% were thought to be healthy by the families, 37% were outpatients whose conditions were stable, 11% were not in good condition but were not expected to die and 18% had some diseases which were left untreated.

A histopathological study

A microscopic examination of the hearts of 200 SCD cases autopsied in 1986 was performed. Among these, 41 cases were estimated as myocardial infarction, 6 myocarditis, and one amyloidosis. Although the other cases exhibited various cardiac lesions, we could not make an exact diagnosis by histological examination alone. We classified these cases into 5 groups by cardiac lesion and severity of coronary sclerosis (Fig. 2). The severity of coronary sclerosis in the three main vessels was graded according to the degree of stenosis; none (–), slight (+), moderate (++), and severe (+++). If more than 75% of the original lumen was retained, the process was categorized as slight. Vessels with residual lumens ranging from 26 to 74% of their original caliber were graded as moderately involved. When the lumen were reduced to less than 25% of original caliber, the process was estimated as severe.

Myocardial infarction (MI) (41 cases)

Different phases of infarction were observed. Discrete coronary thrombosis was found in only 5 cases, but typical acute myocardial lesions such as bleeding, coagulative necrosis of myofibers, cellular infiltration consisting mainly of neutrophils to the interstitium were found in 41 cases.

Fourteen cases suffered from pericardial tamponades by the rupture of myocardium due to MI. There were 21 males and 20 females aged from 31 years to 85 years (mean age 64.3 ± 14.6 years). The frequency of each degree of severity of coronary sclerosis was as follows; (–) 1, (+) 4, (+++) 14, (++++) 22. Past histories of hypertension were recorded in 8 patients, diabetes mellitus in 2 and angina pectoris in 2. Thirteen patients had complained of chest pain from several hours to a few days before death.

Myocarditis (6 cases)

Infiltration of lymphocytes, plasma cells,
neutrophils and giant cells was seen in the interstitium and sometimes in the epicardial region, both patchily and diffusely. Degeneration of myofibers including myolysis was also seen to a limited extent (Fig. 3). All of these cases considered as myocarditis were males aged from 15 years to 64 years (mean age 42.5 ± 19.3 years). One had a history of chronic hepatitis and another had a history of nephritis.

Amyloidosis (1 case)

A 82 year old man found dead at a public bathroom showed a typical cardiac lesion of amyloidosis (Fig. 4). Amyloidosis were not found in other organs and he had not been diagnosed

*Japanese Circulation Journal  Vol. 33, December 1989*
as suffering from amyloidosis before death.

Hypertrophic cardiomyopathy (19 cases)

Nineteen cases showing chiefly marked hypertrophy and disarray of myofibers which were excluded the presence of myocardial infarction, myocarditis and amyloidosis were defined as the hypertrophic cardiomyopathy group (Fig. 5). In this group, cardiac fibrosis was also frequently seen. Frequency of severity of the degrees of coronary sclerosis was as follows; \((-)\) 6, \((+)\) 1, \((++)\) 7, \((+++\)) 4. They consisted of 14 males and 6 females aged from 15 years to 77 years (mean age 51.7 ± 19.5 years). Only 1 patient had been diagnosed as having hypertrophic cardio-

myopathy before death, and past histories of hypertension were seen in 2, diabetes mellitus in 2 and angina pectoris in 1.

Chronic ischemia with severe coronary sclerosis (65 cases)

In the remaining 134 cases, various cardiac lesions were observed to different extents; hypertrophy, atrophy, degenerations of myocytes including contraction band (Fig. 6), fibrosis, cellular and fatty infiltration of the interstitium, and thickening of the intima of intramural small arteries. Then, these cases were divided into 4 groups by severity of coronary sclerosis. Sixty-five cases had severe coronary sclerosis, and were classified as one group. There were 48 males and 17 females aged from 39 years to 89 years (mean age 63.6 ± 12.9 years). Their past histories were as follows; hypertension 14, angina pectoris 5, diabetes mellitus 5.

Chronic ischemia with moderate coronary sclerosis (27 cases)

Twenty-seven cases having cardiac lesions as described above but moderate coronary sclerosis were classified as another group. In general, the cardiac lesions of this group were similar to those of the severe sclerotic group, but lesions were relatively less severe and less frequent in this group than the former group. There were 15 males and 12 females aged from 40 years to 82 years (mean age 62.2 ± 15.2 years). Past histories of hypertension were seen in 8 cases, diabetes mellitus in 4 and angina pectoris in 4.

Small vessel disease (18 cases)

The remaining 41 cases whose coronary sclerosis was mild or not observed, were divided into two groups by the presence or absence of lesions of intramural small arteries. Among them, 18 cases disclosed moderate narrowings of their lumen (Fig. 7) and were identified as small vessel disease. Cardiac lesions of this group, frequency and severity of hypertrophy and atrophy were similar to these in the two former groups, but fibrosis and interstitial edema of was more extensively seen in this group than the chronic ischemia groups. This group was consisted of 10 males and 8 females aged from 35 years to 77 years (mean age 59.8 ± 10.5 years). Histories of hypertension were seen in 7 cases, angina pectoris in 1 and diabetes mellitus in 1.

Unknown (23 cases)

In the remaining 23 cases, no vascular lesions were observed. Although cardiac changes such as hypertrophy, fibrosis and cellular infiltration were rare in this group, we observed atrophy and vacuolative degeneration of myocytes and interstitial edema in about half of the cases. There were 19 males and 4 females aged from 18 years to 74 years (mean 45.1 ± 17.0 years). Most of them were thought by themselves or their families to be healthy. Past histories of hypertension were admitted in 4 cases, diabetes mellitus in 1 and angina pectoris in 1.

DISCUSSION

To investigate the cause and mechanisms of sudden deaths, it is important to examine the situation of each subject in as much detail as possible. We studied sudden death cases autopsied over the last 5 years in Osaka Medical Examiner's Office, where most sudden death cases in Osaka city (population two million) are examined. Among the sudden deaths, sudden cardiac death (SCD) has been reported to be the most frequent, which was confirmed by the present study (66% of sudden deaths). This is in contrast to the report by Hasuo10 that cerebral stroke is the most common cause of sudden death in Hisayama-cho (small town in Kyushu, its population aged above the twenties is about 5,000). This may be due to the difference of environment or to the method. In the present study, SCD cases were most commonly seen in people in their fifties, and males were susceptible than females (about 3 times as much). They were all dead within 24 hours of the onset of fatal symptoms, and most of them (72%) were thought to be dead instantaneously, which may be ascribed to fatal arrhythmias especially ventricular fibrillation as suggested in the former studies.11-13 Fatal onset was most commonly seen in bed, whether asleep or not, and was also frequently seen at bath and at toilet. It was seen relatively rarely at exercise (2%). It is thought that SCD occurs at any time and in any place as previously reported. In the present study, most of SCD subjects (89%) were believed to be healthy before death and did not expect to die. However, some had past histories of hypertension, diabetes mellitus, angina pectoris etc. Though the data are not shown, some patients (about 30%) complained of general fatigue or chest pain. These prodromal symptoms were also reported by Alonzo14 and Goldstein.15 So, even those who had been considered to be healthy might have had some physical difficulties.

On microscopic observation, ischemic heart
disease was seen to be the most common cause of death. Although it has been frequently suggested that ischemic heart disease is important in SCD, it has been difficult to decide whether the cause of SCD is really myocardial infarction or not. This is because of the difficulty of finding pathological changes in the early phase of infarction. Bouchardy and Majno described “wavy fibers” and “contraction bands” as findings of early infarction. Although these findings were observed in various extents in the present cases, we did not diagnostically classify the cases except for those showing changes as myocardial infarction. We finally diagnosed 41 cases (21%) as infarction, of which only 5 cases showed thrombosis. Many reports have discussed thrombosis in myocardial infarction but the exact reason why thrombosis cannot be seen in all cases of myocardial infarction is unknown. Leary and Kmonicik reported coronary spasm as a mechanism for sudden death. In this study, we paid much attention to the role of coronary sclerosis, so we compared the moderate coronary sclerotic group with the severe group. The severe group was about twice the size of the moderate group, and cardiac lesions were relatively larger in the severe group than the moderate group. This may indicate that an extent of coronary sclerosis develops, the possibility of sudden death increases. Moreover, there were 18 cases showing thickening of the lumen of intramural small arteries. They were considered as small vessel disease, which was reported as one of the causes of SCD but the precise mechanisms were unknown. On the other hand, 19 cases were considered as hypertrophic cardiomyopathy. It is also well known that hypertrophic cardiomyopathy is one of the common causes of sudden death especially in young adults but in the present study, it was also found in the aged. There were also 6 cases of myocarditis and one of amyloidosis in the present study, both conditions have been reported as causes of sudden death. The “unknown” cases have been rigorously examined especially in forensic medicine but their true cause and mechanism remains unclear. In conclusion, coronary sclerosis including that of small vessels was thought to play an important role in SCD.

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*Japanese Circulation Journal Vol. 53, December 1989*