A 17-year Follow-up Study of a Family with Idiopathic Hypertrophic Cardiomyopathy and WPW Syndrome

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SUMMARY

Long term clinical courses of a patient and her family with idiopathic cardiomyopathy and WPW syndrome were described. The mother and her brother (the first generation) had died of heart disease, and 1 sibling had also died suddenly of heart disease when the study began. Seven out of the 8 siblings (the second generation) were followed for 17 years from 1958 to 1976. The 4 siblings had both typical or atypical WPW syndrome and cardiomegaly in 1958, 2 of them died suddenly and unexpectedly, 1 of them died of congestive heart failure, and 1 of them did not have any complaint during the period. One was normal in 1958 but developed cardiomegaly and atypical WPW syndrome in 1976. The other 2 were normal in both 1958 and 1976. The 2 children of the second sibling (the third generation) were followed simultaneously for 15 years. Both had WPW syndrome without cardiomegaly.

It was suggested that a late onset of the disease could occur in the family with young onset, that the clinical course might become different mainly by sudden cardiac death which occurred only in the members with abnormal findings, and that WPW syndrome and cardiomegaly could be inherited or occur together in the same generation but separately in the different generation.

Additional Indexing Words:
Familial hypertrophic cardiomyopathy  Sudden cardiac death  WPW syndrome  Cardiomegaly  Atrial flutter

Familial cardiomyopathy was studied most intensively in this decade since the first report by Evans1) in 1949. It occupied 20-32% of idiopathic cardiomyopathy2)–4) and was inherited by an autosomal dominant gene in most cases.5),6)

It is still difficult, however, to prospect the clinical course and the prognosis of each patient because they are so variable in the reported patients.3),4) Various arrhythmias were observed in familial cardiomyopathy. Wolff-
Parkinson-White (WPW) syndrome was also not infrequent in these patients, but its relation to cardiomyopathy is not clear.

This is a long term follow-up study of a patient and her family with idiopathic hypertrophic cardiomyopathy and WPW syndrome.

**Subjects and Method**

The family consisted of 3 generations. The first generation was of 4 members, the second of 8, and the third of 2. Seven out of 8 siblings in the second generation were followed for 17 years and 2 children in the third generation for 15 years. Each member took physical examinations, ECGs, chest X-rays and laboratory examinations in 1958 and in 1976. One patient was autopsied.

**Results**

*Clinical picture of a female in the second generation as a representative case of the family:*

Patient A.H., a 48-year-old female, was admitted to Tokyo University Hospital because of sudden onset of palpitation and dyspnea with atrial flutter on September 20, 1976 (Fig. 1). She had neither complaints nor abnormal

![Fig. 1. Left: atrial flutter with block at the admission of patient A.H. Right: atrial flutter at 27 years old of the 5th sibling.](image-url)
findings in the cardiac examination in 1957 (Fig. 2). She felt shortness of breath on exertion a few times in 1976, and then had a precordial pain for a few minutes 3 weeks before the admission.

Physical examination showed heart rate 84/min, blood pressure 138/78 mmHg, cardiomegaly, grade 2/6 systolic ejection murmur at apex with

Fig. 2. ECGs and chest X-rays of patient A.H. Upper ECG and left chest X-ray were obtained in 1958, and lower ECG and right chest X-ray in 1976. The lower ECG was recorded with 1/2 voltage scale.
normal heart sounds, normal respiratory sound, no hepatomegaly and no edema on legs.

Urinalysis, blood chemistry, and serological tests were within normal values, and chromosome analysis was normal (46 XX type). The chest X-ray showed cardiomegaly and cardio-thoracic ratio was 0.60 (Fig. 2). After conversion to sinus rhythm, short PQ interval, and wide QRS complex appeared on the ECG. Huge and diffuse left ventricular hypertrophy and slight anterior movement of the mitral valve in systole were observed on the echocardiogram.

By cardiac catheterization, no pressure gradient between the inflow and the outflow of left ventricle was observed at rest. Soon after left ventriculography, however, both the systolic and end-diastolic pressures of left ventricle elevated, and significant intraventricular pressure gradient appeared (Fig. 3). The free wall was 1.6 cm in thickness and the hypertrophy was dis-

Fig. 3. No pressure gradient through aortic valve was observed. Intraventricular pressure gradient in the left ventricle was not found at rest (left), but it appeared significantly (right) soon after left ventriculography which showed diffuse hypertrophy and small cavity at end-diastole. Abbreviation: LVout; outflow of left ventricle, LVin; inflow of left ventricle, Ao; ascending aorta
tributed diffusely from septum and posterior wall to apex. The left ventricle contracted more intensively in the mid portion of the long axis and the cavity at end-diastole was very small and slit-like. The volume of left ventricle calculated by Dodge's method was 97 ml at end-diastole and 14 ml at end-systole. The mitral and aortic valves, chordae, and coronary artery tree were normal.

**Clinical course of the family:**

The mother of patient A.H. (the first generation) died of heart disease at the age of 56. Her brother died suddenly of unknown heart disease at 25 years old. The father and his relatives did not have heart disease (Fig. 4). The first female sibling (the second generation) died suddenly of heart disease at 21 years old. These members died before the examination in 1958. Other 7 of the 8 siblings took cardiac examinations in 1958.

The second female sibling was patient A. H. herself.

The third was a 46-year-old male. He was free from any abnormality in 1958 and 1976 (Fig. 5).

The fourth was a 27-year-old male in 1958. He had no complaint. The blood pressure was 128/60 mmHg. However, systolic murmur, marked cardiomegaly on the chest X-ray, and WPW syndrome on the ECG were observed in 1958. Nine years after the examinations, he died suddenly at the age of 36, although he worked without any symptoms during the period (Fig. 6).

The fifth was a 26-year-old male in 1958 when marked cardiomegaly on
the chest X-ray, WPW syndrome, no heart murmur were observed. Blood pressure was 140/70 mmHg. The cardiomegaly on chest X-ray was not observed at 18 years old, but was pointed out at 19 years old, and WPW syndrome was found at 21 years old. He complained of palpitation, shortness of breath on exertion and edema on legs since the age of 21. Idiopathic cardiomyopathy was suspected by cardiac catheterization and angiography at 23 years old. At the age of 26, congestive heart failure deteriorated with atrial flutter (Fig.
1. He died of severe congestive heart failure with tachycardia attacks at 27 years of age in 1960. At autopsy, the heart weight was 1,350 Gm. Both ventricles showed slight dilatation and diffuse marked hypertrophy. Both atrial walls were also moderately thickened. The 4 valves and coronary arteries were normal. The histological examination showed hypertrophied myocardial cell with patchy fibrosis and necrosis. The His bundle and its bilateral branches were atrophic with fibrosis (Fig. 7).

The sixth was a 40-year-old female. She had no complaint and no abnormality in 1958 and 1976 except mild cardiomegaly on the chest X-ray in 1976 (Fig. 8).
The seventh was a 38-year-old female. In 1958, she had mild edema on legs. Systolic murmur was audible at apex and blood pressure was 120/56 mmHg. The cardiomegaly on the chest X-ray and the WPW syndrome were observed. However, after 1958, she worked without symptoms and any cardiac treatments. The cardiomegaly was unchanged in size and the ECG showed the same findings except sinus arrhythmia in 1976 (Fig. 9).

The eighth was a 17-year-old male in 1958 when he did not have any complaint and his blood pressure was 138/70 mmHg. But the cardiomegaly on the chest X-ray and the WPW syndrome were found. He died suddenly
at the age of 21, 4 years after the examinations. He had no symptoms during these years (Fig. 10).

The second sibling (patient A.H.) had 2 daughters (the third generation). Both took the examinations at 8 and 6 years old respectively, when they were normal in physical examination and chest X-ray but their ECG findings were unknown. In 1976, the older was 23 (Fig. 11) and the younger 21 years old (Fig. 12). Both had no complaint and no abnormality in the physical examination and chest X-ray again, but had WPW syndrome on ECG.
Fig. 9. ECGs and chest X-rays of the 7th sibling. Upper ECG and left chest X-ray were obtained in 1958, and lower ECG and right chest X-ray in 1976. The chest leads of both ECGs were recorded with 1/2 voltage scale.

Discussion

Patient A.H. was normal in 1958 when she was 31 years old, but showed hypertrophic cardiomyopathy at the age of 48 in 1976. However, the cardiac
abnormality in other members of the family were found in the second or the third decade. Inoh\textsuperscript{11) reviewed Japanese cases and stated that the onset of symptoms was most frequent in the second decade. Other statistical studies\textsuperscript{2)–4) also showed the frequent onsets in the second or the third decade. This study evidenced that the late onset of the disease could occur in the family that had frequent onsets in the second or the third decade.

The clinical picture of the studied family was very similar in cardiomegaly, WPW syndrome and young onset of the disease, but the clinical course of each member was variable. Six of the family died of heart disease and 4 out of the 6 died suddenly and unexpectedly. Inoh\textsuperscript{11) reported that sudden cardiac death was seen in 75\% of Japanese patients.

The fourth, the seventh, and the eighth siblings showed cardiomegaly
in 1958. However, the eighth died suddenly at the age of 21, 4 years after the examination, and the fourth died suddenly at 36 years old, 9 years after the examination. The seventh did not have any symptom for 17 years till the age of 38 and the cardiac findings did not aggravate except sinus arrhythmia on ECG in 1976. These 3 siblings did not have any complaint nor any cardiac treatment after 1958. Therefore, the difference in their clinical courses seemed to come mainly from sudden cardiac death. On the other hand, the second, the third, and the sixth siblings were normal in 1958, and sudden cardiac death did not occur in these 3 siblings for 17 years.

Congestive heart failure was also one of the causes of death, but less frequent.11) The fifth sibling died of intractable congestive heart failure with tachyarrhythmia. His clinical course was different from the other members in congestive heart failure lasting for at least 6 years. This patient showed
the most marked cardiomegaly, but it was not clear why he did not die suddenly but suffered for long time.

The ECG of patient A.H. showed normal sinus rhythm in 1958, but changed to atypical form of WPW syndrome. WPW syndrome has short PQ interval, prolongation of QRS complex and delta wave. But atypical form which consists of 2 out of the 3 findings, was not infrequently observed in the reported cases with idiopathic cardiomyopathy.4)

Atypical WPW syndrome of this patient appeared together with cardiomegaly and showed neither normal conduction nor paroxysmal supraventricular tachycardia during 10 months hospitalization. In addition, both cardiomegaly and typical or atypical WPW syndrome were common clinical pictures of the second generation of this family. This suggested that both abnormalities could be inherited or occur in combination.
However, 2 children of the third generation had typical WPW syndrome without cardiomegaly. This suggested that these 2 abnormalities could be separated in a different genetic circumstance. WPW syndrome including atypical form was observed in about 10% of the patients with idiopathic cardiomyopathy. However, familial WPW syndrome without cardiomyopathy was also reported but still infrequent. Therefore, familial WPW syndrome might be inherited or occur more frequently together with cardiomyopathy.

The type of WPW syndrome in this family was variable. Types A and B were 3 and 4 out of 7 patients, respectively. Two of the 7 patients had tachycardia attacks, but both showed only atrial flutter on ECG. This was unusual and different from sporadic WPW syndrome with paroxysmal supraventricular tachycardia. However, its relation to cardiomyopathy was not clear in this study.

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