Serial Electrocardiographic Findings in Acute Myocarditis

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The purpose of the present study was to clarify the characteristic findings of electrocardiogram (ECG) in 11 patients with acute myocarditis. ST elevation without reciprocal ST depression was one of the conspicuous findings in the acute stage. Total QRS amplitudes at the acute stage were significantly decreased as compared to those before illness and during the convalescent stage. Abnormal Q waves were present in 7 patients and disappeared in a short period. The number of leads showing Q waves was inversely correlated to left ventricular (LV) ejection fraction ($r=-0.87$, $p<0.01$). Conduction disturbances were present in 7 patients. Second degree and advanced AV block was transient while bundle branch block remained over months. Corticosteroid treatment was effective for patients who had edematous myocardial thickening and AV conduction disturbances. As the serial ECG findings in acute myocarditis are so characteristic, and this help to differentiate it from acute myocardial infarction (AMI).
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Key words: ST elevation, abnormal Q waves, conduction disturbances, corticosteroid treatment, acute myocardial infarction

Introduction

It is now believed that most cases of acute myocarditis are induced by viral infection (1–3). Electrocardiographic findings of these cases often mimic AMI (4–7). The aim of this study is to clarify some very characteristic findings of ECG in acute myocarditis as well as their clinical significance in the severity of disease and prognosis. In addition to this, the effects of steroid therapy in a few cases with severe heart failure and AV block were also evaluated.

Subjects and Methods

The present study included 11 consecutive patients with myocarditis in the Department of Cardiology, Nagasaki Citizens Hospital (Table 1). They consisted of 9 men and 2 women, mean age being 52 years (range, 15–90 years). The diagnosis of myocarditis was made when new cardiac abnormalities developed following symptoms of an acute viral infection. Left ventricular (LV) endomyocardial biopsy samples were obtained in 7 patients. The mean number of interstitial mononuclear cells was calculated under high-power field and considered to be positive when more than 5 cells were found. Consequently, all 7 patients had positive findings. According to the Dallas criteria (8), 2 patients showed active myocarditis and 5 patients showed borderline myocarditis. Blood samples at the acute and convalescent stage were drawn and assayed simultaneously in 9 patients to detect the serum neutralizing antibody titer to Coxsackie B and echo viruses. Five patients showed a greater than four-fold rising or falling antibody titer. Coronary angiography of 8 patients at the convalescent stage disclosed normal findings in all.

In the present study, each patient underwent clinical examination, serum enzyme sampling, chest X-ray, and ECG. Serial ECG changes were analyzed with special reference to ST-T changes, QRS amplitudes, abnormal Q waves, and conduction disturbances. Ventricular tachycardia was diagnosed when six or more consecutive ventricular premature contractions occurred. ST segment level was measured at 60 msec after the J point. ST elevation of 1 mm or more in the limb leads or left precordial leads and 2 mm or more in the right precordial leads was considered significant. Concerning persistent bundle branch block, ST changes were presumed as abnormal when they demonstrated a shift of greater than 2 mm shift (elevation or depression) without any QRS changes throughout the clinical course. Total limb and total chest lead QRS amplitudes were obtained by adding the amplitudes of the individual leads. Any Q waves >40 msec were considered abnormal.

The paired t test was used in determining changes in QRS amplitudes. Linear regression analysis was employed to examine the correlation between the number of leads in which Q waves appeared and the left ventricular ejection fraction (LVEF).

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Table 1. Patients Profile

Patient No.	Age	Sex	Viral symptoms	Type of virus	Antibody titers First	Antibody titers Second	ECG changes	EF (%)	CAG	Myocardial biopsy	Outcome
1	38	M	+	Coxsackie B_3	8×	64×	+	54	Normal	Positive	Incomplete recovery
2	56	M	+	Echo 13	<4×	32×	+	72	Normal	Positive	Complete recovery
3	15	M	+	Negative			+	70	ND	ND	Incomplete recovery
4	54	M	–	Negative			+	62	Normal	Positive	Death
5	41	M	+	Negative			+	38	Normal	Positive	Incomplete recovery
6	71	M	+	ND			+	53	Normal	ND	Complete recovery
7	48	M	+	Echo 3 Echo 4 Echo 9	<4× <4× <4×	16× 32× 32×	+	51	Normal	Positive	Incomplete recovery
8	40	M	+	Coxsackie B_2 Coxsackie B_3 Echo 17	16× 32× <4×	<4× <4× 16×	+	51	Normal	Positive	Complete recovery
9	57	M	+	ND			+	26	ND	ND	Death
10	67	F	–	ND			+	66	Normal	Positive	Incomplete recovery
11	90	F	+	Echo 3	4×	64×	+	64	ND	ND	Incomplete recovery

ECG: electrocardiogram, EF: ejection fraction, CAG: coronary angiography, ND: not done.

A value of $p<0.05$ and $p<0.01$ was considered significant.

Results

NYHA classification: On admission, all patients except one revealed severe heart failure in NYHA class III or IV (Fig. 1). One patient (patient 4) died of progressive heart failure due to restrictive cardiomyopathy following acute myocarditis on the 228th hospital day. One patient (patient 9) died of repetitive ventricular tachycardia on the 9th hospital day. The remaining 9 patients improved to NYHA class I (7 patients) or class II (2 patients) by the time of discharge from hospital. There were no patients who experienced relapse during the 6 months or longer follow-up period.

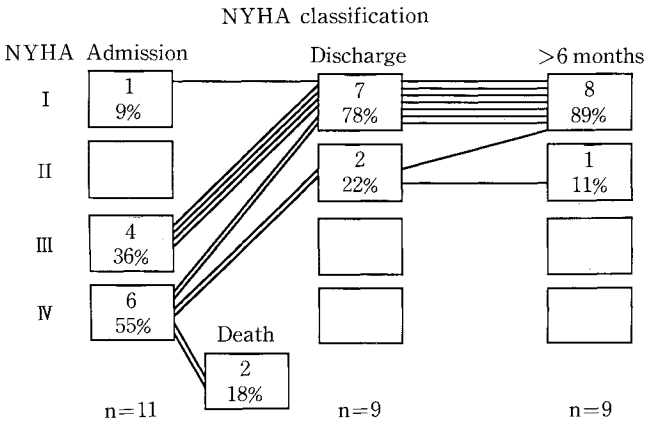

Fig. 1. Clinical course and 6-month follow-up according to New York Heart Association (NYHA) classification.

Electrocardiographic findings: ECG findings are summarized in Fig. 2. All patients had ST-T waves abnormalities. In 7 patients (64%), abnormal Q waves were observed. Low voltage was present in 2 patients (18%). Six patients (55%) had tachyarrhythmia, namely, sinus tachycardia in 5 patients (45%), atrial tachycardia in 2 (18%), atrial fibrillation in 2 (18%) and ventricular tachycardia in 5 (45%). Conduction disturbances were observed in 7 patients. Six patients (55%) had AV block. First degree, second degree, and advanced AV block was

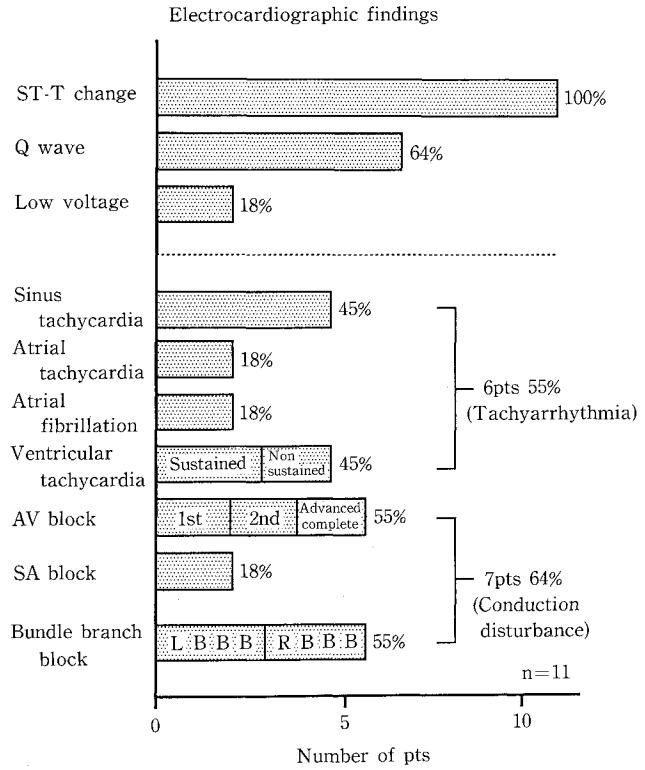

Fig. 2. ECG findings of the 11 patients are summarized. pts: patients, LBBB: left bundle branch block, RBBB: right bundle branch block.

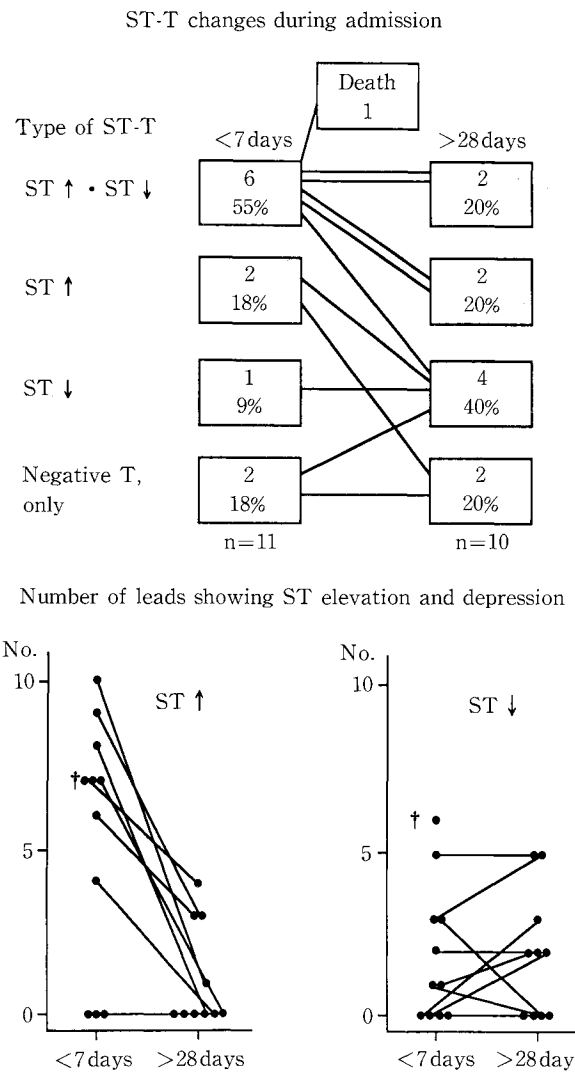

Fig. 3. ST elevation is prevalent at the acute stage (upper and lower left panel) and often replaced by ST depression and negative T waves during the convalescent stage (upper and lower panel).

observed in 2 patients, each. Bundle branch block occurred in 6 patients (55%) with 3 having right and 3 having left bundle branch block.

ST-T changes: ST elevation, observed in 8 patients, was the predominant finding in the acute stage (Fig. 3; upper panel). These patients did not exhibit reciprocal ST depression except for one. From the acute to the convalescent stage, the number of leads showing ST elevation was obviously decreased (Fig. 3; lower left panel) and was often replaced by ST depression and negative T waves (Fig. 3; upper and lower right panel).

QRS amplitudes: QRS amplitudes of limb and chest leads at the acute stage were compared to those before illness and during the convalescent stage (Fig. 4). ECGs before illness which were recorded for health screening were available in 7 patients. Total QRS amplitudes in limb and chest leads showed a significant decrease in the acute stage as compared to those before illness (limb lead 4.7 versus 2.8 mV; $p<0.05$, chest lead 11.9 versus 7.7 mV; $p<0.01$). Furthermore, total QRS amplitudes were significantly increased during the convalescent stage as compared to those at the acute stage (limb lead 3.0 versus 3.9 mV; $p<0.05$, chest lead 7.8 versus 9.2 mV; $p<0.01$). It was clearly demonstrated that the presence of pericardial effusion did not interfere with these results.

Abnormal Q waves: Abnormal Q waves were present in 7 patients and distributed in various regions. The area of ST elevation seemed to have no relation with the appearance of Q waves as shown in Fig. 5. The appearance of Q waves was rather transient as shown in the upper panel of Fig. 6. Q waves disappeared within three days in 4 patients. The number of leads showing Q waves demonstrated an inverse correlation with LVEF on the echocardiogram (Fig. 6; lower panel). In the most seriously ill patient, the Q waves extended up to 6 leads as shown in Fig. 5; he died on the 9th hospital day.

Conduction disturbances: Time course of conduction disturbances could be evaluated in 6 of 7 patients (Fig. 7). Both AV block and bundle branch block were documented in all patients except one (patient 8) through the clinical course. Second degree and/or advanced AV block were observed in 4 patients and disappeared within 5 days, while bundle branch block remained for months.

Illustrative case: Patient 7 (Fig. 8). This patient, a 48-year old man, was admitted to our hospital because of syncope and pulmonary edema following upper respiratory infection. The

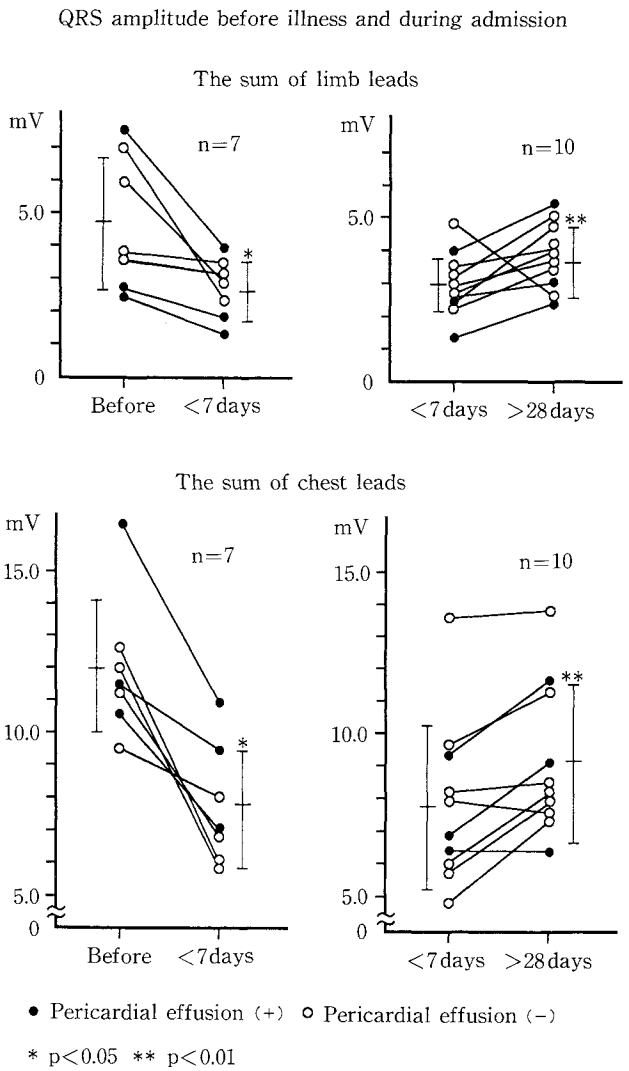

Fig. 4. The sum of QRS amplitudes in limb and chest leads at the acute stage significantly decreased as compared to that before illness and during the convalescent stage.

ECG on admission showed a complete AV block. Three days later, advanced AV block disappeared but both conducted and nonconducted supraventricular premature contractions frequently occurred. The conducted beats showed the prolonged PR intervals with Wenckebach phenomenon and a complete

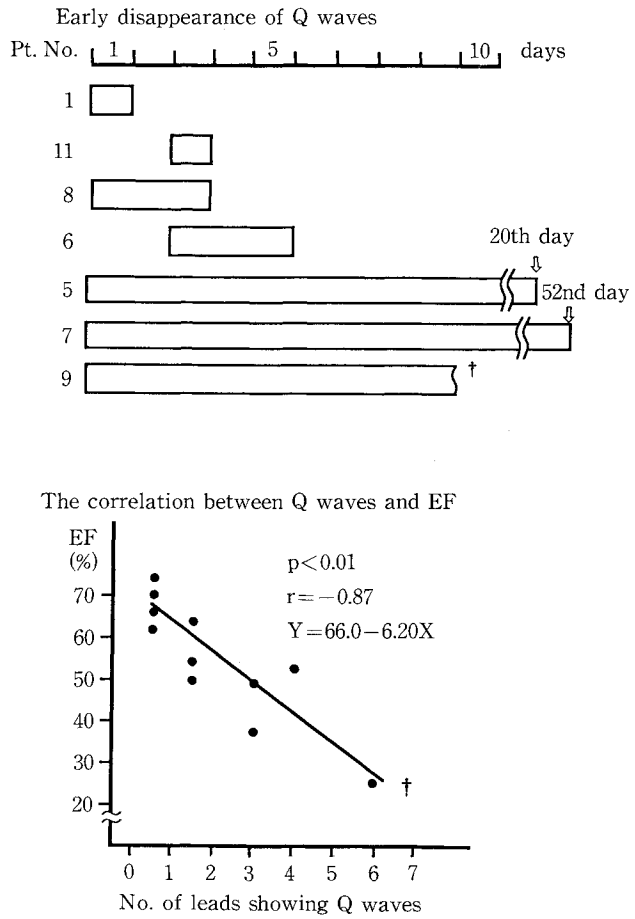

Fig. 6. Q waves in myocarditis are transient (upper panel). Lower panel indicates an inverse correlation between the number (No.) of leads showing Q waves and ejection fraction (EF).

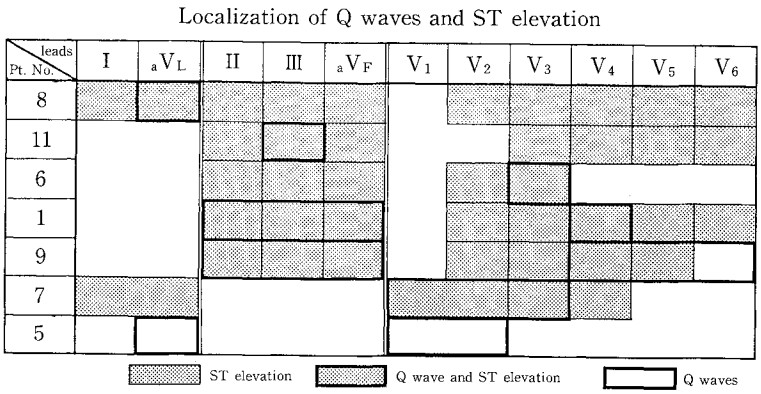

Fig. 5. Q waves are present in 7 patients and distributed in various regions.

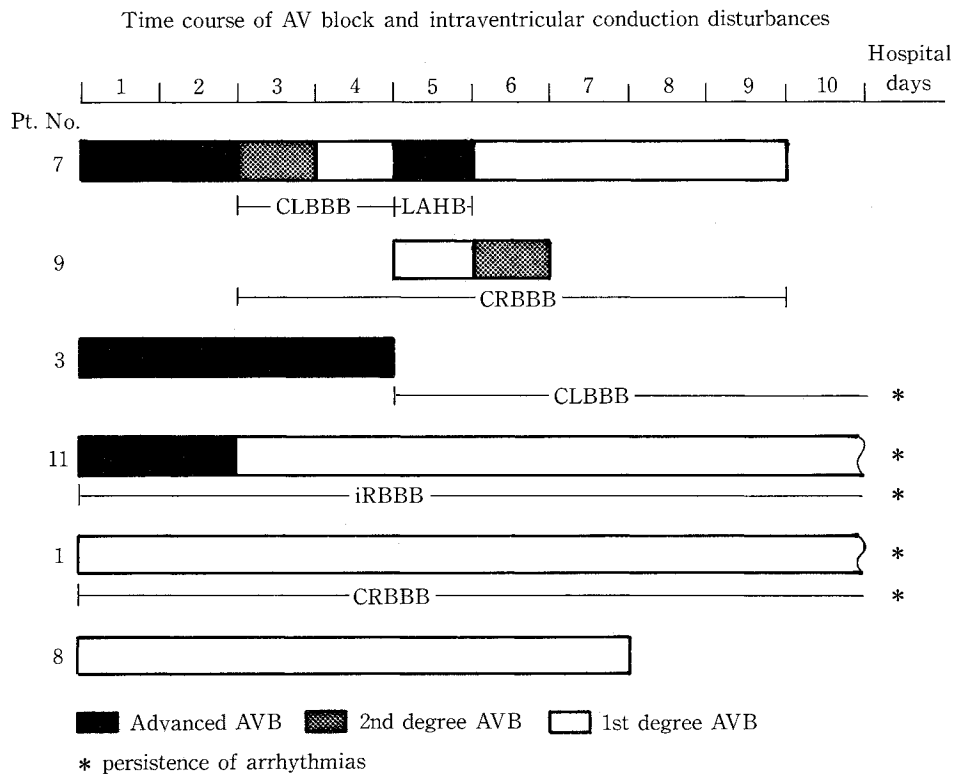

Fig. 7. Time course of conduction disturbances is illustrated. pt: patient, CLBBB: complete left bundle branch block, LAHB: left anterior hemiblock, CRBBB: complete right bundle branch block, AVB: AV block.

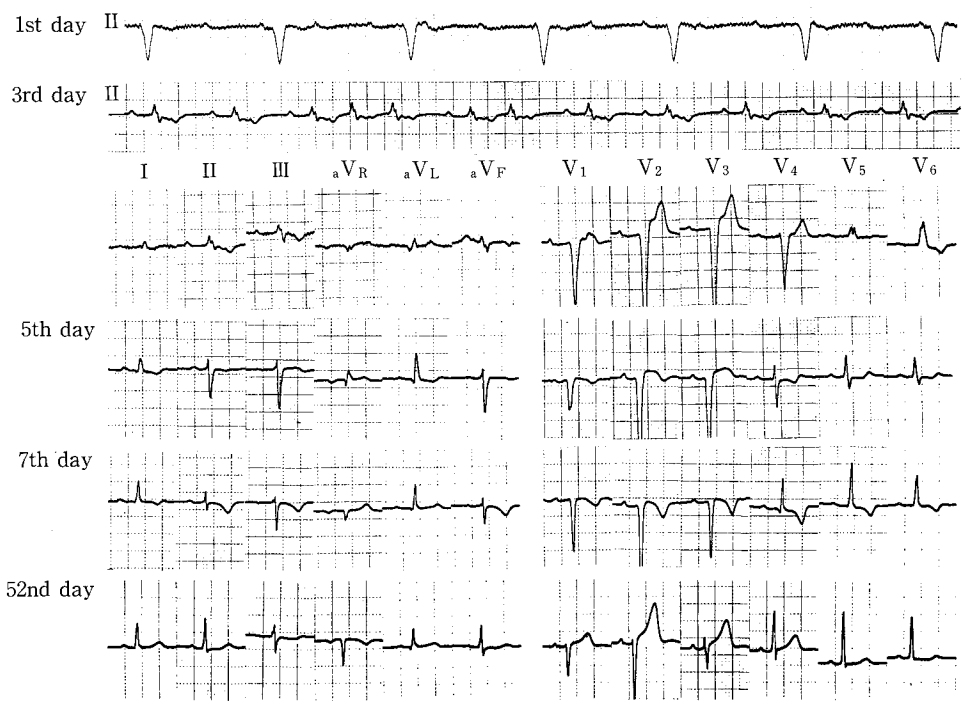

Fig. 8. Serial changes of conduction disturbances and Q waves in patient 7 are illustrated.

left bundle branch block. Five days later, conduction disturbances considerably improved, presenting a left anterior hemiblock. QS pattern was also noted in the right precordial leads. Seven days later, conduction disturbances were much more improved and only a slight PR prolongation (0.22 sec) was present, however, Q waves were apparently demonstrated. Fifty-two days later, Q waves completely disappeared.

The effects of steroid therapy: Three patients received corticosteroid treatment because of severe heart failure and conduction disturbances. Two of these patients, given large doses of intravenous methylprednisolone (500–1,000 mg per day), are illustrated in Fig. 9. Patient 8 was administered methylprednisolone from the 3rd hospital day. Prolonged PR and QRS intervals were normalized on the 8th hospital day (PR 0.28→0.16 sec. QRS 0.12→0.10 sec). Striking improvement was also noted on the echocardiogram; myocardial thickening diminished and LVEF increased with the initiation of steroid therapy. Patient 9 was started on methylprednisolone on the 5th hospital day because of PR prolongation, QRS widening, and cardiogenic shock. Although transient Mobitz type 2 AV block was noted on the 6th hospital day, conduction disturbances disappeared and the improvement of myocardial thickening and LVEF were also noted on the 8th hospital day. However, he died of repetitive ventricular tachycardia on the 9th hospital day. Another patient, patient 1, had first degree AV block, complete right bundle branch block, and myocardial thickening, like the above 2 patients. He was treated with oral prednisolone at an initial dose of 30 mg per day, gradually tapering off to a dose of 5 mg per day. Myocardial thickening was resolved and LV function improved within 3 days with this treatment. However, conduction disturbances remained unchanged.

Discussion

The average incidence of myocarditis in autopsy cases is 0.15% (9); the annual incidence of myocarditis cases has apparently increased from 1974 in Japan (9). Coxsackie B viruses are the most common agents (1–3). In addition to the Coxsackie B viruses, echo viruses and other members of the picorna virus group can cause myocarditis because they are highly cardiotropic for man (10, 11). The main mechanisms by which viruses might produce myocarditis have been considered to include direct viral invasion of myocardium and immune-mediated myocardial injury (11, 12). It is widely accepted that clinical findings of myocarditis may mimic AMI with chest pain, electrocardiographic ST changes, and serum creatinine kinase elevation (4–7). Thrombolytic therapy due to mistaken

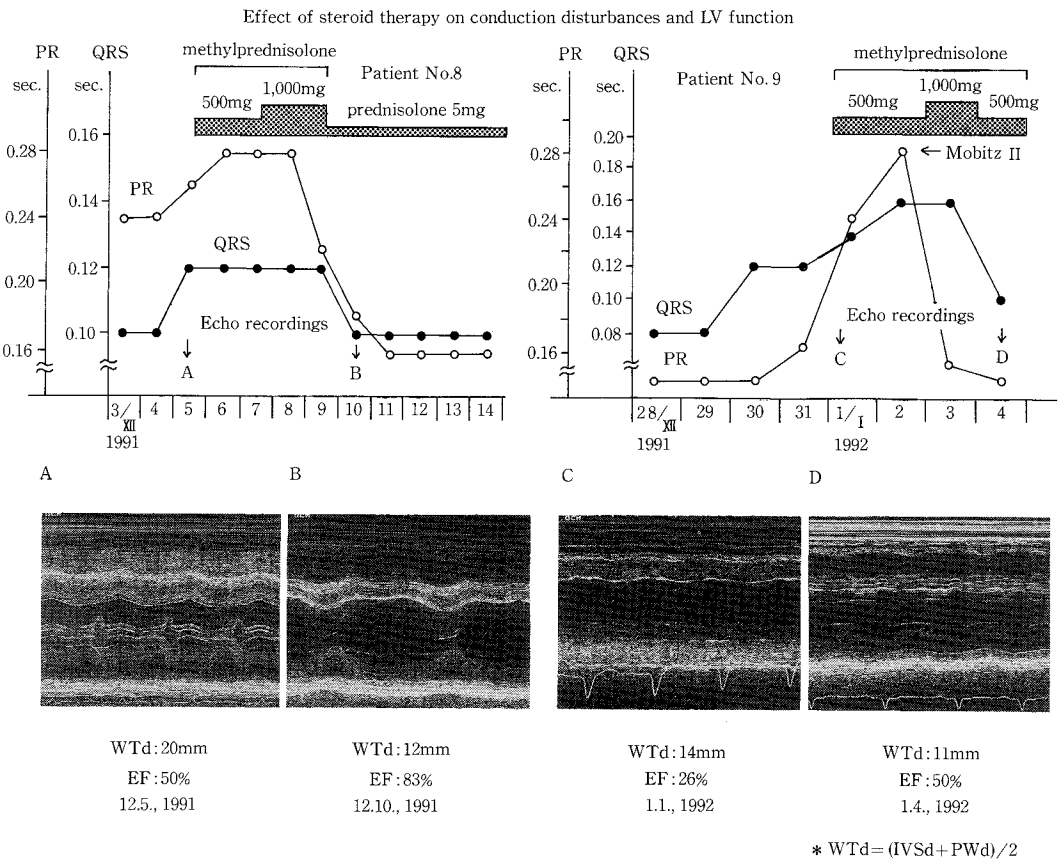

Fig. 9. Effects of corticosteroid treatment are evaluated in patient 8 (left panel) and 9 (right panel). WTd: wall thickness in diastole, IVSd: interventricular septum thickness in diastole, PWd: posterior wall thickness in diastole, EF: ejection fraction.

diagnosis of myocardial infarction can cause a fatal result such as a pericardial tamponade (13).

All of the present 11 patients showed new cardiac abnormalities which included heart failure, cardiogenic shock, and various cardiac arrhythmias. Heart failure was the most common complication. Ten patients (91%) were in NYHA class III or IV. Preceding viral symptoms were observed in 9 patients (82%). All 8 patients who underwent coronary angiography showed no atherosclerotic lesions. However, coronary angiography can not be used as a definite discrimination between the patients presenting myocarditis and those presenting with AMI with normal coronary arteries. While only a few patients in myocarditis demonstrate segmental wall motion abnormalities at the convalescent stage (5), AMI patients inevitably show these abnormalities. The present 8 patients who underwent coronary angiography did not show LV asynergy on left ventriculography in the convalescent stage. Therefore, this finding strongly favored the diagnosis of myocarditis. The diagnosis was further confirmed by a four-fold or greater changing viral antibody titer and/or histological examination of endomyocardial biopsy specimen. It should be noted that serial ECG findings are important to lead to correct diagnosis of myocarditis and treatment.

Characteristic ST-T changes were present in all 11 patients. Heart rate might affect ST depression or elevation. Heart rate during the acute stage tended to be more rapid than that during the convalescent stage. However, the difference in the heart rate of these two stages was not so striking (80 versus 71 bpm; NS). Consequently, heart rate-dependent ST changes might be negligible in this series. Widespread ST elevation which could not be explained by coronary artery distribution was prevalent at the acute stage. A clear relation could not be found between the leads showing ST elevation and showing Q waves in this study. Therefore, the mechanism of ST elevation might differ from that of myocardial infarction. Severe inflammatory change of myocardium and/or pericardial involvement might contribute to ST elevation. Eight of the present patients with ST elevation did not show reciprocal ST depression except one. Previously, only two cases of myocarditis who had reciprocal ST depression have been reported (6, 7). ST elevation without reciprocal ST depression is quite distinct from AMI and can be a diagnostic hallmark in myocarditis.

QRS amplitudes at the acute stage were significantly decreased as compared to those before illness and during the convalescent stage. Pericardial effusion may be considered as a factor in the decreased QRS amplitudes. However, in the present cases, decreased QRS amplitudes were observed regardless of pericardial effusion. Interstitial edema and inflammatory myocardial lesion may also have been associated with this finding.

Abnormal Q waves had been considered to be relatively rare findings (3). In previous reports (1–3), the frequency of abnormal Q waves ranges from 0 to 14% in myocarditis. Abnormal Q waves (occurring in 7 patients), however, was a common finding in the present study. It might be emphasized that Q waves show only a transient appearance in myocarditis. Likewise, Sainani et al (1) and Smith (2) found that 2 of 2 patients and 2 of 3 patients having Q waves were transient, respectively. Because of early disappearance of Q waves, frequent ECG recordings might be essential. Another important finding is that Q waves have a close relation to LV function. An inverse correlation was clearly observed between the number of leads showing Q waves and LVEF. Impaired LV function during the acute stage improved to a normal level until the convalescent stage. It is well known that the majority of Q waves in myocardial infarction persist for a long period (14). The fact consequently indicates an irreversible myocardial lesion. It is presumed that early disappearance of Q waves indicates a reversible myocardial lesion in cases of myocarditis. Q waves might disappear on resolution of inflammatory process. We speculate that Q waves in myocarditis might reflect the transiently decreased electrical and mechanical activity in those myocardial lesions, and the Q waves do not necessarily imply cellular necrosis.

Conduction disturbances are quite common findings as compared to myocardial infarction. Kawamura et al (15) found that conduction disturbances occurred in 43% of 214 patients, including 25% with complete AV block. The present study revealed that conduction disturbances were present in 7 patients (64%). AV block and bundle branch block were frequently observed in the same patients as described in Fig. 7. Second degree and advanced AV block were transient, but bundle branch block did not disappear during the illness except in one patient (patient 7).

Immunosuppressive treatment is controversial in myocarditis (12, 16–18). Paradoxical results are noted between experimental and clinical studies. Experimental viral infection in mice reveals that the administration of cortisone results in extensive and disseminated myocardial necrosis (16). Steroid-induced impairment of interferon production may be related to enhancement of the lesion (12). Several clinical studies, however, have revealed that histologic findings and LV function are often improved by immunosuppression (17, 18).

In the present study, 3 patients were given large doses of corticosteroids because of intractable heart failure and conduction disturbances. Echocardiographic findings of all 3 patients showed poor LVEF and LV thickening. LV thickening was remarkable in 2 patients and echocardiographically interpreted as reflecting severe interstitial edema. Prolonged PR and QRS intervals were rapidly shortened in 2 patients by corticosteroid treatment (Fig. 9). Likewise, in all 3 patients, LV thickening diminished to normal values and LV function strikingly improved within 7 days of the initiation of therapy. Since natural course of LV thickening gradually disappeared months later in myocarditis (19), these effects were considered attributable to corticosteroids. The most severe patient (patient 9) whose ejection fraction was 26% died of repetitive ventricular tachycardia. Although the relation between corticosteroid treatment and ventricular tachycardia is uncertain, rapid intervention in inflammatory process by this agent might cause electrical instability leading to ventricular tachycardia.

Corticosteroids are not necessarily given to all patients with myocarditis because the majority of the patients show clinical

improvement by usual management. This therapy should be restricted to fluminant myocarditis characterized by refractory heart failure.

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