CASE REPORT

A patient with sustained ventricular tachycardia : identification of a responder to amiodarone using signal-averaged electrocardiogram

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Abstract : A75-year-old man suffered sustained ventricular tachycardia with syncopal attack. Ventricular tachycardias appeared repeatedly, and an electrical defibrillator was used after an anti-arrhythmic drug, such as lidocaine or mexiletine, proved ineffective. The tachycardias had multiple origins, and the signal-averaged electrocardiogram (SAECG) showed ventricular late potential before the administration of amiodarone. After administration, the filtered QRS and duration of the late potential increased, but the recurrence of tachycardias was suppressed. The reason for this is thought to be that amiodarone blocked the sodium channel and delayed conduction, consequently blocking reentry, because amiodaron has antiarrhymic properties with a prolongation of refractoriness and minimal effect on conduction velocity in ventricular myocardium, and inhibits sympathetic activity, and blocks L-type calcium channel besides the depression of the fast sodium channel. In this case, SAECG predicted to some degree whether or not this patient's ventricular tachycardia would respond to amiodarone.

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Keywords **:** *amiodarone, signal-averaged electrocardiogram, ventricular late potential, ventricular tachycardia.*

INTRODUCTION

Meta-analysis has shown that amiodarone treatment significantly inhibits ventricular arrhythmias in cases of post-acute myocardial infarction and chronic heart failure(1-5). Amiodarone decreases arrhythmic death caused by non-ischemic heart failure, thereby improving the total mortality rate. Furthermore, this drug may be able to control ventricular arrhythmia during the electrically unstable stage caused by acute myocardial infarction (1-5).

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However, amiodarone does not control all lethal ventricular arrhythmias, and it does not improve prognosis unlike the case with the implantable cardioverter defibrillator. Therefore, the application of both amiodarone and an implantable cardioverter defibrillator should be considered in patients whose cardiac dysfunction causes sustained ventricular arrhythmias (6).

If the mechanism underlying amiodarone's suppression of ventricular tachycardias is easily identified, it might be possible to delay implanting the cardioverter defibrillator. In the present study, we report that a patient could be identified as a responder or nonresponder to amiodarone treatment for ventricular tachycardia by using signal-averaged electrocardiogram (SAECG). We also found that ventricular tachycardia was suppressed by amiodaron.

CASE REPORT

A75-year-old man was referred to the Tokushima University Hospital because of a syncopal attack. The patient, whose family had no history of sudden cardiac death, had noted a previous syncopal attack on October 10, 2003, during a walk, and was transported to the nearest emergency hospital. There, ventricular tachycardia was recognized and, after an anti-arrhythmic drug (sodium channel blocker, such as lidocaine or mexiletine) proved ineffective, an electrical defibrillator was used to obtain a normal sinus rhythm. Thereafter the patient experienced repeated ventricular tachycardias. After 7 days at the emergency hospital, he was referred to our cardiovascular department for further examination.

At his physical examination, the patient's pulse was 54/minute and regular, and his blood pressure was 120/60 mmHg. In auscultation, no heart murmurs were heard and breathing sounds were normal. His abdomen was flat and soft, and his liver and spleen were not palpable. No edema was found in the lower limbs. Except for the increase in brain natriuretic peptide (BNP, 486pg/dl), there were no abnormalities in the patient's blood biochemical data, which were as follows: leukocyte count 4800/μl, erythrocyte count 486×10^4/μl, hemoglobin 13.4g/dl, hematocrit 42.7%, platelet count 20.8×10^4/μl, glutamic oxaloacetic transaminase (GOT) 45U/L, glutamic pyruvic transaminase (GPT) 39 U/L, lactate dehydrogenase 250U/L, alkaline phosphatase 244U/L, gamma-glutamyl transferase 34U/L, creatine kinase 85U/L, total bilirubin 0.5mg/dl, total protein 6.9mg/dl, total cholesterol 147mg/dl, triglyceride 176 mg/dl, HDL-cholesterol 29mg/dl, blood urea nitrogen 12mg/dl, creatinine1.22mg/dl, Na 142 mEq/L, K 4.5mEq/L, Cl 104mEq/L, C-reactive protein 0.06 mg/dl.

The patient's electrocardiogram (ECG) taken at admission to our department is shown in Figure 1. Negative P-waves appeared in leads II, III, and and aV_F, and the QRS axis showed left-axis deviation and a deep S-wave appeared in lead V_6. In chest X-ray (Figure 2), the cardiothoratic ratio was 61%, demonstrating cardiomegaly. However, there were no findings of pulmonary congestion.

A standard 12-lead ECG during a sustained ventricular tachycardia is shown in Figure 3. The patient's heart rate was 255/minute, and QRS showed left-axis deviation and right bundle branch block. The echocardiogram in the sinus rhythm demonstrated that the left ventricular endo-diastolic dimension (LVDd) was 5.8cm, the left ventricular endo-systolic dimension (LVDs) was 3.9cm, the thickness of the interventricular septum was 24.9mm, the posterior wall of the left ventricle was 11.4 mm, fractional shortening was 33%, and the ejection fraction of the left ventricle was 57%; in addition, hypertrophic cardiomyopathy (asymmetric septal hypertrophy) was recognized. In the coronary angiography, no significant stenosis was seen in either the left or the right coronary artery.

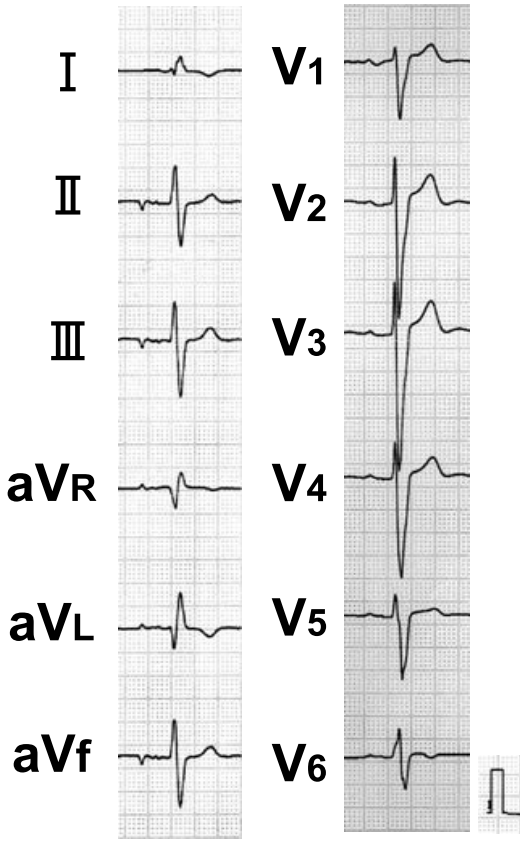

Figure 1 Patient's electrocardiogram at admission.

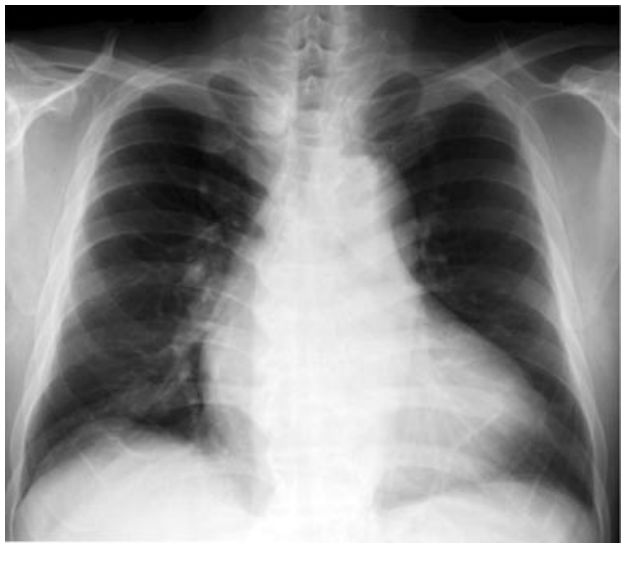

Figure 2 Chest X-ray at admission.

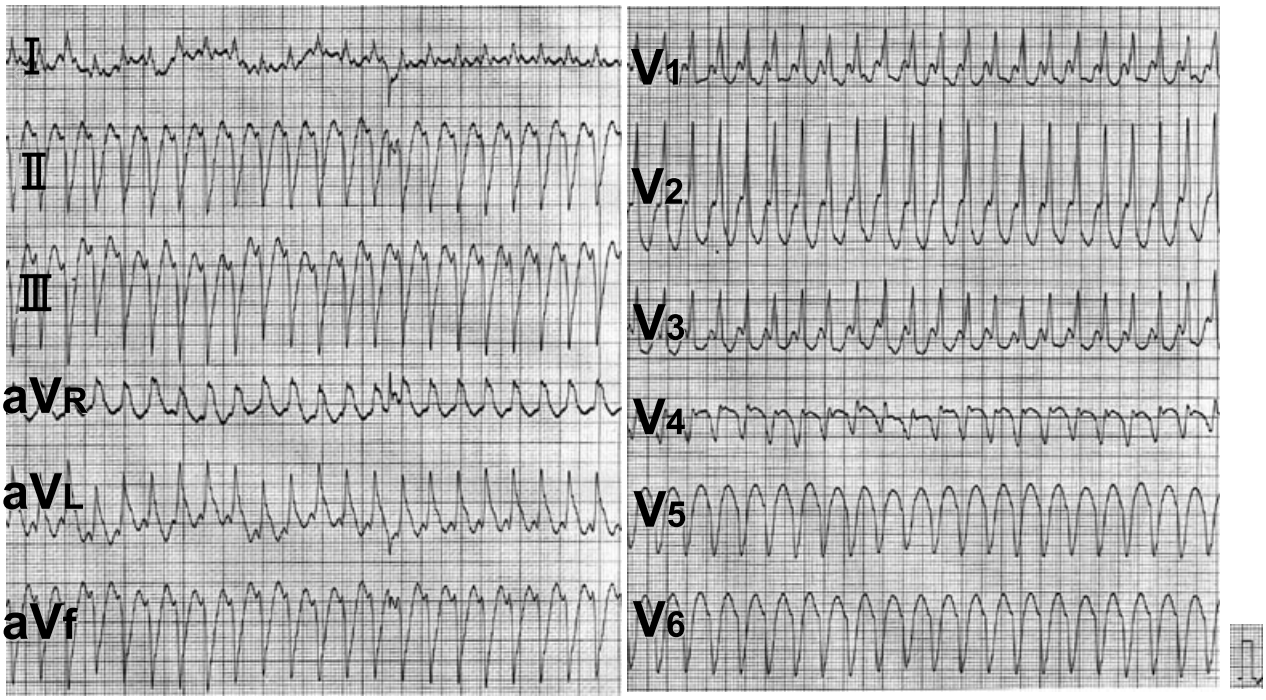

Figure 3 Standard 12-lead ECG during sustained ventricular tachycardia.

Figure 4 shows body surface maps of two types of ventricular extrasystole. These maps were recorded during a clinical spontaneous attack using a multi-purpose electrocardiograph (VCM-3000, Fukuda Denshi Co., Ltd., Tokyo, Japan). In Figure 4a, the minimum was located at the G-5 lead and maximal at the D-4 lead. The origin of the ventricular arrhythmia was predicted to be the anterior wall of the left ventricle to the mid-base of the septum. In Figure 4 b, the lateral base of the left ventricle was the site of origin of the ventricular arrhythmia because the minimum was located at the I-5 lead and the maximum at the F-3 lead.

SAECG was recorded using a VCM-8000 electrocardiograph (Fukuda Denshi Co., Ltd., Tokyo, Japan). Using the vector magnitude method reported by Simson *et al*.(7), signals obtained by bipolar leads corresponding to the three axes of the X, Y, and Z leads of Frank leads were averaged to obtain values for $(X^2+Y^2+Z^2)^{1/2}$. Signals from 256 heartbeats were averaged using a high-cut filter (300 Hz) and a low-cut filter(40 Hz). Three parameters were measured : 1) the filtered-QRS (f-QRS) duration (in milliseconds),

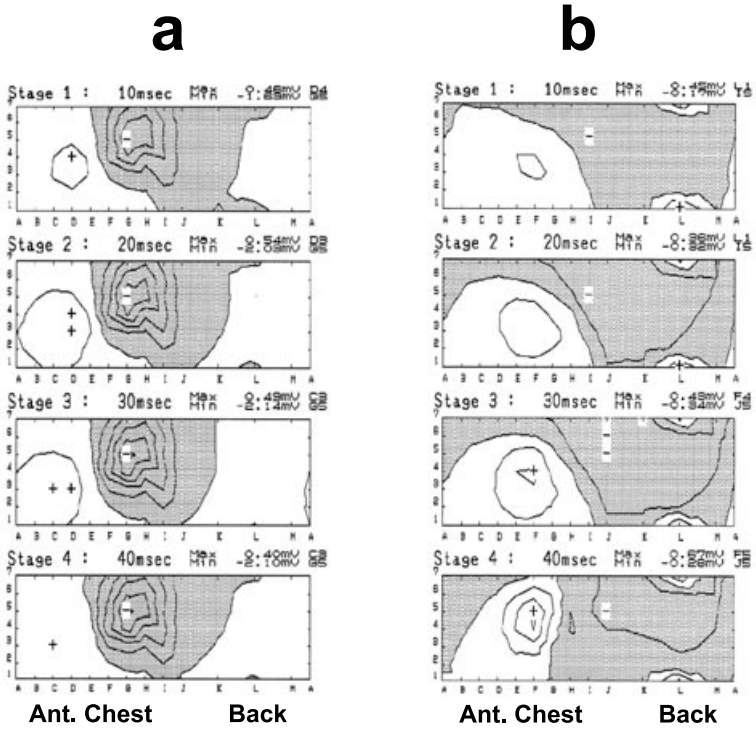

Figure 4 Body surface maps 10, 20, 30, and 40msec after the onset of QRS waves on two types of ventricular extrasystole.
Left half of frame is the chest (horizontal axis; A-I) and right half (horizontal axis; I-M) is the back. Gray area is negative potential, white area is negative and +, − denote the maximum (Max) and minimum (Min) respectively. Lines represent the isopotential line increments.

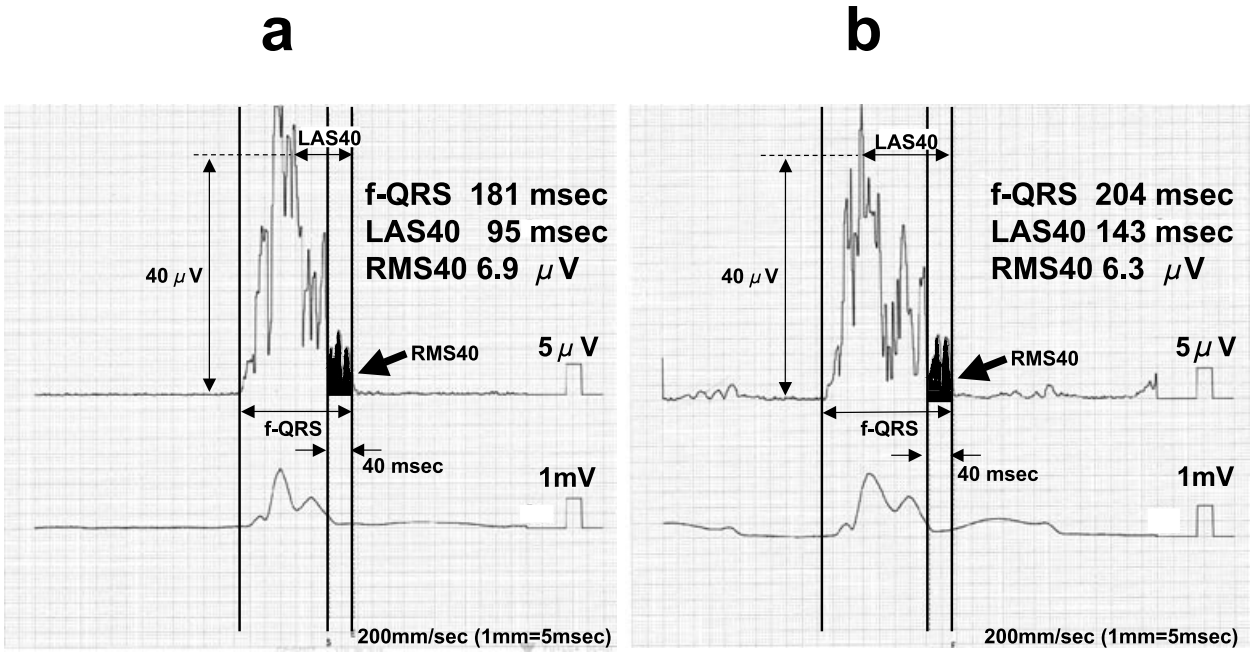

Figure 5 SAECG before (panel a) and after (panel b) administration of amiodarone.

Table 1. Percent change of three parameters of SAECG

	Before administration of amiodarone	After administration of amiodarone	percent change of parameter
f-QRS	181 msec	204 msec	+12.7%
LAS40	95 msec	143 msec	+50.1%
RMS40	6.9 μV	6.3 μV	-8.7%

f-QRS, filter-QRS duration;LAS 40, duration over the last 40msec under the 40μV duration ; RMS 40, root mean square voltage of the terminal 40 msec of the f-QRS waveform.

2)the root mean square (RMS) voltage (in microvolts) of the terminal 40 msec of the f-QRS waveform (RMS-40), and 3)the last duration (in millisecond) of the terminal f-QRS waveform within 40μV (LAS40). The late potential were defined to be present if the SAECG showed at least the two items of the following criteria : f-QRS>130 msec, RMS40<15μV, or LAS40>40msec.

Figure 5 shows SAECG before (panel a) and two weeks after (panel b) administration of amiodarone. The f-QRS, LAS40, and RMS40 parameters of SAECG before and after administration of amiodarone were 181 msec and 204 msec, 95 msec and 143 msec, and 6.9μV and 6.3 μV, respectively. In the present case, the late potentials before and after administration of amiodarone were positive. Table 1 shows the percent changes of the three SAECG parameters in this patient. The percent changes of f-QRS, LAS40, and RMS40 were+12.7%,+50.1% and -8.7%, respectively, from before to after the administration of amiodarone.

The electrophysiological study revealed two types of sustained ventricular tachycardia:the right bundle branch block type with left-axis deviation, and the left bundle branch block type with a normal axis (Figure 6). Catheter ablation was not performed because of the multiple origins of the ventricular tachycardias. After the administration of amiodarone for 2 weeks, an electrophysiological study was performed again. Amiodarone was thought to prevent ventricular tachycardias from appearing after the coupled stimulation at the right ventricular apex. Figure 7 shows the clinical course of this patient. The frequency of ventricular tachycardia in the short run decreased and finally the episode disappeared. Oral amiodarone was started out at 400 mg/day for 3 days and thereafter was continued at 100 mg/day. By the patient's 10th day at our hospital, ventricular tachycardia was no longer recognized.

Although amiodarone eliminated ventricular tachycardia in this patient, a cardioverter defibrillator was implanted as a backup because the patient had symptoms of a syncopal attack. The patient is now being followed up at an outpatient department. His ventricular tachycardia has thus far been suppressed without the operation of the defibrillator.

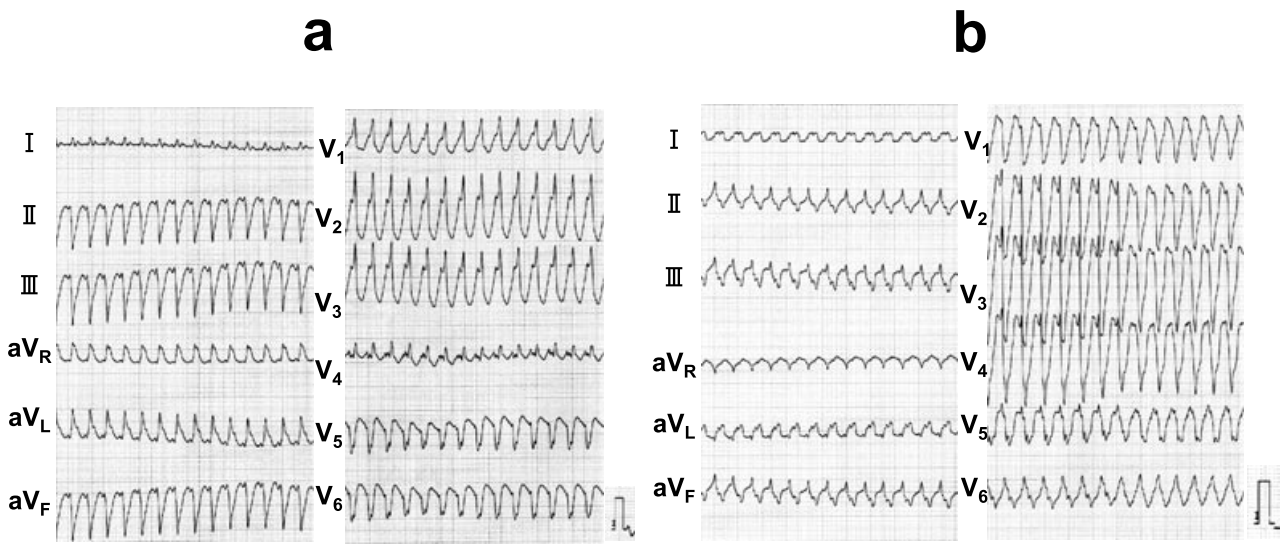

Figure 6 Electrophysiological study of this case.
Two types of suspended ventricular tachycardia are induced.

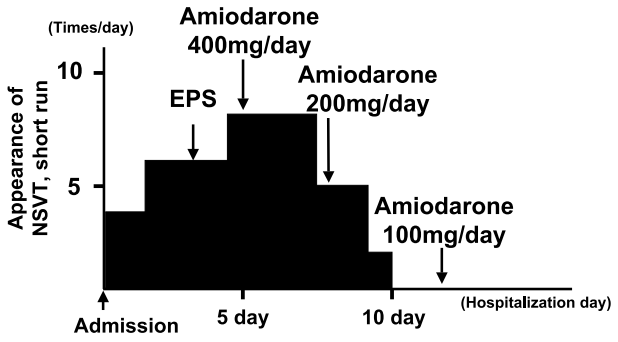

Figure 7 Clinical course of this patient.
EPS, Electrophysiological study ; NSVT, non-sustained ventricular tachycardia

DISCUSSION

Brembilla-Perrot *et al.*(8) reported that SAECG was useful for distinguishing responders from non-responders to amiodarone for treatment of ventricular tachycardia. They did not explain why the increased filtered QRS duration and the prolonged late ventricular potential indicated the effectiveness of anti-arrhythmic action. In agreement with their study, amiodarone controlled ventricular tachycardia in our patient, since the three parameters of SAECG show marked change from before to after administration of amiodarone. These findings indicate that this patient is a responder to amiodarone. Amiodarone has a sodium channel-blocking effect in addition to its potassium channel-blocking effect. The SAECG is more sensitive than the standard ECG in detecting changes in QRS duration resulting from the slowing down of conduction by amiodarone.

The relationship between the ventricular late potential in SAECG and ventricular tachycardias has reported a number of times (9-11). A high possibility of occurrence of ventricular tachycardias has been reported in cases where ventricular late potential is positive; conversely, the possibility of ventricular tachycardia is low in cases where the ventricular delay potential is negative (12).

Late ventricular potential appears in damaged myocardium due to myocardial infarction or cardiomyopathy. This delayed potential reflects a conduction disturbance that creates a reentry circuit. This reentry circuit is thought to be the cause of reentrant ventricular arrhythmia. Moreover, hypertrophic cardiomyopathy is related to sudden death caused by ventricular arrhythmias, although it was reported that ventricular hypertrophy has a relatively good prognosis (13,14). This suggested that a slow conduction caused ventricular tachycardia in hypertrophic myocardium with strong degeneration.

Fauchier *et al.* (15) reported the positive rates of a ventricular late potential are 5-20% and 1-5% in hypertrophic cardiomyopathy and hypertensive cardiomyopathy, respectively. Furthermore, it has been reported that ventricular late potential is frequently seen in cases with left ventricular dysfunction, although it has also been reported that ventricular late potential and cardiac function are independent of each other (16).

In the present case, no obvious abnormalities of cardiac function appeared, despite the ventricular late potential. This suggested that a conduction delay exists in hypertrophic myocardium with strong degeneration. In our patient, ventricular late potential still existed after the administration of amiodarone. Instead, ven-

tricular tachycardia was suppressed after the administration. Prolongation of QRS and of the late potential duration by other sodium channel-blocking drugs correlates with prolongation of the ventricular tachycardia cycle length (17). Therefore, it is suggested that in patients with longer filtered QRS and late potential, amiodarone causes a greater conduction delay and suppresses reentrant tachycardias. Amiodarone suppresses conduction in morbid myocardium more than it does in normal myocardium. Amiodarone completely inhibits the conduction disturbance of hypertrophic lesions. Therefore, the three parameters of SAECG might have been worse than they actually were. The percent changes of f-QRS and LAS40 were increased, and RMS40 were deceased after the administration of amiodarone.

Furthermore, the occurrence of tachyarrhythmias greatly influences the prognosis and strategy of medical treatment. In order to treat ventricular tachycardias in patients with heart failure, a drug with little influence on cardiac function is required. To prevent sudden arrhythmic cardiac death, an implantable cardioverter defibrillator has been introduced in addition to amiodarone treatment, to improve the prognosis of ventricular tachycardia (18).

The present case was diagnosed as a non-obstructive hypertrophic cardiomyopathy. Even though heart failure was not recognized, medical treatment with an anti-arrhythmic drug (sodium channel blocker) was not effective. Because syncopal attack occurred in this case, amiodarone administration and the implantation of a cardioverter defibrillator were both necessary to prevent sudden cardiac death.

It is dangerous to prescribe amiodarone aimlessly, since its side effects including interstitial pneumonia (19), hypofunction of the thyroid gland (20), and liver injury (21). Therefore, it is necessary to stop amiodarone treatment at an early stage if an anti-arrhythmic effect does not appear imminent. In the present case, we were able to identify the effect of amiodarone by examining the SAECG parameters.

Even though responders to amiodarone can be identified with SAECG, this will not reduce the indication for an implantable cardioverter defibrillator. That is because in organic heart disease, ventricular tachycardia is caused by the interaction of many factors, such as an anatomical barrier by the cardiac tissue, a conduction delay in abnormal myocardium, and an increase in endogenous catecholamines followed by cardiac dysfunction. Since the implantable cardioverter defibrillator decreases the likelihood of sudden cardiac death and improves the prognosis in cases with fatal arrhythmia, it may be the first choice of treatment for patients with ventricular tachycardia with cardiac dysfunction. However, the implantation of a cardioverter defibrillator remarkably reduces the patient's quality of life. Therefore, this approach needs to be combined with drug treatment, such as that with amiodarone, or catheter and/or surgical ablation. In the present case, we combined an implantable cardioverter defibrillator with amiodarone treatment, and the patient is doing well.

CONCLUSIONS

We experienced a patient with sustained ventricular tachycardia. Amiodarone was effective in maintaining sinus rhythm. Our results suggested that the effectiveness of amiodarone can be predicted by examining the parameters of SAECG.

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