Acute Myocardial Infarction and Fatal Ventricular Arrhythmia: a Case of Fatal Ventricular Tachycardia Induced by Coronary Vasospasm

Susumu Ui, Junko Honye

Purpose: The purpose of this study is to predict the mechanism of cardiac sudden death (CSD) by analyzing the fatal events associated with acute myocardial infarction (AMI). Methods and Results: To predict the mechanism of CSD, clinical characteristics were analyzed in 5 AMI cases which presented early ventricular tachyarrhythmia over the 7 months from January, 2011. Case 1: 30-year-old (y/o) male underwent primary percutaneous coronary intervention (PCI) for acute inferior MI. He was wearing an ambulatory electrocardiography 2 days before the onset of AMI. ST segment depression with prolonged QTc interval followed by ventricular tachycardia (VT) was shown in the recording at night. Intracoronary injection of acetylcholine revealed multivessel spasm with subsequent prolonged QTc and ventricular ectopy. Case 2 and 3; two 67 y/o males were treated with primary PCI after direct current (DC) shock for ventricular fibrillation (VF). Case 4; 62 y/o male whose VF was treated with DC shocks in the emergency room (ER), and died of pulseless electrical activity (PEA) with heart rupture after successful PCI for acute anterior MI. Case 5; 71 y/o female with acute inferior MI due to stent thrombosis presented cardiogenic shock and VF which was treated in the ER. Conclusions: The fatal events associated with AMI were VF, VT induced by prolonged QTc via multivessel spasm, and PEA due to heart rupture. Coronary spasm is also suspected to be an important factor to induce VT, resulting in CSD.

KEY WORDS: cardiac sudden death, coronary artery disease, ventricular fibrillation, ventricular tachycardia, coronary vasospasm

I. Introduction

In Japan, cardiac sudden death (CSD) accounts for about 60% of sudden death. The cases of out-of-hospital cardiac arrest are about 100,000 per year according to the data, carried out by the "Implementation Working Group for the All-Japan Utstein Registry of the Fire and Disaster Management Agency." This means that the occurrence of out-of-hospital cardiac arrest is about 7 cases per hour in Japan. According to "Guidelines for Risks and Prevention of Sudden Cardiac Death (JCS 2010)," arrhythmia is a major cause of sudden death. Ventricular tachycardia (VT) and ventricular fibrillation (VF) especially have important roles in CSD. Bradyarrhythmia and pulseless electrical activity (PEA) are also shown as its etiology. Coronary artery disease (CAD) is a major baseline disease of CSD in U.S. and the percentage of CAD is about 60% in CSD. In Japan, CAD accounts for around 35–50%. Several factors are supposed to influence the mechanism of CSD due to CAD.

II. Purpose

To predict the mechanism of CSD due to CAD in Japan, we retrospectively investigated the acute myocardial infarction (AMI) patients with the fatal events in our percutaneous coronary intervention (PCI) database.

III. Patients and methods

1. The cases selected for this study

We retrospectively analyzed the consecutive ST-elevation MI (STEMI) patients treated with primary PCI from January to July, 2011 in our PCI database. Among these patients, cases with fatal events were selected. The fatal events include death (VF, cardiogenic shock, mechanical complication such as cardiac rupture and non-cardiac death) and non-fatal events (VT/VF, cardiac tamponade, cardiogenic shock and advanced block). Because VT and VF are the major causes of out-of-hospital CSD and these deaths mostly occur before the patients reach the medical contact, we focused on the early ventricular tachyarrhythmia in AMI.

2. The definition of VT

VT is defined as an abnormally rapid ventricular rhythm usually in excess of 150 beats per minute (bpm). VT is called as "monomorphic VT" with the uniform QRS-complex
morphologies and, is called as “polymorphic VT” with variations in morphology. The ventricle may beat independently of the atrial beating (atrio-ventricular dissociation). Torsades de Pointes is a malignant form of polymorphic VT with the heart rate (HR) between 200 and 250 bpm, and QRS complexes with changing amplitude and twisting of the points. VT is designated as “sustained VT” if it persists for longer than 30 seconds.

3. Provocation test of coronary spasm by acetylcholine (ACh)\(^{11}\)

All the AMI patients do not undergo this provocation test. This test applies only to the cases that coronary spasm possibly contributes to the onset of ventricular arrhythmia or AMI, without its documentation by ECG monitoring or other noninvasive studies.

This provocation test is performed when the patient recovers from AMI into a stable stage of the convalescence.

It is judged to be positive for the provocation test if the coronary artery develops angiographical stenosis more than 90% in diameter, with chest pain and ischemic ST-T change.

4. Analysis of QT interval

Corrected QT interval (QTc) was measured by the modification of Bazett’s formula by Hodges and coworkers, as follows: QTc=QT+0.00175 (ventricular rate-60).\(^{12}\)

IV. Results

The number of the STEMI patients was 31 for 7 months from January, 2011 in our institute, and 30 patients were treated with primary PCI. Among these patients, early ventricular tachyarrhythmia was shown in 5 cases around admission (Table 1). Case 2–4 and 5 patients were treated in an emergency room (ER) or a cardiac catheterization room for VF with direct current (DC) shock before primary PCI. PCI was successful in all the cases. Two patients died among these 5 cases, one of cardiac rupture and the other of pneumonia. During the follow-up for the 8 months until March, 2012, 29 AMI patients are doing well without any event.

1. Case 1

30-year-old Japanese male was transferred to an ER in our institute at 16:42 on June 12, 2011, because of frequent palpitation and chest pain at rest. These symptoms were noticed at 13:00, 14:00, and 16:00 with each lasting duration of about 10 minutes followed by a spontaneous relief. He also noticed the same symptom 3 days ago. He has no history of known diseases and no current medication. His coronary risk factors are current smoker of 20 cigarettes per day for the last 12 years and a family history of cardiac sudden death. His father suddenly died at sitting position in his library at the age of 48. The cause of his death was diagnosed of acute myocardial infarction by autopsy.

In the ER, his body temperature (BT), heart rate (HR), blood pressure (BP) and arterial oxygen saturation (SaO2) were 35.8°C, 71 bpm, 138/82 mmHg and 98% (room air), respectively. Physical examination disclosed no clinically significant findings except for the low body mass index of 17.3, and occasional skipped heart beat. ECG monitoring showed a regular sinus rhythm with monofocal premature ventricular contraction (PVC). There was also no abnormal finding in 12-lead ECG, chest X-ray and blood sample (including electrolyte, lipoprotein A and protein C). The emergency physician diagnosed him unstable angina pectoris (UAP) and ordered him to be admitted to hospital immediately, however he rejected it. He visited our cardiology outpatient department on June 13 of the next day, and the finding of ultrasound echocardiography was within normal limits. Because the medical record in ER of the day before

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)/Sex</th>
<th>Infarct-related coronary artery</th>
<th>Type of fatal ventricular arrhythmia (its time from the onset of AMI, minutes)</th>
<th>QTc interval at the onset of arrhythmia (msec)</th>
<th>Outcome</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30/M</td>
<td>RCA</td>
<td>VT</td>
<td>480</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>67/M</td>
<td>RCA</td>
<td>VF (50)</td>
<td>445</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>67/M</td>
<td>RCA</td>
<td>VF (75)</td>
<td>440</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>62/M</td>
<td>LAD</td>
<td>VF (55)</td>
<td>432</td>
<td>Died at 20 hours</td>
<td>Cardiac rupture</td>
</tr>
<tr>
<td>5</td>
<td>71/F</td>
<td>RCA</td>
<td>VF (40)</td>
<td>438</td>
<td>Died at 3 months</td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>

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Table 1 Clinical characteristics of patients with ST elevation myocardial infarction and fatal ventricular arrhythmia
showed the presence of monofocal PVC, the attending doctor instructed him to wear a Holter monitor. He was equipped with a Holter monitor (FUKUDA DENSII recorder system FM-190, Holter analysis system SCMS000, Fukuda Denshi Electronics, Tokyo, Japan) at 12:47 on the same day. On June 14, he visited our hospital again to remove the monitor without any complaint. However, nonsustained polymorphic VT of about from 180 to 250 bpm was recorded at 1:37 40 at midnight. The attending doctor ordered him to be admitted immediately, however he rejected the admission, again. Detail analysis of ECG tracing disclosed QTc prolongation of 480 msec with upsloping ST depression just before the onset of VT (Fig. 1A). One minute later, VT spontaneously reverted to regular sinus rhythm with normalized QTc of 360 msec (Fig. 1B). On June 16, he suddenly woke up to develop palpitation and chest pain at 7:00 and he was delivered to our ER at 8:29. His vital signs were HR of 64 bpm, BP of 136/91 mmHg and SaO2 of 100% (at room air). ECG showed ST elevation in leads of II, III and aVF with QTc of 400 msec. Sublingual nitrate resolved the ECG change and his symptom at ER. Under the diagnosis of UAP, he was admitted to CCU at 9:30. The levels of cardiac enzymes including troponin T were within normal limits. After admission to CCU, his clinical condition was stable. However, chest pain suddenly re-emerged at 11:25. ECG showed ST elevation in leads of II, III and aVF with complete ativoventricular block and QTc interval of 400 msec (Fig. 2A, B). Acute inferior MI was diagnosed because of no relief of chest pain and elevated ST-T change after sublingual nitroglycerine. The patient was delivered to a cardiac catheterization room for urgent CAG. Right coronary artery was completely occluded at mid-portion (Fig. 2C). No significant stenosis was noticed in left coronary arteriogram (Fig. 2D).

Primary PCI was carried out using a 6 Fr TAIGA™ SAL1.0 guiding catheter (Medtronic, Inc. Minneapolis, USA). After crossing the culprit lesion by a 0.014 inch coronary guidewire (Runthrough NS Extra Floppy, TERUMO CORPORATION, Tokyo, Japan), intravascular ultrasound (IVUS; ViewIT, TERUMO Co. Tokyo, Japan) was performed. In the IVUS imaging, media was thickened, which means there is a suspected coronary spasm with negative remodeling, mild atherosclerosis, and thrombus in the occluded portion. Aspiration catheter was successfully applied, using a Thrombust III GR 6 Fr (KANEKA Co. Osaka, Japan). The IVUS image after using an aspiration catheter showed larger diameter of coronary artery at culprit lesion than the pre-aspiration image. Angiogram disclosed the reperfusion with TIMI 2 grade flow of RCA and the presence of high-grade stenosis at mid-RCA (Fig. 2E). Balloon angioplasty was performed with 4x13 mm non-slipping balloon (Lacrosse NSE, GOODMAN CO. LTD. Aichi-ken, Japan). Residual stenosis was angiographically 25% with TIMI 3 flow (Fig. 2F). The time of onset to reperfusion by balloon was 60 minutes. The patient’s clinical course after primary PCI was uneventful and he left our institution on June 28 (hospital stay of 13 days).

2. Provocation test of coronary spasm by Ach

Because coronary spasm possibly influence on the onset of the polymorphic VT followed by acute inferior MI in this case, provocation test of coronary spasm by Ach was scheduled after getting a written informed consent.
In the morning on July 12 (after 26 days from the onset of AMI), the provocation test was performed. ECG just before the provocation test already showed prolonged QTc (480 msec) with positive u wave (Fig. 3A). Its angiogram of RCA looked diffusely spastic. The QTc was prolonged to 540 msec with PVC at 25 sec after the injection of ACh 50 μg into RCA, followed by negative U wave with QTU of 680 ms at 60 sec after the injection (Fig. 3B). Its angiogram at 60 sec after injection of ACh 50 μg disclosed the induction of 90% stenosis of distal segment in RCA (Fig. 4A). As shown in Fig. 3C, just after the provocation test in LCA with 50 μg, the prolonged QTc of 520 msec accompanied PVC of R-on-T, followed by negative U wave as in Fig. 3D. 90% stenosis of distal segment in LCA was disclosed in the angiogram (Fig. 4B). Because he presented severe chest pain, nitroglycerin of 1mg was injected into both LCA and RCA, resulting in a symptom relief and normalization of QTc to 440 msec without U wave. Final angiogram after intracoronary nitrate showed a dilatation of both coronary arteries (Fig. 4C, D). Coronary vasospasm was considered to contribute to the onsets of VT and AMI in this patient.

3. Therapeutic strategy
Polymorphic VT was accidentally disclosed by Holter monitoring before the attack of AMI and the patient has a family history of CSD. Because he has no history of syncope or faintness and his organic stenosis in RCA has already been recanalized, we have decided to treat him not with ICD implantation but with oral medication. After discharge from our institute, he is doing well without any limit in daily lives with the medication of aspirin 100 mg, nifedipine CR 40 mg and isosorbide dinitrate 40 mg daily. Holter ECG monitoring disclosed no arrhythmia or QT prolongation, any longer. It was acknowledged that the patient’s oral intake of medication was controlling the patient’s vasospasm, having studied the result of repeated Holter monitoring and patient’s clinical course.

Fig. 2 Electrocardiogram at the onset of acute myocardial infarction (AMI) and coronary arteriogram, followed by primary percutaneous coronary intervention.
A: ECG shows ST elevation in leads of II, III and aVF with complete atrioventricular block and QTc interval of 400 msec when chest pain suddenly developed at 11:25 on June 16, 2011 after admission to CCU.
B: Precordial leads show ST depression as the reciprocal change of the ST elevation in limb leads.
C: Right coronary artery (RCA) is completely occluded at mid-portion in the left anterior oblique view (LAO).
D: No significant stenosis is noticed in left coronary arteriogram in the right anterior oblique view (RAO).
E: High-grade stenosis became evident in middle segment of RCA after successful aspiration of much thrombus.
F: Final angiogram (LAO) is shown after successful balloon angioplasty.
Fig. 3  ECG at coronary spasm provocation test by acetylcholine (ACh).
A: Baseline ECG. Prolonged QTc (480 msec) with positive u wave (arrows) is shown, just before the provocation test.
B: ECG at 60 seconds after injection of ACh 50 µg into RCA. Prolonged QTc (540 msec) with negative u wave (arrows) is shown with QTU of 680 msec.
C: ECG at 10 seconds after injection of ACh 50 µg into LCA. The QTc is prolonged to 520 msec and PVC of R-on-T is shown.
D: ECG at 60 seconds after injection of ACh 50 µg into LCA. The QTc is prolonged to 540 msec and negative u waves (arrows) are evident with QTU of 680 msec.

Fig. 4  Angiogram at coronary spasm provocation test by acetylcholine.
A, B: Intracoronary injection of ACh provokes 90% stenosis (arrows) in both coronary arteries.
C, D: Both coronary arteries dilate with intracoronary nitroglycerin.
V. Discussion

1. Early ventricular fibrillation

VF at acute phase of AMI is particularly fatal arrhythmia in CAD.

We experienced 4 cases of VF (2 cases without CHF and 2 ones with CHF), among 31 AMI patients for over the period of 7 months in 2011. Early VFs were shown at 50, 75, 55 and 40 minutes, respectively, after the onset of AMI symptom.

2. Polymorphic ventricular tachycardia due to prolonged QTc interval induced by coronary spasm

We were fortunately able to detect polymorphic VT by Holter monitoring in 30-years-old male who had a family history of sudden cardiac death. The VT was preceded by upsloping ST depression and prolonged QTc interval at midnight. However, at the attack of AMI, the QTc interval was within the normal limits. In the provocation test of coronary spasm by ACh, the QTc interval became markedly prolonged with negative u wave and PVC of R-on-T. These findings show that VT was possibly induced by the electrophysiologic derangement due to coronary spasm, and possibly multi-vessel spasm. He had one vessel disease and no ventricular arrhythmia was noticed at the attack of AMI. Therefore, it was considered that VT was mainly induced not by the ischemia of organic stenosis, but by the prolonged QTc interval due to multi-vessel spasm. Finally, ventricular arrhythmia due to coronary spasm is possibly one of the causes of the out-of-hospital CSD. This is different from VF on the mechanisms, because such VF suddenly appears via reentrant mechanism with abnormal automaticity and triggered activity without precedent VT. The mechanism of polymorphic VT due to coronary spasm is unclear, and few previous reports records the prolongation of QTc due to coronary spasm. However, prolongation of QT interval induced by the coronary spasm probably results in Torsades de pointes VT, which is usually nonsustained or may evolve into VF in some conditions.

Concerning coronary spasm, in 1998, among the consecutive 2251 patients with angina pectoris at 15 institutes in Japan, vasospastic angina accounted for 40.9 percent, reported by Kaikita, et al. Moreover Coronary Spasm Association in Japan shows that 38 resuscitated patients from out-of-hospital cardiac arrest were younger (55±15 vs 65±10 years old, P<0.001), showed higher rate of spasm provocation in LAD (71 vs 47 percent, P=0.005) and multi-vessel spasm (42 vs 27 percent, P=0.04). Regarding metabolic syndrome, those with obesity, dyslipidemia, higher blood pressure and/or hyperglycemia have recently been increasing in Japan, as shown via the data of National Health and Nutrition Examination Survey by Japanese Ministry of Health, Labour and Welfare in 2007. Considering the report on the increasing rate of coronary abnormal response, endothelial dysfunction mainly plays the role of coronary spasm in metabolic syndrome. Our case presenting multivessel spasm does not suffer from metabolic syndrome, but has risk factors of current smoking and the family history of CSD. This study reveals that coronary spasm is possibly one of the causes of the out-of-hospital CSD. This is different fromVF on the mechanisms, because such VF suddenly appears via reentrant mechanism with abnormal automaticity and triggered activity without precedent VT. The mechanism of polymorphic VT due to coronary spasm is unclear, and few previous reports records the prolongation of QTc due to coronary spasm. However, prolongation of QT interval induced by the coronary spasm probably results in Torsades de pointes VT, which is usually nonsustained or may evolve into VF in some conditions.

3. IVUS finding in the case of coronary spasm

In the case of our patient, IVUS disclosed the thickened media with negative remodeling, mild atherosclerosis and thrombus in the culprit lesion. It is generally considered that severe ischemia due to coronary spasm induces the production of NO, which releases the spasm of the narrowed vessel, and coronary ischemia is finally resolved without myocardial necrosis. However, as shown in our case, coronary spasm mostly accompanies baseline atherosclerosis as the reports and these clinical conditions easily induce the thrombus formation focally followed by an onset of AMI. Moreover, it is reported that gene mutation reduces the endothelial NO production, and this patient has a family history of CSD, suspecting the presence of genetic abnormality.

4. Heart rupture

Cardiac rupture rarely occurs in the early phase of AMI, and is typically presented 3 to 5 days after AMI. It is suspected that a cardiac rupture possibly becomes one of the causes of CSD in the case of painless AMI as well as late arrival to a medical institution from onset.

5. Bradycardia

Bradycardia such as sick sinus syndrome or advanced atrioventricular block is known as one of the causes of CSD. However, there was no such patient evident in our study.

6. To reduce cardiac sudden death

a. Education for the general public

Because CSD occurs at the early stage of AMI, the general public should be taught on the "Chain of Survival." This means "Early Access," "Early CPR," "Early Defibrillation," and "Early Advanced Care."

b. Confirmation of the significance of coronary vasospasm for healthcare professionals

As Sueda reports, the rate of the patients with metabolic
syndrome is rising in Japan, and endothelial dysfunction of coronary artery with abnormal reactivity is increasing.\textsuperscript{17} This results in a higher frequency of coronary spasm development. For managing acute coronary syndrome, we have to recognize not only organic stenosis, but also the functional abnormality of coronary artery.

c. Problem in our case

Although case 1 was diagnosed as UAP, we could not persuade him to enter to hospital. More efforts were indispensable for him to be admitted at early stage of UAP.

VI. Study limitations

1. Patients selection

Because our cardiovascular center has not been running long, the number of cases with AMI is not high. Fortunately we have experienced the patients with early VF, and impressive VT case with prolonged QTc interval induced by coronary spasm. Measurement of QTc is necessary for more cases of provocation test with ACH, and we have to identify whether our case is rare or not.

2. Hardware ability

The data of ECG monitor in ER is not kept in a server and it is not possible for us to analyze the VF shown in ER retrospectively.

3. PEA

One patient died of PEA due to cardiac rupture after successful primary PCI. Because this event happened after the intervention in our case, it couldn’t be concluded that PEA due to heart rupture is one of the causes of out-of-hospital cardiac death.

VII. Conclusion

Causes of CSD in the early phase of acute coronary syndrome were VF and VT induced by prolonged QTc due to coronary spasm. Death due to heart rupture was noticed after admission, however not in the early stage of AMI. Considering the characteristics of early ventricular arrhythmia, not only should the general public be educated on the “Chain of Survival,” but also an awareness of coronary spasm to healthcare professionals is mandatory in Japan.

References


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