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Letter to the editor

Repeated syncope caused by intractable vasospastic angina: A case report

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Coronary vasospastic angina (CVA) plays an important role in the pathogenesis of a variety of ischemic heart disease, including not only variant angina but also effort angina, acute myocardial infarction, and other related conditions [1–4]. Most attacks of CVA can be controlled by coronary vasodilators, such as nitrates and calcium channel blockers. However, in some patients, episodes of vasospastic angina resist these two drugs, defined as intractable coronary vasospastic angina (ICVA) [3]. For patients with repeated cardiac arrest caused by refractory spasm-induced ventricular tachycardia and ventricular fibrillation, a comprehensive treatment, including an implantable cardioverter defibrillator (ICD), should be considered. In this study, we present a case with ICVA who represented life-threatening complications of malignant arrhythmias and cardiac arrest, and discuss the managements about ICVA.

A 56-year-old man without traditional coronary risk factors (including hypertension, diabetes, hyperlipidemia, smoking), had a 6-year history of paroxysmal chest pain, meanwhile administration of sublingual nitroglycerin tablets could relieve the symptom. 1 week before admission, at eight o'clock after breakfast, the patient suffered a sudden chest pain, vomiting, and subsequent unconsciousness. After a successful cardiopulmonary resuscitation (CPR), he was transferred to Ningxia People's Hospital, Yinchuan, China. In hospital, abnormalities in serum electrolytes, renal function, liver function, electrocardiogram QT intervals, chest X-ray and echocardiogram were not observed. On November 3, 2008, selective coronary angiography (CAG) revealed an 85% stenosis in the middle segment of the left anterior descending (LAD) artery (Fig. 1A, and B), and an 80% stenosis in the middle segment of the right coronary artery (RCA) (Fig. 1C, and D),which could not be relieved by intracoronary injection of nitroglycerine. A 3.0 × 13 mm Firebird™ stent (MicroPort, China) at the LAD lesion (Fig. 1E) and a 3.0 × 15 mm Partner™ stent (Lepu Medical, China) at the RCA lesion (Fig. 1F) were successfully implanted; both were drug-eluting stents.

Two weeks after discharge from hospital, the patient was admitted in another local hospital again, due to sudden chest pain, syncope and unconsciousness. Fortunately, the CPR succeeded once more. On December 12, 2008, the results of the second CAG showed no apparent stenosis (Fig. 2). However, during the hospitalization, attacks of sudden chest pain and syncope occurred frequently, meanwhile electrocardiogram monitor showed ST-segment elevations, ST-segment depressions, ventricular tachycardias and sinus bradycardias (Fig. 3). Thus, the third CAG was operated 1 week after the second CAG. Intense spasms in the entire LAD were observed. After intracoronary boluses an infusion of 400 μg nitroglycerine, the LAD spasms were relieved (Fig. 4).

Subsequently, the patient was treated with two types of vasodilators (isosorbide dinitrate 10 mg, and diltiazem 30 mg, for 3 times a day) and amiodarone 20 mg per day. The dosage of atorvastatin was increased from 20 mg to 40 mg per day. Unfortunately, the patient suffered vasospastic angina and unconsciousness again 6 months later, and survived after CPR. The dosage of diltiazem was increased to 60 mg, and that of isosorbide dinitrate to 15 mg for 3 times a day. However, attacks of intractable vasospastic angina and syncope didn't stop. Due to the low level blood pressure and heart rate, the dosages of these two vasodilators were not increased further.

On July 12, 2010, an implantable cardioverter defibrillator (ICD) was implanted. Three months following the implantation, 5 mg of nicorandil was added 3 times a day (which can't be prescribed before). Later, the symptom of intractable vasospastic angina was repeated intermittently, however attacks of syncope and unconsciousness discontinued. During the 4-year follow-up, data about ICD showed no antitachycardia pacing, low-energy cardioversion and high-energy defibrillation, but part time represented antibradycardia pacing.

In 1959, Prinzmetal et al. [5] first described the special form of coronary angina with transient ST-segment elevation. At present, the term of coronary vasospastic angina (CVA) was used to depict angina caused by coronary vasospasm, instead of Prinzmetal's variant angina. Previous data provided racial heterogeneity in coronary artery vasomotor reactivity, East Asian people (such as Japanese) have a higher incidence of variant angina than Caucasian persons [6,7]. However, provocation tests were scarcely performed in western countries. Recently, an American study enrolled a total of 921 consecutive patients

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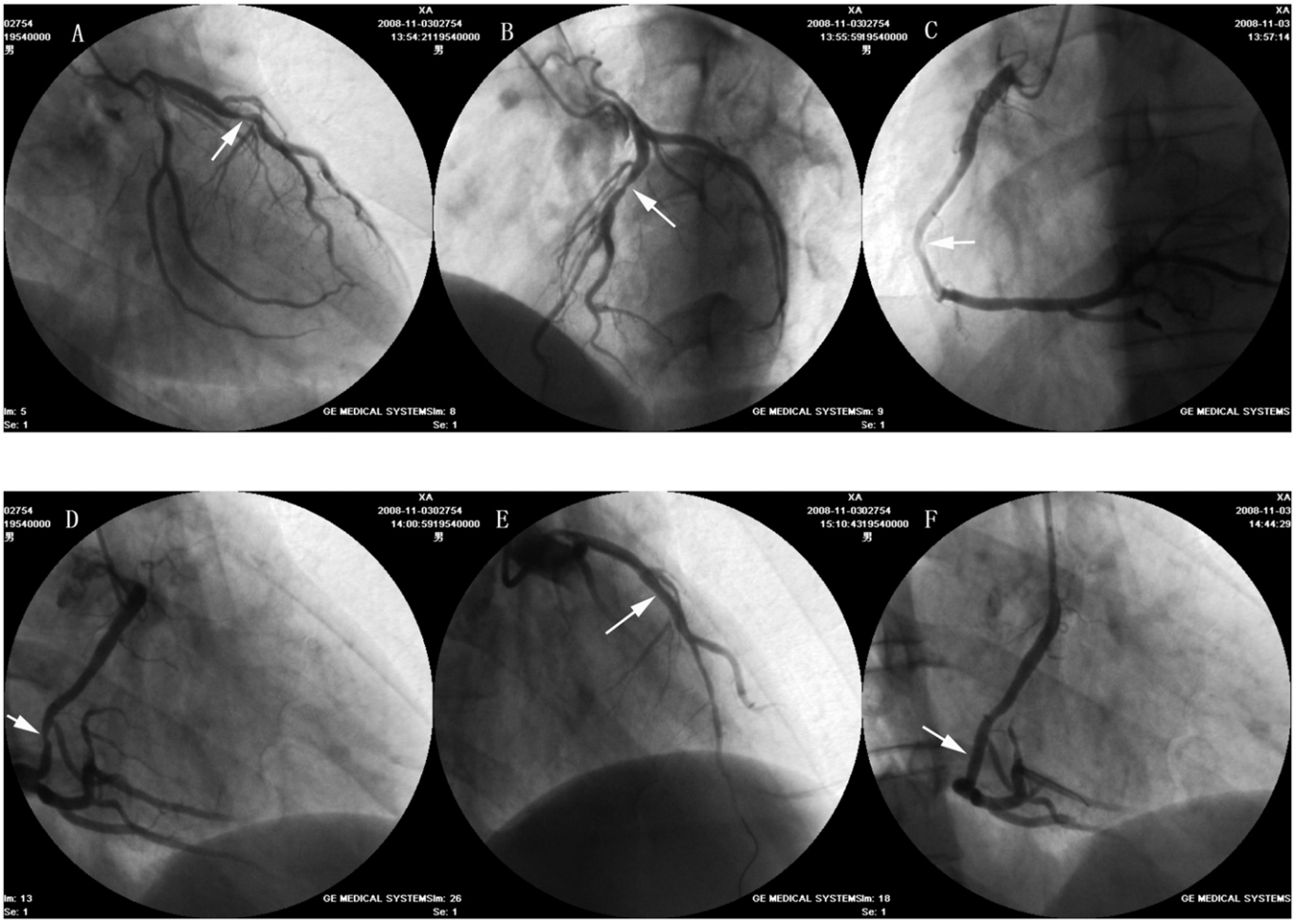

Fig. 1. Coronary angiography first time. An 85% stenosis in the middle segment of the left anterior descending artery (1A, 1B); an 80% segmental stenosis in the middle segment of the right coronary artery (1C, 1D). There was no residual stenosis after implantation of drug-eluting stents (1E, 1F).

who had unobstructed coronary arteries. After diagnostic angiography, the intracoronary acetylcholine provocation testing was performed according to a standardized protocol. The overall frequency of epicardial spasm was 33.4%, and the frequency of microvascular spasm was 24.2%, which indicated that coronary vasospasm may be underestimated in white patients previously [8].

A lot of risk factors have been identified to relate with coronary vasospasm, including smoking, drinking, lipid abnormalities, diabetes mellitus, and stress. Persons with coronary vasospasm are often familial, which suggests that genetic factors may also be involved. In 1988, Fischell et al. [9] first found that spontaneous coronary artery vasoconstriction after percutaneous transluminal coronary angioplasty occurred routinely at and distal to the site of balloon dilatation. In the era of stent, patients with coronary vasospasm following stent implantation were reported frequently, the spastic vessels included stent-related arteries [10,11] and non-stent-related arteries [12]. Previous studies have shown that, compared with bare metal stents, drug-eluting stents (DES) are more likely to cause coronary vasospasm [13,14]. However, postoperative coronary vasospasm mechanisms are not fully elucidated, which may be related to impaired endothelial function, emotional stress and allergic reactions caused by stent drugs and polymers. Most coronary vasospasms during percutaneous coronary intervention are easily relieved by intracoronary administration of vasodilators, but some cases are intractable [11,12].

Most attacks of vasospastic angina can be controlled by coronary vasodilators, such as nitrates and calcium channel blockers. However, in some patients, episodes of vasospastic angina are intractable, and induce major adverse cardiac events (MACE). In order to evaluate the prognosis of patients with vasospastic angina, Japanese Coronary Spasm Association (JCSA) developed a comprehensive clinical risk score system [15]: history of out-of-hospital cardiac arrest (4 points), smoking, angina at rest alone, organic coronary stenosis, multivessel spasm (2 points each), ST-segment elevation during angina, and beta-blocker use (1 point each). According to the total score in individual patient, 3 risk strata were defined: low (score 0 to 2, $n = 598$), intermediate (score 3 to 5, $n = 639$) and high (score 6 or more, $n = 192$). The incidences of MACE in the low-, intermediate-, and high-risk patients were 2.5%, 7.0%, and 13.0%, respectively ($p < 0.001$).

No universal definition exists concerning intractable coronary vasospastic angina (ICVA). According to the Japanese Circulation Society, ICVA was defined as angina that cannot be controlled even with the administration of two types of coronary vasodilators [3]. Smoking cessation, drinking restriction, maintenance of ideal body weight, blood pressure control, avoidance of excessive fatigue and mental stress are helpful for the prevention of coronary spasm. Nitrates and calcium channel blockers are deemed coronary vasodilators of first choice for the treatment of vasospastic angina. Since nitrates exert effects by different mechanisms from that of calcium channel blockers, combinations of nitrates with different classes of calcium antagonists may be reasonable for patients with ICVA. If patients with vasospastic angina have no significant stenosis of coronary artery, β-blockers are not recommended [3]. Nicorandil, an adenosine triphosphate-sensitive potassium channel opener, increases the outflow of K^+, shortens the action potential, decreases the inflow of Ca^{2+} and intracellular Ca^{2+}