CASE REPORT

Syncope caused by coronary artery spasm without chest pain leading to ventricular fibrillation

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SUMMARY

We present a case of syncope caused by coronary artery spasm without chest pain leading to ventricular fibrillation despite of vasodilator therapy with a calcium channel blocker (CCB). A 68-year-old man presented with two episodes of syncope without chest pain. Ergonovine provocation test induced a diffuse spasm in the right coronary artery (RCA) and subsequently, ventricular fibrillation. Under the therapy with multiple vasodilators including two CCBs, a second ergonovine provocation induced a spasm of the proximal RCA resulting in complete obstruction. Owing to drug-resistant coronary spasm complicated by ventricular fibrillation, an implantable cardioverter defibrillator (ICD) was implanted. This case report highlights the occurrence of syncope caused by coronary artery spasm without chest pain that was refractory to single CCB therapy and needed ICD implantation. Therapy with multiple vasodilators, including two or more CCBs, along with ICD implantation may be required to treat such refractory coronary artery spasms leading to lethal arrhythmia.

BACKGROUND

Coronary artery spasm resulting in arrhythmia is a rare but recognised cause of syncope and sudden cardiac death.^{1–4} Preventing coronary artery spasms is crucial to preventing ventricular fibrillation (VF), and calcium channel blockers (CCB) are the primary drugs used for this purpose.⁵ However, if the coronary artery spasm does not cause chest pain, the diagnosis and management is very difficult. Diagnosis of the silent coronary artery spasm is possible if the attack occurs under ECG monitoring; however, it may not occur during ambulatory monitoring and exercise test may not be helpful.⁶ Long-term surveillance such as repeated ambulatory Holter ECGs, or an implantable loop recording, may be needed to establish the diagnosis.⁷ The efficacy of CCB cannot be monitored in the absence of chest pain. In such cases, combination therapy with CCB and implantable cardioverter defibrillator (ICD) may be appropriate.

CASE PRESENTATION

A 68-year-old man presented with two episodes of syncope (15 and 3 months ago) without chest pain. The patient lost consciousness suddenly during the day and subsequently suffered head injuries at both times and cerebral contusion at latest time and needed rehabilitation for 3 weeks. At the time of presentation, the patient was hypertensive and was therefore administered benidipine (8 mg once daily)

and valsartan (160 mg twice daily). He was an exsmoker; no other relevant medical history was noted. Findings of physical examination, echocardiography, 12-leads ECG (figure 1A), in-hospital ECG monitoring, MRI of the head and electroencephalography showed no significant abnormalities. Since his transient loss of consciousness caused serious head injuries, we performed coronary angiography (CAG), electrophysiological study (EPS) and ergonovine provocation test in order to investigate the presence of the sick sinus syndrome or an advanced atrioventricular block (AV block) and to induce coronary spasm leading to VF or an AV block. No organic stenosis was detected by CAG (figure 1B). Subsequently, no spasm was induced by the intracoronary infusion of 32 µg of ergonovine into the left coronary artery. A diffuse spasm in the right coronary artery (RCA) was observed 3 min after 20 µg of ergonovine infusion into the RCA; however, no chest pain occurred (figure 1C). At 8 min after infusion, a marked elevation was observed in the ST segments in the II, III and aVF leads despite the continuing absence of chest symptoms (figure 1D); subsequently, atrioventricular block and VF was induced, and the patient lost consciousness (figure 1E). We performed immediate cardiac compression and nitrate injection into the coronary artery; VF was successfully defibrillated by electrical cardioversion and the spasm was relieved by the nitrate injection. The patient was therefore diagnosed with ischaemic-induced VF mediated by coronary spasm, and started on therapy with an additional CCB (diltiazem, 400 mg twice daily) and other vasodilators (nicorandil (15 mg three times a day) and isosorbide dinitrate (40 mg twice daily)). A second ergonovine provocation test was performed 2 weeks after drug therapy was initiated (before provocation: figure 2A); this induced a spasm of the proximal RCA resulting in complete obstruction after 20 µg of ergonovine infusion without chest pain (figure 2B, C), which was released by nitrate injection into the coronary artery. Because we were concerned that despite increased medication, a future spasm resulting in arrhythmia may occur, an ICD was implanted. After discharge, the patient has remained asymptomatic with an uneventful clinical course; no further episodes of syncope or ICD-detected ventricular arrhythmias have occurred during 12 months of follow-up following ICD implantation.

OUTCOME AND FOLLOW-UP

The patient has remained asymptomatic with an uneventful clinical course; no further episodes of

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Figure 1 (A) ECG at baseline. (B) Coronary angiography at baseline. (C) A diffuse spasm in the right coronary artery by the intracoronary infusion of ergonovine. (D) ECG at 8 min after infusion. A marked elevation was observed in the ST segments in the II, III and aVF leads despite the continuing absence of chest symptoms. (E) Atrioventricular block and ventricular fibrillation was induced with loss of consciousness.

syncope or ICD-detected ventricular arrhythmias have occurred during 12 months of follow-up following ICD implantation.

DISCUSSION

Coronary artery spasm is a rather common disease in East Asia,⁸ provably owing to the polymorphism of genes related to endothelial function such as endothelial nitric oxide synthase.⁹ In a white population with acute coronary syndrome without a culprit lesion, 49% of German¹⁰ and 16% of French¹¹ had a positive intracoronary provocation test, whereas 79% of similar Japanese patients developed coronary artery spasm by intracoronary ergonovine provocation test.¹² In addition, recent studies have reported that coronary artery spasm is one of important causes of out-of-hospital cardiac arrest.^{13–14} Given the infrequency of the attacks, an implantable loop recorder would be recommended¹⁵; however, given the severity of the head injury caused by syncope, an urgent and thorough investigation was needed. Hence, after the monitoring of ECG and the exclusion of structural heart disease, CAG, EPS, and an ergonovine provocation test were planned.

This patient was diagnosed with refractory spasm despite administration of multiple CCBs, benidipine and diltiazem. It has been reported that the coronary response to acetylcholine is not completely inhibited after 6-month CCB administration despite the absence of symptomatic angina.¹⁶ Moreover, 12 months CCB administration does not improve abnormalities

in the uptake of a fatty acid tracer, indicating residual ischaemia in the myocardium.¹⁷ However, CCBs remain the mainstay of the current clinical therapy for patients with coronary artery spasms,⁵ and benidipine is the most selective CCB for coronary spasm as compared with other CCBs.¹³

Both the efficacy and limitations of ICD therapy in patients with refractory variant angina have been reported by Meisel *et al*.³ Among eight patients with refractory variant angina, they implanted ICDs in seven patients. Appropriate ICD shocks were documented in four patients; however, one patient died of electromechanical dissociation despite CCB treatment. In the present case, therapy with multiple vasodilators could effectively control the coronary spasm. The ICD has demonstrated, using its monitoring capabilities, that no further tachy-arrhythmias have occurred on the increased medication. The importance of continued medical treatment for coronary spasms has been previously reported, with any reduction or discontinuation in medical therapy resulting in a significantly increased incidence of cardiac death and myocardial infarction.¹³

This case report highlights the occurrence of syncope caused by coronary artery spasm without chest pain that was refractory to single CCB therapy and needed ICD implantation. Therapy with multiple vasodilators, including two or more CCBs, along with ICD implantation may be required to treat such refractory coronary artery spasms leading to lethal arrhythmia.

Figure 2 (A) Coronary angiography (CAG) under medication of two CCBs. (B) ECG on a second ergonovine provocation test to the right coronary artery under medication of two CCBs. (C) Complete obstruction in the right coronary artery was induced.

Learning points

- This case report highlights the occurrence of syncope caused by coronary artery spasm without chest pain that was refractory to single calcium channel blocker (CCB) therapy and needed implantable cardioverter defibrillator (ICD) implantation.
- Therapy with multiple vasodilators, including two or more CCBs, along with ICD implantation may be required to treat refractory coronary artery spasms leading to lethal arrhythmia.
- Coronary artery spasm resulting in arrhythmia is a rare, but a recognised cause of syncope or cardiac arrest even if not accompanied by chest pain.
- Cardiac monitoring may show evidence of ST changes associated with brady-arrhythmias or tachy-arrhythmias in this condition.

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