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CASE REPORT
Coronary intervention

Sudden cardiac arrest due to recurrent coronary spasm in a young woman: a case report

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Background Coronary artery spasm (CAS) is a pathological condition resulting from transient functional narrowing of the coronary arteries leading to myocardial ischaemia and in some rare cases even to sudden cardiac arrest (SCA). The most important preventable risk factor is use of tobacco, whereas possible precipitating factors include some medications and psychological stress.

Case summary A 32-year-old woman was hospitalized with burning chest pain. The immediate investigations revealed the diagnosis of non-ST-segment elevation myocardial infarction, because of ST elevations in one single lead and increased high-sensitivity troponin. Due to ongoing chest pain and a severe impaired left ventricular ejection fraction (LVEF) of 30% with apical akinesia, a prompt coronary angiography (CAG) was scheduled. After aspirin administration, she developed anaphylaxis with pulseless electrical activity (PEA). She could be resuscitated successfully. CAG revealed multi-vessel CAS for which she received calcium channel blockers. Five days after, she suffered from a second SCA due to ventricular fibrillation and was resuscitated again. Repeated CAG showed no critical coronary artery occlusion. LVEF improved progressively during hospitalization. Drug therapy was increased, and a subcutaneous implantable cardioverter defibrillator (ICD) was implanted for secondary prevention.

Discussion CAS may in some instances lead to SCA, especially in case of multi-vessel involvement. Allergic and anaphylactic events can trigger CAS, which are frequently underestimated. Regardless of the cause, cornerstone of CAS prophylaxes remains optimal medical therapy as in the avoidance of predisposing risk factors. In case of life-threatening arrhythmia, the implantation of an ICD should be considered.

Keywords Coronary artery spasm • Sudden cardiac arrest • Anaphylaxis • Case report

ESC Curriculum 3.2 Acute coronary syndrome • 3.4 Coronary angiography • 5.6 Ventricular arrhythmia • 5.10 Implantable cardioverter defibrillators • 7.2 Post-cardiac arrest

Learning points

- Coronary artery spasm may lead to cardiac arrest, especially in cases of multi-vessel involvement.
- By sudden cardiac arrest after coronary artery spasm, a strict adherence to medical therapy is mandatory, and the implantation of implantable cardioverter defibrillator should be considered.
- Allergic and anaphylactic events can trigger coronary artery spasm.

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Introduction

Coronary artery spasm (CAS) was described first by Prinzmetal *et al.*[1] in 1959 as abnormal constriction of coronary arteries. Typically, CAS presents at rest with corresponding ST-segment deviation on electrocardiogram (ECG). Smoking and psychological stress are known risk factors. Various pharmacological agents can trigger CAS, e.g. cocaine, beta-blockers, and ergot alkaloids (ergonovine, ergotamine, etc.), sympathomimetics (epinephrine, norepinephrine, etc.), as well as parasympathomimetics (methacholine, pilocarpine, etc.). Furthermore, activated platelets may trigger CAS through the release of vasoconstrictor substances, including thromboxane and serotonin.[2] Clinical manifestation can vary from transient angina attack to myocardial infarction (MI) and is generally associated with a good prognosis. However, patients may suffer from life-threatening arrhythmia (LTA), especially when multiple vessels are involved. We present a case of a young woman with multi-vessel CAS, who suffered sudden cardiac arrest (SCA) twice.

Timeline

Date	Event
11 March 2022	10.00 a.m.: hospital admission
	12.15 p.m.: aspirin administration
	12.30 p.m.: first cardiac arrest
	3.00 p.m.: coronary angiogram: severe multi-vessel coronary artery spasm.
16 March 2022	Second cardiac arrest
22 March 2022	Implantation of subcutaneous implantable cardioverter defibrillator
26 March 2022	Hospital discharge to cardiovascular rehabilitation
12 May 2022	First ambulatory follow-up

Case presentation

A 32-year-old woman presented to the emergency department with ongoing burning chest pain, which had occurred 1 h earlier. She reported a stressful emotional situation: her father recently died, and her mother was hospitalized for stroke. She stated that she smoked and regularly took budesonide/formoterol for bronchial asthma. Allergies to metamizole and non-steroidal anti-inflammatory drugs were reported.

On admission, she was haemodynamically stable, and the physical examination did not show any pathological findings, especially regarding the cardiovascular one (normal heart sounds without murmurs, no pericardial rub, no oedema, and normal pulmonary sound). ECG showed ST-segment elevation (STE) in aVL coupled with slight depression in the inferior and hyperacute T-waves in the precordial leads (*Figure 1A*). Elevated high-sensitivity troponin (hsTn) of 435 ng/L was found, with normal creatine kinase value. The transthoracic echocardiography (TTE) demonstrated impaired left ventricular ejection fraction (LVEF) of 30% with apical akinesia (see Supplementary material online, *Video S1*). Based on these findings, a diagnosis of non-ST-segment elevation myocardial infarction (NSTEMI) was made. Due to ongoing chest pain and the severe reduced LVEF, an urgent coronary angiogram (CAG) was scheduled. Immediately after aspirin administration of 250 mg intravenously, she developed symptoms and signs of anaphylaxis including dyspnoea, palpitations, dizziness, hypotension, tachycardia, and a drop in oxygen saturation to 88%. She received methylprednisolonum (125 mg), clemastinum (2 mg), and adrenaline inhalation with instant resolution of symptoms. Pulseless electrical activity (PEA) occurred unexpectedly during CAG preparation. Manual resuscitation was performed, and atropine (1 mg) and adrenaline (1 mg) were administrated with returning of spontaneous circulation (ROSC) after several minutes. CAG revealed subtotal stenosis of the left anterior descending artery, left circumflex artery, and right coronary artery suggesting multi-vessel CAS, which resolved immediately after intracoronary infusion of nitrate (*Figure 2*; see Supplementary material online, *Video S2*). Drug treatment with calcium channel blockers (CCBs) was initiated, and aspirin was discontinued.

Five days later, the patient suddenly complained chest pain and the ECG showed new STE in V1-V2 (*Figure 1B*). She received immediately nitrate. A few minutes later, she suffered another SCA, this time due to ventricular fibrillation (VF), and was successfully resuscitated again. Following ROSC, CAG was repeated and showed no relevant coronary artery occlusion. The follow-up TTE showed improvement of the LVEF (50%) with still some diffuse hypokinesia (see Supplementary material online, *Video S3*). Subsequently, a subcutaneous implantable cardioverter defibrillator (S-ICD) was implanted for secondary prevention in addition to optimized drug therapy with increased CCB dosage and molsidomine (*Figure 3*).

Until discharge, she remained asymptomatic and presented no other arrhythmias. At the first ambulatory follow-up, any cardiac symptoms were denied, and she reported an excellent adherence to the therapy. During S-ICD interrogation, no arrhythmia could be detected.

Discussion

On admission, diagnosis of NSTEMI was made because of chest pain, STE in only one lead, and abnormal wall motion. Consequently, a CAG was performed allowing the differentiation of type 2 MI with CAS according to the guideline.[3] During preparations for the CAG, the patient developed anaphylaxis that ended in PEA. Based on the patient's distressing emotional situation and the TTE findings, we hypothesize that the patient originally suffered from stress cardiomyopathy (SC). The following inflammatory reaction (activation of mast-cell and platelet, interrelated and interacting inflammatory cells, such as macrophages and T-lymphocytes) after aspirin administration associated with acute coronary syndrome—known as Kounis syndrome—may have triggered or exacerbated CAS, which typically results as type I variant from endothelial dysfunction.[4] TTE is the preferred imaging tool for suspected SC, which typically shows regional left ventricular wall motion abnormality with apical hypo- and akinesia, the so called 'apical ballooning'.[5] In addition, there is a discrepancy between minimal biomarker elevation and extensive wall motion abnormalities. However, the level of biomarker hsTn does not allow the differentiation between MI and SC.[6] The InterTAK diagnostic score asses the likelihood of SC with high sensitivity and specificity; however, the evaluation was performed in a small retrospective analysis.[7]

Five days after the presentation, she again complained of chest pain, and this time showed new STE in V1 and V2. This was followed by a second SCA due to VF, for which she was again successfully resuscitated. The second CAG showed no critical coronary artery occlusion. An explanation for unremarkable CAG is the previous application of nitrate, which may have prevented visualization of CAS. An alternative

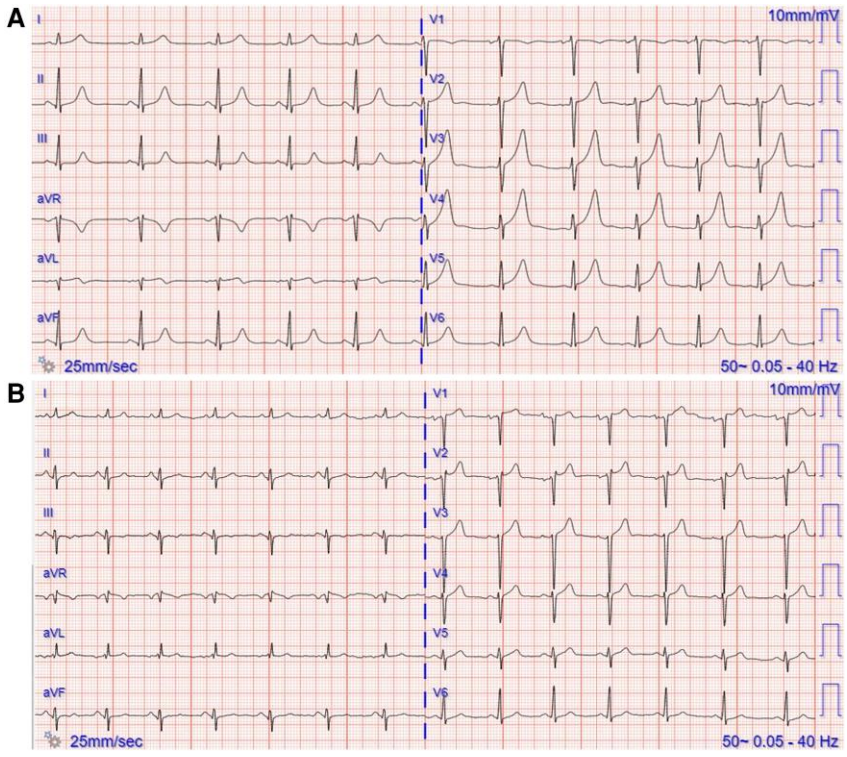

Figure 1 (*A*) Electrocardiogram on 11 March 2022 by the hospital admission and (*B*) electrocardiogram on 16 March 2022 by the second episode of chest pain.

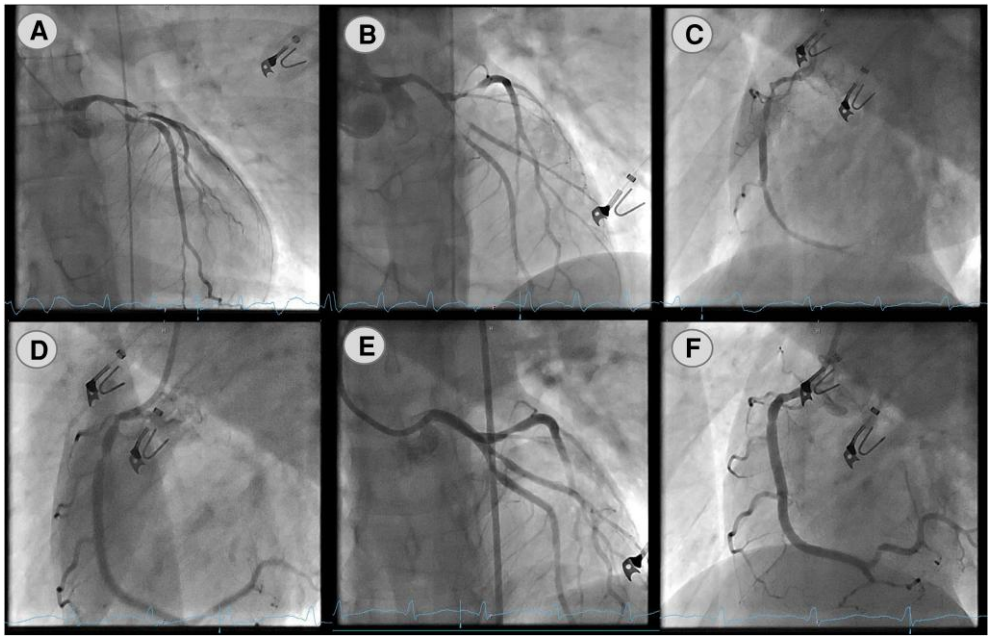

Figure 2 Coronary angiogram on 11 March 2022. (*A–D*) Left coronary artery and right coronary artery angiogram before nitrate administration. (*E–F*) Left coronary artery and right coronary artery angiogram after nitrate administration with resolution of multi-vessel narrowing.

explanation is the presence of microvascular vasospasm. As described in a prospective study by Jansen *et al.*[8] the prevalence of epicardial spasm is higher in men, whereas microvascular spasm is more common in women.

Arrhythmic events in CAS are described with a prevalence of one in every four cases.[9,10] PEA is an uncommon complication. Thus, we explain PEA in the context of anaphylactic reaction after aspirin.[11] The gold standard for diagnosis of CAS remains CAG with provocation tests, such as acetylcholine or ergonovine.[12] Although these provocation tests are feared due to their complications (e.g. LTA), they show an acceptable safety if performed lege artis[12] (*Figure 4*).

Medication	Dose	Date
Amlidipine	5mg twice daily	12.03.2022 – 16.03.2022
Diltiazem	90mg twice daily	17.03.2022 – 24.03.2022
Diltiazem	180mg twice daily	25.03.2022 – 12.05.2022 (follow-up)
Molsidomine	8 mg twice daily	18.03.2022 – 26.03.2022 (discharge)
Molsidomine	4 mg three times daily	12.05.2022 (follow-up)

Figure 3 Drug therapy scheme during hospitalization and at follow-up.

During hospitalization, the patient received CAS treatment based on avoidance of risk factors and indefinite drug therapy, with a combination of CCB and nitrate. Continuous therapy is recommended because discontinuation of medication has shown a higher recurrence rate.[13] Under this treatment regimen, LVEF gradually improved. Persistent impairment of LVEF on follow-up supports the initial diagnosis of SC. Otherwise it may be interpreted as stunning myocardium after resuscitation.[3]

The current guideline indicates the implantation of ICD after LTA in the absence of reversible causes (e.g. coronary revascularisation by MI type I),[14] Formally, CAS can be classified as reversible cause; however, patients who survive SCA show a high risk of recurrence, and according to the guideline, an ICD implantation should be considered.[14] As recommended in the guideline, the S-ICD was preferred because pacing therapy for bradycardia, cardiac resynchronization, or antitachycardia pacing was not anticipated, thus avoiding complications with transvenous leads[14] (*Figure 4*).

Conclusion

We hypothesize that initially SC was presented and the subsequent iatrogenic Kounis syndrome triggered or aggravated CAS. The role of allergic events in triggering CAS should be considered due to possible complications. Survivors of SCA after CAS are at high risk of LTA recurrence. In this population, a strict adherence to medical

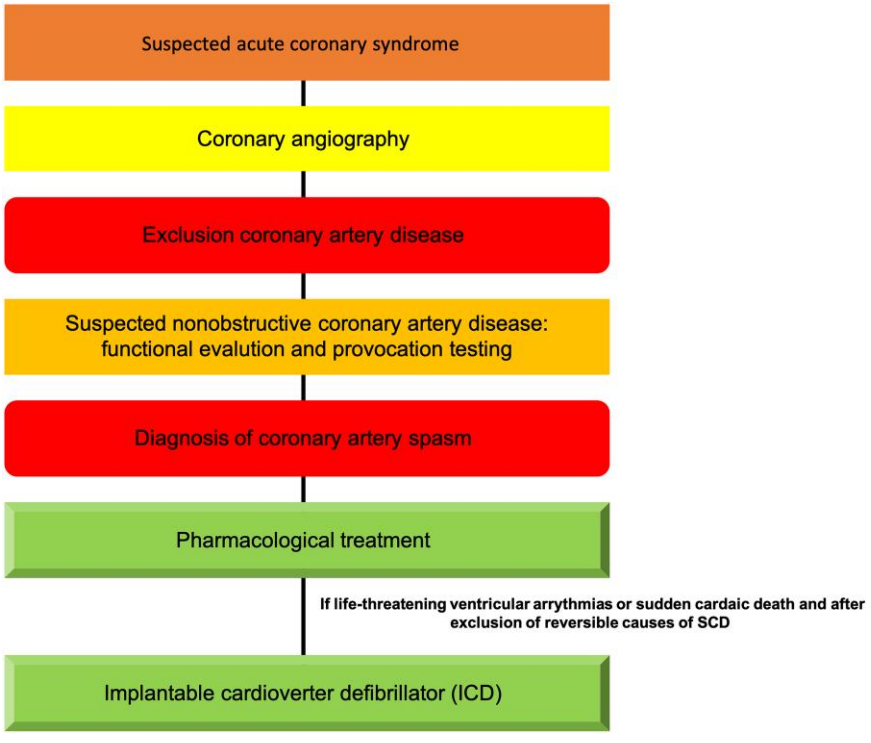

Figure 4 Flow chart diagram with stepwise approach to diagnostic and management strategies of coronary artery spasm and implantable cardioverter defibrillator implantation.

therapy and avoidance of risk factors is mandatory. Further, the implantation of ICD should be considered according to the guideline.

Lead author biography

Serena Favorini practiced at Cardiology Department of Uster Hospital, Switzerland. She graduated from the University of Genova, Italy. She attended her residency programme in Internal Medicine at IRCCS San Martino Hospital Genova, Italy, and her residency programme in Cardiology at Swiss Cardiovascular Center Inselspital University Hospital Bern, Switzerland; Department of Cardiology Aarau Hospital, Switzerland; and Heart Center University Hospital Zürich, Switzerland.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: In accordance with COPE guideline, written informed consent was obtained from the patient.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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