

# Fibrinolysis-treated myocardial infarction in a patient with missed spontaneous coronary artery dissection associated with takotsubo syndrome: case report

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## Background

Spontaneous coronary artery dissection (SCAD) is an under-recognized acute cardiac disease entity. It is often missed, or misdiagnosed as coronary spasm, coronary atherosclerotic lesion, or thrombotic coronary occlusion. During the last years, SCAD also has been reported to be 'misdiagnosed as takotsubo syndrome (TS)' in patients with features consistent with both conditions. Spontaneous coronary artery dissection may present as an acute coronary syndrome and sometimes as sudden cardiac death.

## Case summary

We report on the case of a 67-year-old woman who presented with features of ST-elevation myocardial infarction treated with fibrinolysis. The patient showed to have obtuse-marginal SCAD, which was misdiagnosed as fibrinolysis caused lysis of a coronary thrombus. The patient had moreover all other features of TS.

## Discussion

This case report teaches important information about SCAD. The association between SCAD and TS are discussed.

## Keywords

Spontaneous coronary artery dissection • Takotsubo • Acute coronary syndrome • fibrinolysis • Myocardial infarction • Myocardial stunning • Case report

## Learning points

- Spontaneous coronary artery dissection (SCAD) was misdiagnosed as fibrinolysis caused lysis of a coronary thrombus.
- Spontaneous coronary artery dissection was associated with takotsubo syndrome (TS). This association is a novel one, often overlooked, and only a limited number of cases are reported.
- The causal links between SCAD and TS are discussed.

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## Introduction

Spontaneous coronary artery dissection (SCAD) is defined as a non-traumatic, non-iatrogenic, and non-atherosclerotic spontaneous separation of the coronary artery wall due to either intimal rupture initiating a tear with intramural haematoma formation or spontaneous bleeding into the coronary arterial wall also with intramural haematoma compressing the true lumen resulting in acute coronary stenosis or occlusion.<sup>1</sup> The most frequent presentation of SCAD is clinical signs and symptoms of acute coronary syndrome (ACS).<sup>1</sup> SCAD may be missed or misdiagnosed as coronary spasm or coronary atherosclerotic lesion and consequently mismanaged. Takotsubo syndrome (TS) also presents with signs and symptoms indistinguishable from ACS.<sup>2,3</sup> The left ventricular wall motion abnormality (LVWMA) in TS has a characteristic circumferential pattern resulting in a conspicuous ballooning of the left ventricle during systole.<sup>3</sup> Spontaneous coronary artery dissection and TS are two cardiovascular diseases with a special predilection for women. During the last few years, a number of investigators have reported on the occurrence of left ventricular ballooning resembling that of TS in patients with SCAD.<sup>4,5</sup> These cases have been deemed by some of them as 'SCAD misdiagnosed as TS'. Herein, we describe a case of fibrinolysis-treated myocardial infarction in a patient with SCAD in the obtuse-marginal branch, which initially was missed. Moreover, the patient had all features of left ventricular mid-apical TS.

## Timeline

Symptoms	Clinical examination	Laboratory findings	Initial treatment	Clinical investigations	Final treatment	Follow-up and outcome
Day 1				Day 2	Days 3 and 4	10 months
Chest pain Nausea Dyspnoea	Blood pressure 150/110 mmHg ECG sinus rhythm ST-elevation in inferior and antero-lateral leads	Troponin elevation (6390 ng/L)	Fibrinolysis (metalyse)	Coronary artery angiography (CAG) showing spontaneous coronary artery dissection of marginal branch, which initially was missed. Cardiac magnetic resonance imaging showing transmural lateral myocardial infarction. Mid-apical ballooning.	Conventional and conservative treatment for acute coronary syndrome and heart failure	Patient was almost fully recovered. CAG showed normalization of the marginal branch lesions. Echo showed Resolution of left ventricular wall motion abnormality apart from the infarcted segment.

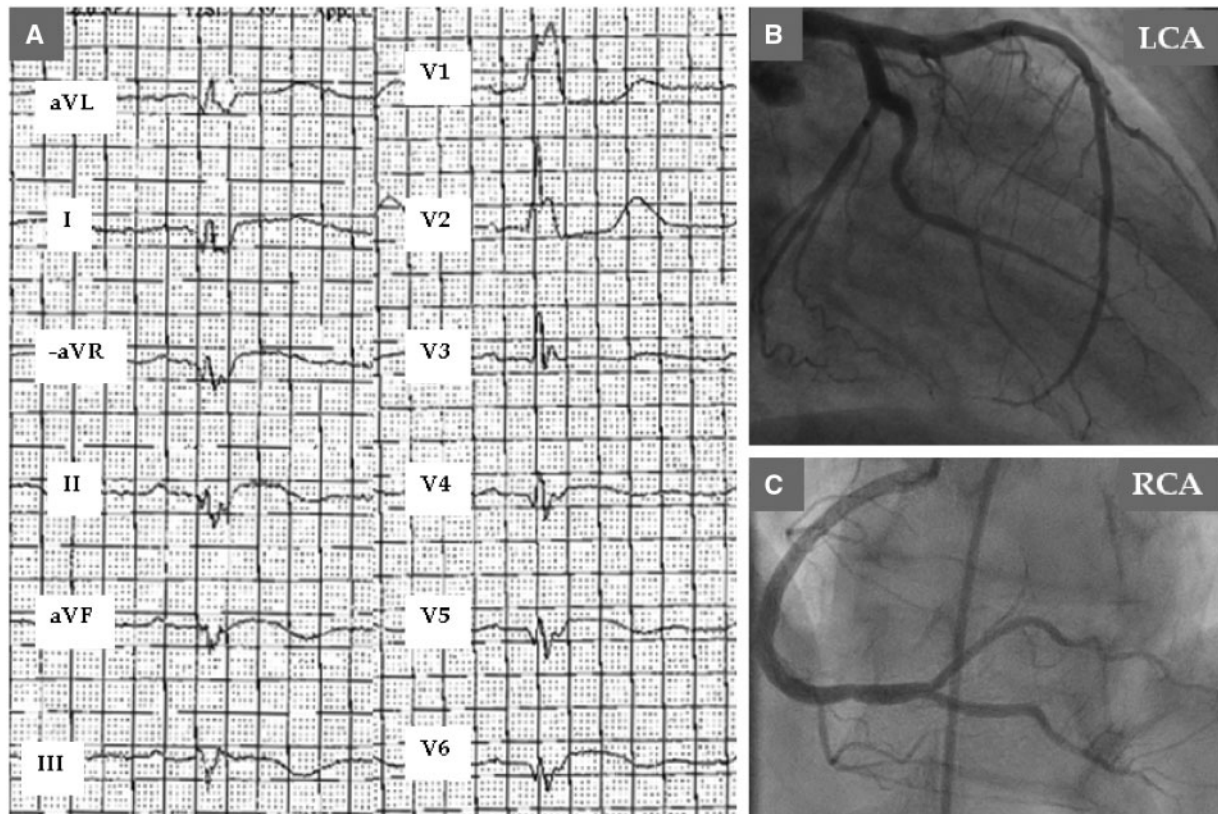
## Case presentation

A 67-year-old woman presented with 21 h duration of chest pain associated with nausea and dyspnoea. The chest pain was intensive during the first 4–6 h of onset and decreased in intensity thereafter. The chest pain was not preceded by an emotional or an extreme physical exercise. She had history of hypothyroidism medicated with thyroxin and hypertension medicated with oral drugs. There was no other past medical history. The patient was a chronic smoker but had no history of other cardiovascular risk factors as diabetes mellitus or

obesity. She had no history of depression/anxiety or connective tissue disease. The clinical examination was not remarkable apart from a blood pressure which was 150/101 mmHg. Normal heart sounds, no murmurs or bruits. The expiratory examination was normal.

The electrocardiogram revealed regular sinus rhythm and ST-segment elevation in the inferior and lateral leads, and in leads V4 through V6, and intraventricular conduction delay of right bundle branch block morphology (Figure 1A). There was marked troponin elevation (6390 ng/L), normal range <15 ng/L. The patient deemed to have infero-lateral ST-elevation myocardial infarction. The attending physician after discussion selected fibrinolysis treatment with metalyse (Tenecteplase). The patient was given 45 mg of Tenecteplase intravenously. Because of persistent chest pain and ST-elevation, the patient was referred to a percutaneous coronary intervention (PCI) centre for rescue PCI (Figure 1B,C). The attending cardiologist decided to perform cardiac magnetic resonance (CMR) imaging before the invasive coronary angiography (CAG) on the same day. Cardiac magnetic resonance imaging showed ballooning of the mid-apical region with normal contractions in the basal segments (Figure 2A–D, and cine CMR videos of 2-, 3-, and 4-chamber views as [Supplementary material online](#)). The left ventricular ejection fraction (LVEF) was 26% (normal 58–76%). Contrast CMR imaging revealed transmural myocardial infarction with signs of microvascular obstruction in the lateral segments corresponding to the left circumflex artery (LCx) supply territory whereas the remainder hypokinetic segments showed no late gadolinium enhancement (Figure 2E,F). The invasive CAG, which was done about 12 h after fibrinolysis administration, deemed initially to be normal apart from mild atheromatous changes (Figure 1B,C). Left

ventriculography revealed circular mid-apical ballooning with normal contractility in the basal segments. Because of patent coronary arteries, the preliminary diagnosis at this stage was LCx thrombosis, lysed by fibrinolysis treatment with myocardial infarction in the LCx territory. The mid-apical ballooning, which extended beyond the LCx territory, was deemed to be takotsubo syndrome (TS) triggered by the acute coronary ischaemic insult. However, because of the persistent and relatively wide-spread ST-segment elevation and the CMR infarction changes, the CAG was reviewed carefully. This resulted in suspicion of peripheral marginal branch SCAD where the vessel was



**Figure 1** (A) Twelve-lead electrocardiogram showing ST-elevation with T-wave inversion in anterolateral and inferior leads. (B and C) Left coronary artery (LCA) and right coronary artery (RCA) initially deemed to be normal apart from some atherosclerotic changes.

narrowed and had the appearance of broken lines (Figure 3A with amplification B, thin white arrows and 2 videos in 2 projections during index presentation as [Supplementary material online](#)). The patient was treated conservatively and received conventional treatment for acute coronary syndrome and heart failure. The patient had in addition during admission days paroxysmal atrial fibrillation treated with amiodarone. There was no history of known paroxysmal atrial fibrillation before the index presentation. For the purpose of confirming the diagnosis of obtuse marginal branch SCAD, repeated CAG 10 months later was performed, which showed complete angiographic normalization of the obtuse-marginal branch lesions (Figure 3C with amplification in D thick white arrows and 2 videos in 2 projections during follow-up 10 months later as [Supplementary material online](#)). Follow-up echocardiography also showed resolution of the LVWMA except in the infarcted lateral segments causing mild depression of LVEF 49%. These findings confirm the diagnosis of obtuse-marginal branch SCAD, which caused myocardial infarction and possibly triggered mid-apical TS.

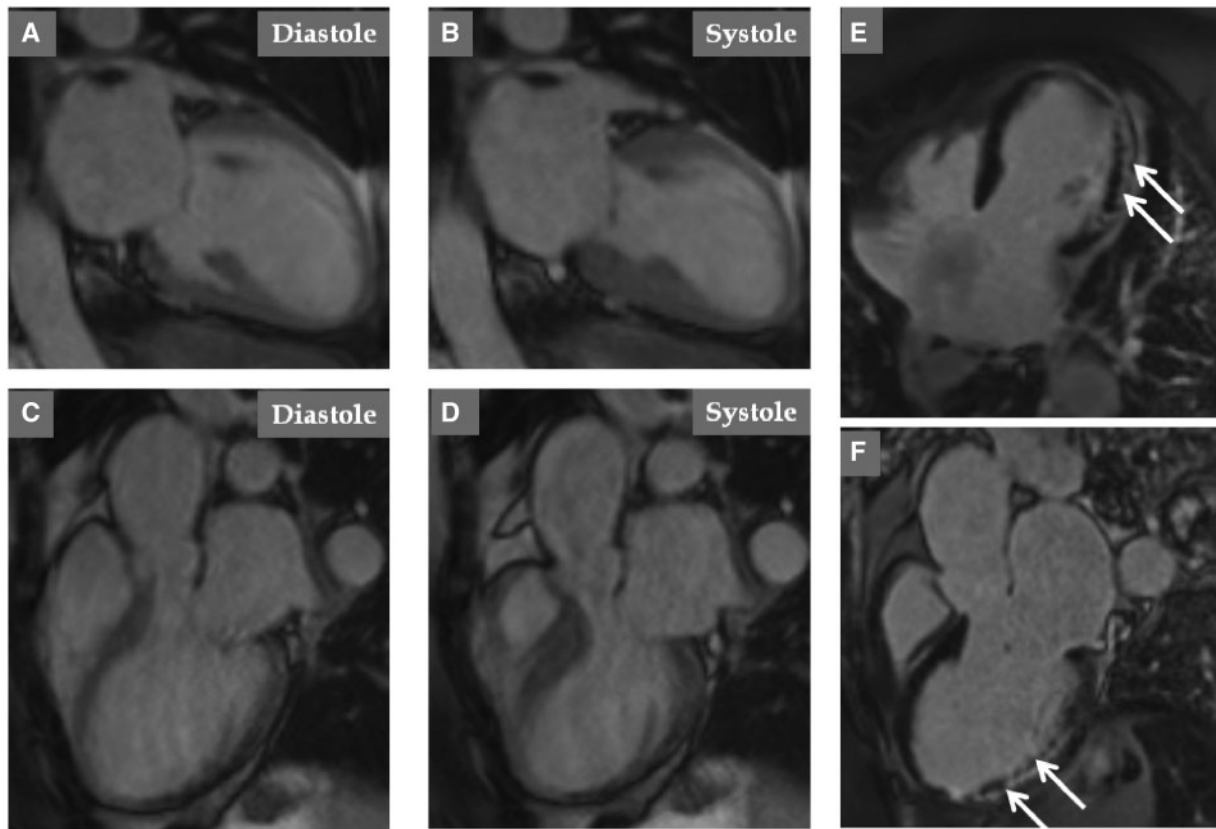
## Discussion

The main findings, which deserve discussion, in the current patient are: the patient was treated with fibrinolysis, where the indication should be questioned on several points. Spontaneous coronary

artery dissection in the obtuse-marginal branch, which was the cause of myocardial infarction in the LCx territory, was initially missed. Moreover, the patient had features typical for that of mid-apical TS. The marked troponin elevation is induced mainly by the SCAD-caused myocardial infarction. The association of SCAD and TS is discussed.

### Treatment with fibrinolysis in a patient with spontaneous coronary artery dissection and takotsubo syndrome

The case was diagnosed as myocardial infarction presumed to be caused by thrombosis in the LCx, which was deemed to be resolved by fibrinolysis treatment in the form of Tenecteplase. The attending physician initiated treatment with fibrinolysis 21 h after the onset of chest pain, where the efficacy of fibrinolysis therapy in such a case should be questioned. Persistent ST-elevation after fibrinolysis therapy argues against successful therapy and lysis of the thrombus in LCx. In hindsight, the persistent and wide-spread ST-elevation was partly attributed to subtotal occlusion of the obtuse-marginal branch due to SCAD and partly to TS. In general, fibrinolysis therapy is associated with certain risks of bleeding including intra-cerebral bleeding. In addition to be futile, fibrinolysis therapy in this patient may have augmented the coronary intramural bleeding, which has caused SCAD in the LCx artery. Furthermore, TS may be triggered in some



**Figure 2** Cardiac magnetic resonance (CMR) imaging showing mid-apical ballooning during systole in two projections (A–D). Contrast cardiac magnetic resonance-imaging showing late gadolinium enhancement (LGE) in the inferolateral wall with signs of microvascular obstruction (E and F, white arrows) and no late gadolinium enhancement in the remainder of the stunned mid-apical segments.

cases by occult bleeding as in subclinical subarachnoid haemorrhage and fibrinolysis therapy in such a case may result in serious consequences. This problem is well demonstrated in a case published by Vyas *et al.*<sup>6</sup> Fortunately, the present patient did not develop any overt complications related to fibrinolysis therapy.

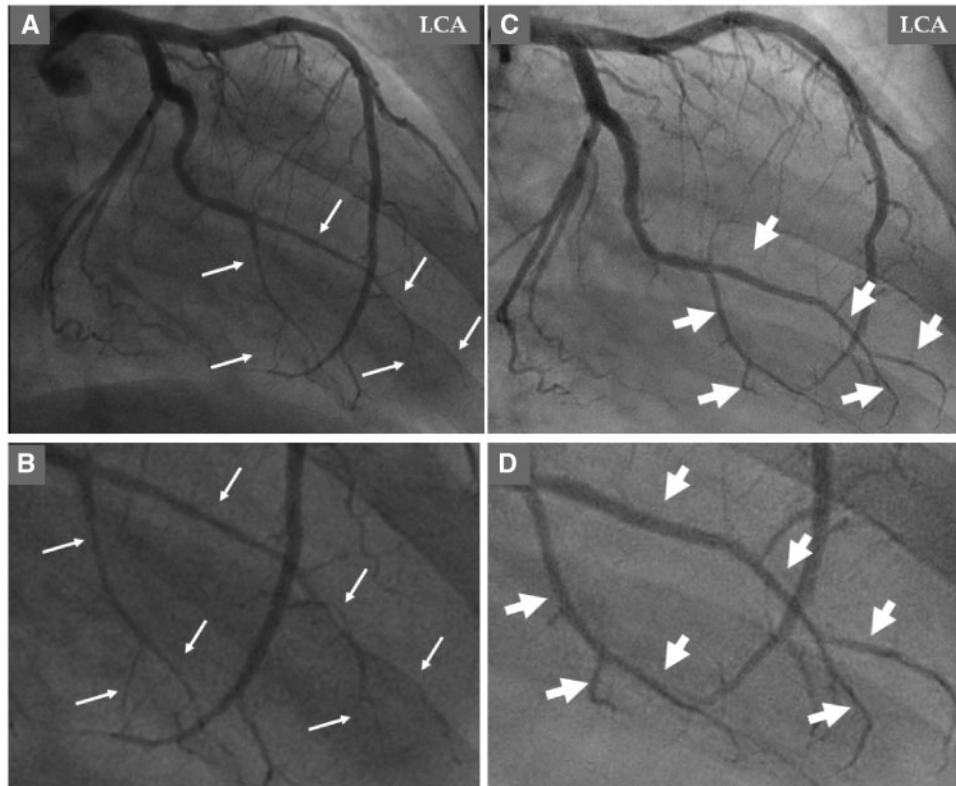
### Missing and misdiagnosis of spontaneous coronary artery dissection

Spontaneous coronary artery dissection is still an under-recognized and therefore an under-diagnosed disease entity. Spontaneous coronary artery dissection may be missed especially in patients with angiographically invisible type II and type III lesions according to Saw classification of SCAD.<sup>7</sup> Spontaneous coronary artery dissection may also be misdiagnosed as a coronary spasm. The persistence of the lesion more than 1 day after the onset of chest pain and routine nitroglycerin administration, and the peripheral localization of the lesion argue against coronary spasm in the current case. Type IIB SCAD may be interpreted as a normal tapering vessel variant. Type III SCAD may be misdiagnosed as an atherosclerotic coronary artery lesion.<sup>8</sup> During the last few years, several investigators have reported cases with 'SCAD misdiagnosed as TS'.<sup>5,9–11</sup> Some of these investigators have explained the apical ballooning induced by coronary ischaemia caused by lesions in a LAD with a long wrap-around course.<sup>5,10</sup>

However, the mid-apical ballooning has occurred even in cases of other non-LAD coronary lesions. We have reported on LAD-SCAD triggering mid-apical ballooning,<sup>4</sup> diagonal-SCAD triggering mid-apical ballooning,<sup>12</sup> and obtuse-marginal-SCAD inducing also mid-apical ballooning.<sup>13</sup> Consequently, there is evidence supporting the coexistence of SCAD and TS as in the current case.

### The causal link between spontaneous coronary artery dissection and takotsubo syndrome

Four possible causal links between SCAD and TS may be discussed. First, the ischaemia caused by SCAD may induce post-ischaemic myocardial stunning (PIMS).<sup>14</sup> Myocardial stunning may extend beyond the supply region of the dissected coronary artery territory resulting in LVWMA with a pattern, features, and course consistent with TS. Consequently, the ischaemic insult caused by SCAD may, as any other physical stress factor, have acted as a trigger factor for PIMS (TS) through the sympathetic hyperactivation with local cardiac sympathetic disruption and norepinephrine seethe and spillover.<sup>15–17</sup> Second, the acute chest pain and the severe discomfort associated with myocardial infarction due to SCAD may also act as a major physical stress factor, which may trigger TS as any other physical



**Figure 3** Careful review of left coronary artery revealed narrowing of the peripheral part with appearance of broken line and even subtotal occlusion in some peripheral branches of the obtuse-marginal branches (thin white arrows in A and with amplification in B). Ten months later, the changes in the obtuse-marginal branches are angiographically resolved (thick white arrows in C and with amplification in D).

stress factor. Third, in addition to the similarities in the clinical and electrocardiographic features between TS and ACS (including SCAD), SCAD and TS have also three other important features in common which are: (i) both diseases afflict predominantly women<sup>1,3</sup>; (ii) SCAD and TS are usually preceded by an emotional or a severe physical exercise<sup>1,3</sup>; (iii) 'restitution ad integrum' of the lesions in both SCAD and TS occurs in the majority of cases.<sup>1,3,18</sup> A complex interaction between neuro-hormonal, genetic, anatomic, and other factors may play a role in the pathogenesis of SCAD and TS. Consequently, a common pathological mechanism triggering both TS and SCAD cannot be excluded. It remains for the future research to disclose this conundrum. Fourth, Madias,<sup>19</sup> proposed that the hyperkinetic basal segments, in conjunction with the akinetic apical or mid-apical segments in TS could form a pre-requisite anatomic/functional substrate for the causation of SCAD in a predisposed individual. However, this hypothesis may explain SCAD in the proximal and not the peripheral coronary segments. Furthermore, Madias<sup>20</sup> in a comment on one of our case report on the association of obtuse-marginal SCAD and TS,<sup>13</sup> has added that the dissected obtuse-marginal branch was at a distance from the hinging point does not exclude this hypothesis with the explanation that the hinging point between the well and poorly contracting regions may have been closer to obtuse-marginal artery, since it has been reported that the regional contraction abnormalities occasionally migrates to the various parts

of the left ventricle in the course of the same TS attack.<sup>20</sup> Further explanation as indicated by Madias is that 'one could conceive maximal mechanical force being applied in one part of the coronary artery, with SCAD occurring in different part, more vulnerable, of the same artery'. This hypothesis is reasonable but needs to be confirmed. If this is the case, SCAD will be regarded as a complication of TS. Spontaneous coronary artery dissection in such a case should occur after the development of TS and there should be cases where the patients primarily admitted because of TS with completely normal CAG and then develop SCAD during admission days; a new CAG is necessary to confirm the SCAD occurrence. Our case report on the obtuse-marginal SCAD and TS<sup>13</sup> had not proximal RCA-SCAD on admission day but developed proximal RCA-SCAD few days after admission. However, recurrence in SCAD (without association with TS) is not unusual during the sub-acute stage and on long-term bases.<sup>21</sup>

## Conclusion

We have presented a case of fibrinolysis-treated myocardial infarction in a patient with SCAD in the obtuse-marginal branch, which initially was missed. Spontaneous coronary artery dissection was associated PIMS with features typical for mid-apical TS. This is an additional report supporting the notion that SCAD and TS may coexist.

## 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:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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