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CASE REPORT
Cardiovascular imaging

An unusual case of two acute coronary syndrome episodes caused by allergic and non-allergic coronary artery dissection with potential coronary vasospasm association: a case report

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Background Type I variant Kounis syndrome is characterized by coronary spasm following an allergic or anaphylactic reaction. Coronary spasm is also recognized as a contributing factor in spontaneous coronary artery dissection (SCAD).

Case summary A 46-year-old woman presented to the emergency room with a chief complaint of chest discomfort following the ingestion of a steamed bun. A marked decrease in systolic blood pressure and a prominent rash on her forearms and groin suggested anaphylactic shock. Upon stabilization of vital signs, acute coronary syndrome (ACS) was suspected based on electrocardiogram findings and symptoms, prompting an emergency coronary angiography (CAG). The CAG revealed severe stenosis with coronary artery dissection in the right coronary artery (RCA), and a stent implantation was performed. Given the suspicion of type I variant Kounis syndrome, a spasm provocation test was performed, yielding a positive result. Six years later, she experienced chest discomfort while sleeping and was admitted to our emergency department. An electrocardiogram showed ST-segment elevation in leads II, III, and aVF. An emergency CAG identified a severely stenotic lesion with coronary artery dissection in the RCA, leading to a diagnosis of SCAD. Direct stenting was performed at the stenotic site. The patient was discharged following intensification of medication.

Discussion This report describes a rare case of a middle-aged woman with two episodes of ACS caused by both allergic and non-allergic coronary artery dissection. These episodes suggest that a shared underlying coronary vasospasm in both conditions may be a common trigger for coronary artery dissection.

Keywords Kounis syndrome • Spontaneous coronary artery dissection • Anaphylactic shock • Coronary vasospasm • Case report

ESC curriculum 3.2 Acute coronary syndrome • 2.1 Imaging modalities • 3.1 Coronary artery disease

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Learning points

- Cases of coronary artery dissection resulting from allergic or anaphylactic reactions in acute coronary syndrome are extremely rare.
- Type I variant Kounis syndrome involves coronary spasm following an allergic or anaphylactic reaction, and this spasm is also considered a factor in spontaneous coronary artery dissection (SCAD).
- Spasm provocation tests at the appropriate timing for SCAD patients with suspected coronary vasospasm may be helpful in determining a pharmacotherapeutic strategy.

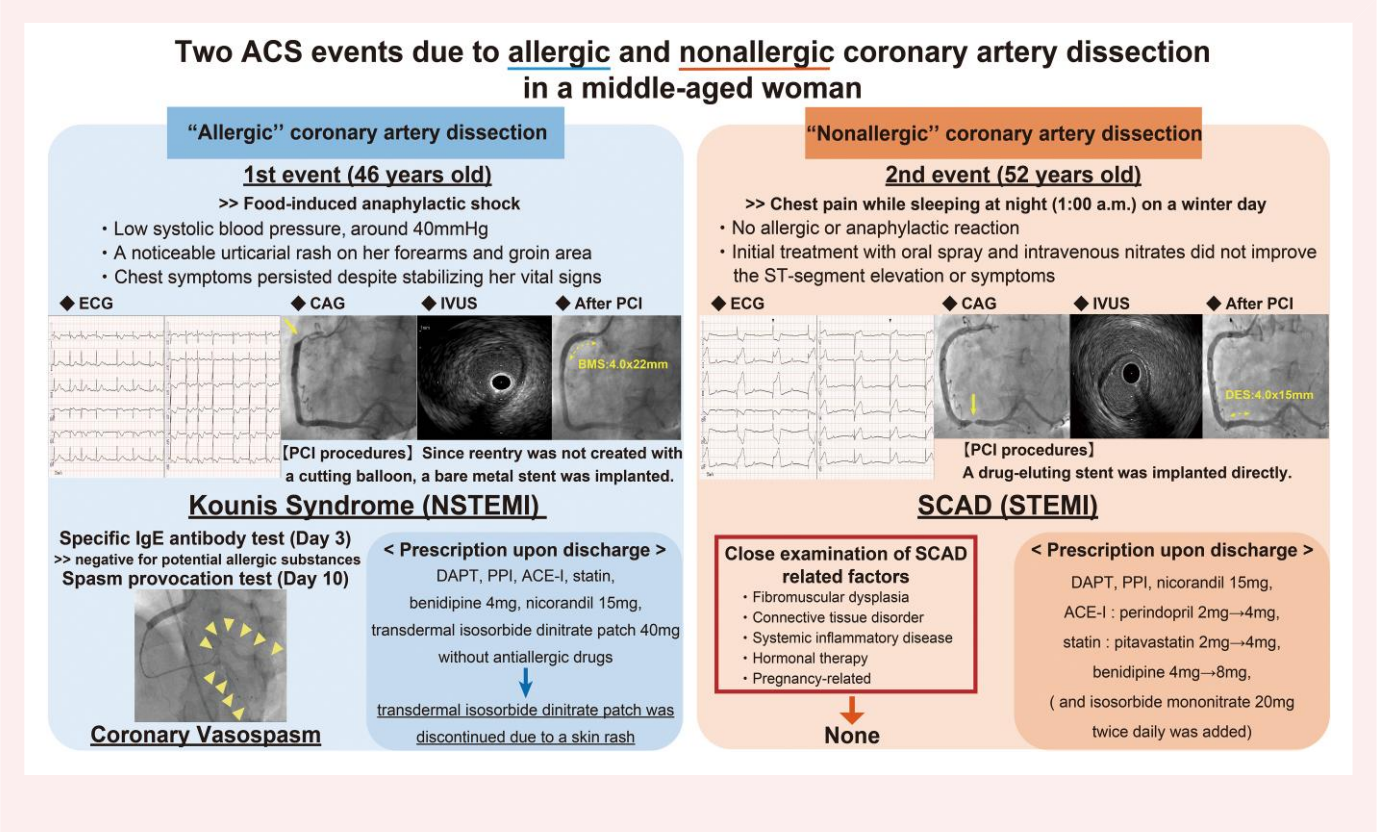
Introduction

Kounis syndrome, initially described in 1991, refers to allergic angina resulting from histamine-induced coronary spasm during an acute allergic reaction.[1] Subsequently, in 2016, its definition expanded to include the simultaneous occurrence of acute coronary syndrome (ACS) with mast cell and platelet activation due to an allergic or anaphylactic reaction.[2] This syndrome is categorized into three variants, with type I involving ACS associated with coronary spasm.

In contrast, spontaneous coronary artery dissection (SCAD) is a relatively rare cause of ACS, particularly in young–middle-aged women, and is notable for its absence of atherosclerosis.[3] The aetiology of SCAD remains unclear, though potential predisposing arteriopathies, including coronary spasm, have been identified.[3]

This report presents an exceedingly rare case of a middle-aged woman who experienced two episodes of ACS. These episodes were attributed to both allergic and non-allergic coronary artery dissection, with coronary spasm appearing to be a common trigger in both scenarios.

Summary figure



Case presentation

A 46-year-old woman was brought to our hospital with a chief complaint of pharyngeal and chest discomfort that developed immediately a few minutes after ingestion of *momiji manju*, a Japanese sweet cake. She was a current smoker with a history of childbirth four times. Regarding allergies, she had a history of severe abdominal pain, nausea, flushing, and transient syncope after previously taking cefaclor at age 30, which was diagnosed as an allergy to cephem antibiotics, but she had no history of food allergies or similar episodes after food ingestion. At the time of ambulance contact, her level of consciousness was Japan Coma Scale II-10, oxygen saturation was 81% in room air, and oxygen administration (10 L/min of oxygen by reservoir mask) was started. Upon arrival at the hospital, her systolic blood pressure was found to be low at 40 mmHg, pulse was 42 b.p.m., body temperature was 35.7°C, and oxygen saturation was 100% on 10 L/min of oxygen by reservoir mask. Noticeable urticarial rash was observed on her forearms and groin area. Although pharyngeal and chest discomfort persisted for about 40 min from onset, there were no complaints of dyspnoea, and no wheezing in the lung field was heard on auscultation. Chest X-ray and computed tomography findings showed no evidence of pulmonary congestion. Anaphylactic shock was strongly suspected based on the

Table 1 Laboratory data

	1st admission (A)	2nd admission (B)	Normal range
White blood cell ($\times 10^3/\mu L$)	12.7	12.8	(A) 4.0–9.0/(B) 3.3–8.6
Basophil (%)	0.1	0.4	0.0–3.0
Eosinophil (%)	1.3	2.8	0.0–10.0
Neutrophil (%)	48.6	42.0	50.0–70.0
Lymphocytes (%)	44.3	47.5	30.0–45.0
Monocytes (%)	5.7	7.3	2.0–8.0
C-reactive protein (mg/dL)	0.0	0.02	(A) 0.0–0.7/(B) 0.00–0.14
AST (U/L)	163	15	(A) 10–40/(B) 13–30
ALT (U/L)	164	14	(A) 4–45/(B) 7–23
BUN (mg/dL)	12.2	16.6	8–20
Creatinine (mg/dL)	0.65	0.63	(A) 0.46–0.82/(B) 0.46–0.79
CK (U/L)	73	99	(A) 30–165/(B) 41–153
CK-MB (IU/L)	10	14	0–12
Qualitative TnT	—		—
hs-TnT (ng/mL)		0.004	<0.100
BNP (pg/mL)	26.1	19.5	0–18.4
Peak CK (U/L)	129	622	
Peak CK-MB (IU/L)	13	74	

AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; CK, creatine kinase; CK-MB, creatine kinase-MB; TnT, troponin T; hs-TnT, high-sensitive troponin T; BNP, brain natriuretic peptide.

pharyngeal and skin symptoms that developed suddenly after food ingestion and the marked decrease in blood pressure. Despite stabilizing her vital signs with rapid hydration and anti-allergic medications (intravenous administration of *d*-chlorpheniramine maleate 5 mg, famotidine 20 mg, and hydrocortisone sodium succinate 300 mg), her chest symptoms persisted. Laboratory results at the time of her arrival are detailed in *Table 1* (A), indicating a slight elevation in brain natriuretic peptide levels at 26.1 pg/mL (normal range: ≤18.4 pg/mL), but no increase in creatine kinase (CK) at 73 U/L (30–165 U/L), CK-MB fraction at 10 IU/L (≤12 IU/L), and negative for qualitative cardiac troponin T. An electrocardiogram showed ST-segment depression in leads V3–6 and atrial fibrillation (*Figure 1A*). Transthoracic echocardiography revealed mild wall motion abnormalities in the left ventricular inferior region. Emergency coronary angiography (CAG) for suspected ACS revealed 90% stenosis in the right coronary artery (RCA) ostium to the proximal portion (see Supplementary material online, *Video S1*; *Figure 1B*). Intracoronary nitrate administration failed to alleviate the stenosis. Intravascular ultrasound (IVUS) revealed a coronary artery dissection and intramural haematoma with no evidence of atherosclerotic lesions (see Supplementary material online, *Video S2*; *Figure 1B'*). Attempts to create reentry using multiple dilatations with a cutting balloon Flextome (Boston Scientific, Natick, USA) were unsuccessful, leading to the placement of a bare metal stent (Integrity 4.0 × 22 mm; Medtronic, Santa Rosa, CA, USA; *Figure 1C*). Subsequent IVUS showed successful stent expansion and coverage of the dissected lumen (*Figure 1C'*).

During her hospital stay, a spasm provocation test was performed (*Figure 2A–C*). The administration of 20 μg acetylcholine in the RCA revealed a 99% stenosis due to spasm (see Supplementary material online, *Video S3*; *Figure 2B*). The patient experienced severe chest pain, and the test confirmed a diagnosis of coronary vasospastic angina. Specific IgE testing (a radioallergosorbent test) was performed in the evaluation of allergen sensitivity to confirm the allergic diagnosis (*Table 2*). As a result, all potential allergens, mainly milk, egg white, egg yolk, soybean, and rice, which are the ingredients of buns, were negative, and the causative agents could not be identified. Mast cell tryptase test was not performed. She was prohibited foods suspected of triggering anaphylaxis, instructed to quit smoking, and discharged with a prescription for a calcium channel blocker (benidipine 4 mg) and vasodilators (nicorandil 5 mg three times daily and a transdermal isosorbide dinitrate patch 40 mg) for managing coronary spasm, without anti-allergic drugs. Additionally, she was prescribed aspirin 100 mg, clopidogrel 75 mg, esomeprazole 20 mg, pitavastatin 1 mg, and perindopril 2 mg.

Six years after her initial presentation, the patient returned to our emergency department with chest discomfort while asleep on a winter night. She had continued with her calcium channel blocker and nicorandil treatment since her last discharge but discontinued the transdermal isosorbide dinitrate patch at her own discretion approximately 6 months ago because of a skin rash related to its use. An electrocardiogram revealed ST-segment elevation in leads II, III, and aVF with complete atrioventricular block (*Figure 3A*). Laboratory results at the time of her arrival are shown in *Table 1* (B), indicating a slight elevation in CK-MB fraction at 14 IU/L (≤12 IU/L), but no increase in CK at 99 U/L (41–153 U/L) and high-sensitivity cardiac troponin T at 0.004 ng/mL (<0.10 ng/mL). Initial treatment with oral spray and intravenous nitrates did not improve the ST-segment elevation or symptoms.

Consequently, an emergency CAG was performed, revealing a severe focal stenosis in the RCA (see Supplementary material online, *Video S4*; *Figure 3B*). An intracoronary injection of nitrate failed to ameliorate the stenosis. Intravascular ultrasound revealed the coronary artery dissection and intramural haematoma with no evidence of atherosclerotic lesions, leading to a diagnosis of SCAD (see Supplementary material online, *Video S5*; *Figure 3B'*). Post-implantation of a drug-eluting stent (Ultimaster Nagomi 4.0 × 15 mm; Terumo Corporation, Tokyo, Japan; *Figure 3C*), IVUS confirmed effective stent expansion and coverage of the dissected lumen on the proximal side (*Figure 3C'*). Neither fibromuscular dysplasia nor

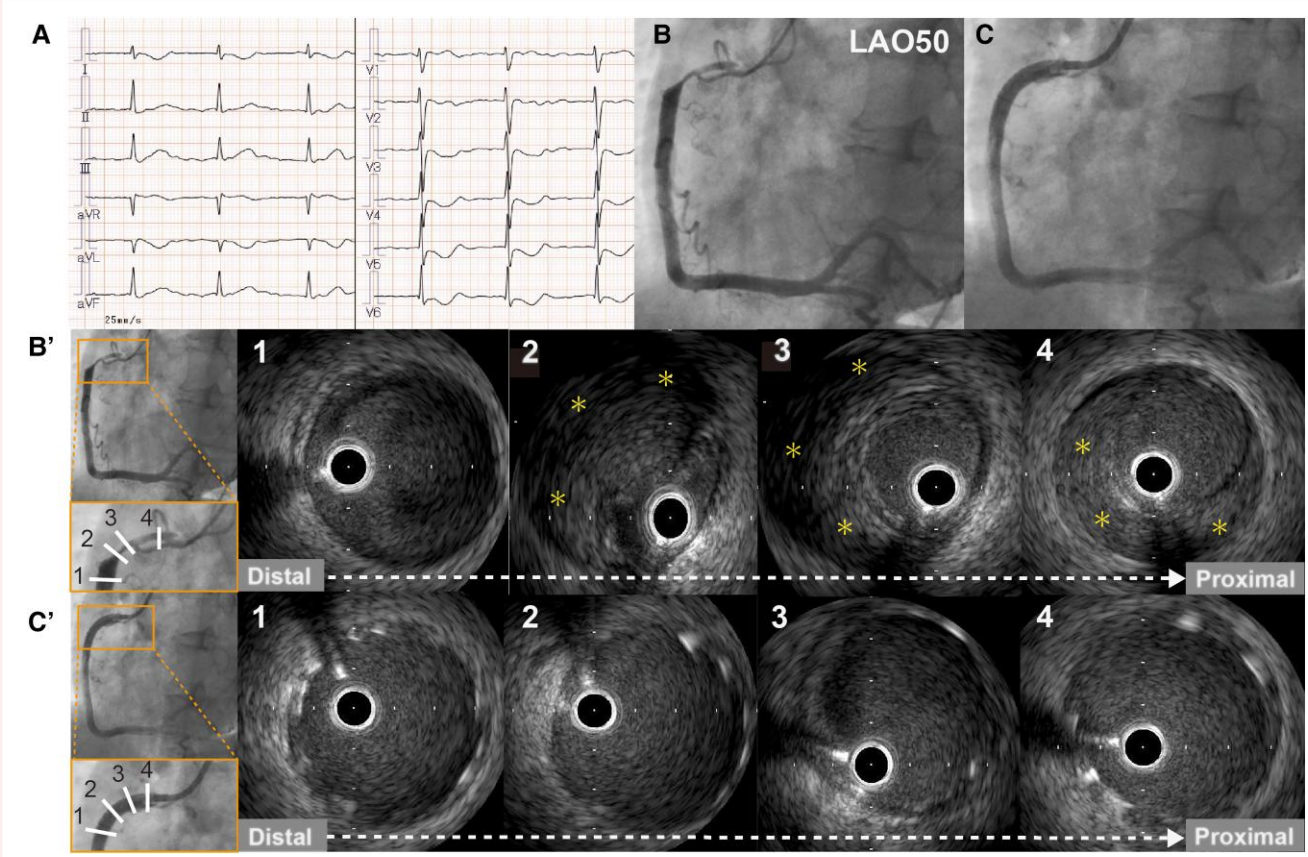


Figure 1 (*A*) Twelve-lead electrocardiogram taken upon arrival. (*B*) Coronary angiography demonstrating a severely stenotic lesion in the right coronary artery #1. (*B': 1–4*) Pre-stenting intravascular ultrasound images displaying true lumen compression with coronary artery dissection and intramural haematoma (asterisks). (*C, C': 1–4*) Post-stenting coronary angiography and intravascular ultrasound illustrating effective stent expansion.

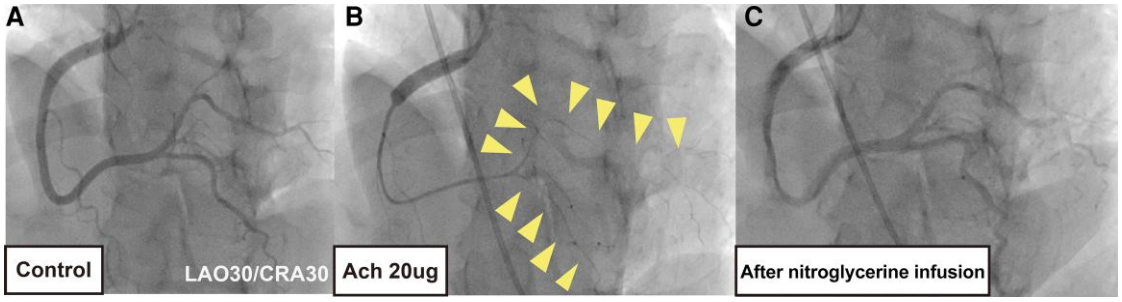


Figure 2 Results of the spasm provocation test. (*A*) Baseline contrast imaging prior to nitroglycerine administration. (*B*) Following the administration of 20 μg acetylcholine, the area beyond the stent became narrower, with 99% stenosis resulting from spasm (triangles). (*C*) Contrast imaging after nitroglycerine administration.

connective tissue disorder was identified as a contributing factor to the SCAD. The patient was discharged following cardiac rehabilitation and intensification of medication (perindopril increased to 4 mg, benidipine to 4 mg twice daily, pitavastatin to 4 mg, and isosorbide mononitrate 20 mg twice daily was added). After discharge, the patient has continued to receive medical treatment at our outpatient clinic and has been doing well for about 2 years without any recurrence.

Discussion

Cases of coronary artery dissection in ACS following an allergic or anaphylactic reaction are exceedingly rare. To the best of our knowledge, this is the first report of an ACS case in a middle-aged woman who experienced coronary artery dissection after anaphylactic shock. It is also the first documented instance of two separate ACS episodes, one due

Table 2 Specific IgE antibody test

Type of allergens	Patient range (UA/mL)	Normal range (UA/mL)
Dermatophagoides farinae	1.94	≤0.34
House dust	1.54	≤0.34
Cryptomeria japonica	0.52	≤0.34
Milk	<0.1	≤0.34
Egg white	<0.1	≤0.34
Egg yolk	<0.1	≤0.34
Wheat	<0.1	≤0.34
Rice	<0.1	≤0.34
Soba (*Fagopyrum esculentum*)	<0.1	≤0.34
Soybean	<0.1	≤0.34
Almond	<0.1	≤0.34
Crab	<0.1	≤0.34
Shrimp	<0.1	≤0.34
Beef	<0.1	≤0.34
Tuna (*Thunnus thynnus*)	<0.1	≤0.34
Salmon (*Oncorhynchus keta*)	<0.1	≤0.34
Cheese	<0.1	≤0.34
Chicken	<0.1	≤0.34
Mackerel	<0.1	≤0.34
Squid	<0.1	≤0.34
Octopus	<0.1	≤0.34
Horse mackerel (*Trachurus japonicus*)	<0.1	≤0.34
Chamaecyparis obtusa	<0.1	≤0.34
Anthoxanthum odoratum	<0.1	≤0.34
Phleum pratense	<0.1	≤0.34
Ambrosia artemisiifolia	<0.1	≤0.34
Artemisia princeps Pampanini	<0.1	≤0.34
Penicillium sp.	<0.1	≤0.34
Cladosporium sp.	<0.1	≤0.34
Aspergillus sp.	<0.1	≤0.34
Candida albicans	<0.1	≤0.34
Alternaria alternata	<0.1	≤0.34
Cat skin scraps	<0.1	≤0.34

to an allergic and the other non-allergic, both resulting from coronary artery dissection in the same patient within a 6-year span. These episodes may have been triggered by coronary spasm.

Mast cells play a crucial role in the onset of Kounis syndrome. Their degranulation and subsequent release of chemical mediators can exacerbate local coronary spasms.[1,2] Research indicates a higher density of mast cells at the site of coronary spasm in patients, suggesting that chemical mediators such as histamine, released from vascular wall mast cells, could initiate spontaneous coronary spasm episodes even in non-allergic conditions.[4] The relationship between coronary spasm and coronary artery dissection has been highlighted in several clinical reports,[5–8] and experimental animal models have also shown that severe coronary spasm often leads to intramural haematoma.[9] Notably, in the present case, there was no evidence of organic atherosclerotic lesions at the site of the two coronary artery dissection lesions. The term SCAD is typically used interchangeably with non-atherosclerotic SCAD (NA-SCAD), although instances of atherosclerotic SCAD (A-SCAD) in patients with organic atherosclerotic lesions have been documented.[10,11] The mechanism underlying A-SCAD remains elusive; however, it has been suggested that the disruption of the vasa vasorum within the atheroma may precipitate intraplaque haemorrhage and dissection.[12] Given the divergent management approaches for each condition, it becomes crucial to evaluate organic atherosclerotic lesions through not only CAG but also through imaging modalities such as IVUS or optical coherence tomography (OCT) to determine the aetiology of the dissection.[13] Furthermore, the presence of organic coronary stenosis has been identified as a significant prognostic marker for cardiovascular events in individuals with coronary spasm.[14,15] Optical coherence tomography imaging of organic stenosis in patients experiencing coronary artery spasm has revealed features such as layered plaques, macrophages, and microchannels within the plaques.[16] The absence of such atherosclerotic lesions in this case might indicate that pathologies such as congenital vascular endothelium abnormalities and vascular fragility, frequently observed in SCAD patients,[3,17,18] could evolve into dissection via severe coronary spasm.

With regard to pharmacotherapy for SCAD, the efficacy of beta-blockers is not conclusively established, but their use has been reported to be significantly associated with a decreased risk of recurrent SCAD.[19]

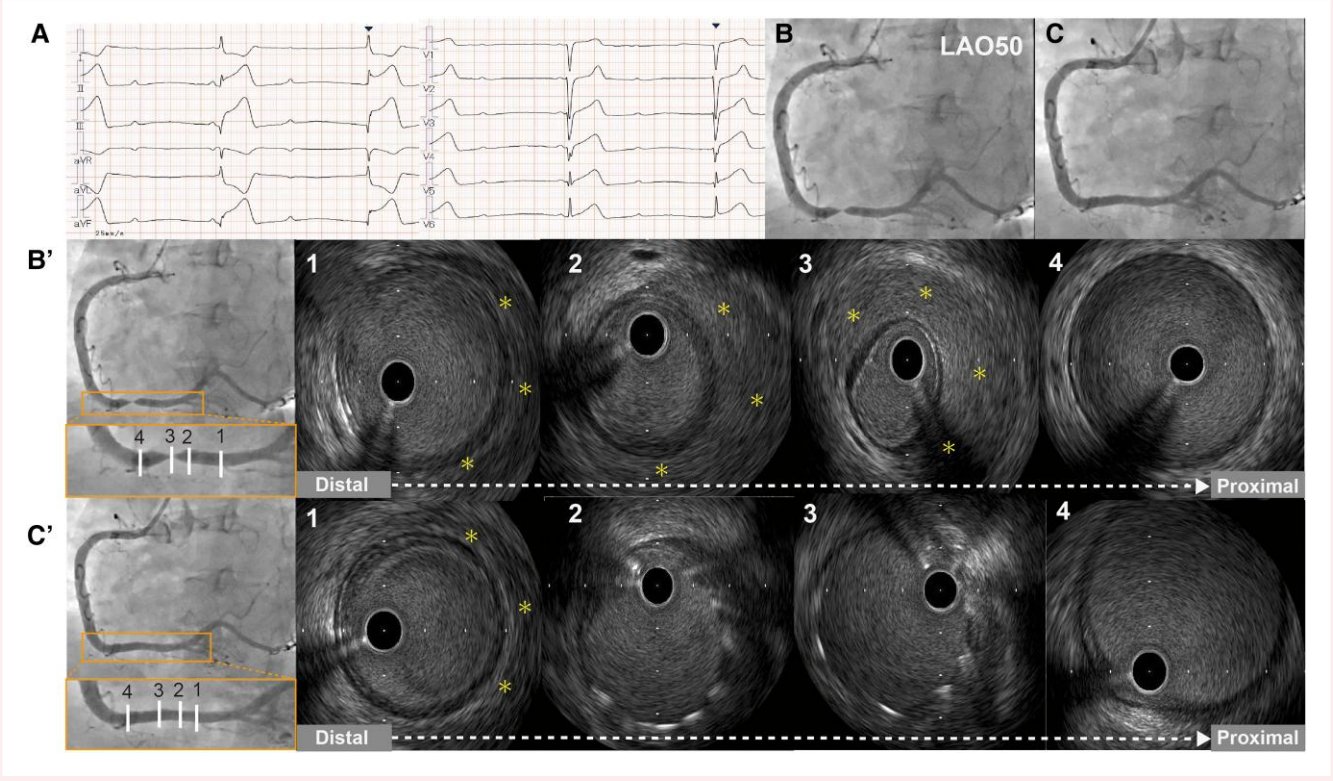


Figure 3 (*A*) Twelve-lead electrocardiogram taken upon arrival. (*B*) Coronary angiography demonstrating a severely stenotic lesion in the right coronary artery #3. (*B': 1–4*) Intravascular ultrasound pre-stent implantation showing true lumen compression, coronary artery dissection, and intramural haematoma (asterisks). (*C, C': 1–4*) Post-stenting coronary angiography and intravascular ultrasound images showing effective stent expansion and coverage of the dissected lumen on the proximal side.

However, beta-blockers may exacerbate coronary spasm and could be unsuitable for SCAD patients experiencing this condition. Therefore, this case underscores the potential utility of a well-timed spasm provocation test in SCAD patients with unidentified relevant factors, aiding in the stratification of pharmacotherapy involving calcium channel blockers or beta-blockers.

In summary, we report an exceedingly rare case of a middle-aged woman with coronary spasm who developed food-induced allergic coronary artery dissection, potentially related to type I variant Kounis syndrome, and SCAD under seemingly distinct conditions. The same factor triggering coronary spasm might explain both ACS events. This case highlights that a shared underlying coronary spasm in both conditions could have been the common cause of coronary artery dissection.

Lead author biography

Tomohiro Yoshino graduated from the Faculty of Medicine at Jichi Medical University in 2013. He is a cardiologist in the Department of Cardiovascular Medicine, Tsuyama Chuo Hospital, Okayama, Japan.

Supplementary material

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

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Consent: The authors confirm that written consent for the submission and publication of this case report, including images and associated text, has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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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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