

Acute coronary syndrome due to plaque erosion likely triggered by insect bites: a case series of Kounis syndrome

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Background

Kounis syndrome is the concurrence of acute coronary syndrome (ACS), including coronary spasm, acute myocardial infarction, and stent thrombosis due to an allergic and/or anaphylactoid insult.

Case summary

We present two cases of Kounis syndrome likely triggered by insect bites, with plaque erosion demonstrated using optical coherence tomography (OCT). Three common findings were derived from this case series. First, the patients developed a rash after an insect bite followed by ACS. Second, immunoglobulin E levels were increased. Finally, OCT identified the aetiology of ACS in this case series as erosion of the culprit lesions.

Discussion

Kounis syndrome, which is ACS following allergic reactions due to insect bites, is a rare complication. Kounis syndrome is probably not uncommon, but underdiagnosed. It is important for physicians to consider the treatment of Kounis syndrome in the complex course of ACS associated with allergic reactions. Furthermore, patients with a history of Kounis syndrome should avoid antigen exposure during secondary prophylaxis. In some cases, it may take several days from antigen exposure to the onset of ACS. Considering Kounis syndrome is beneficial for early diagnosis and appropriate treatment.

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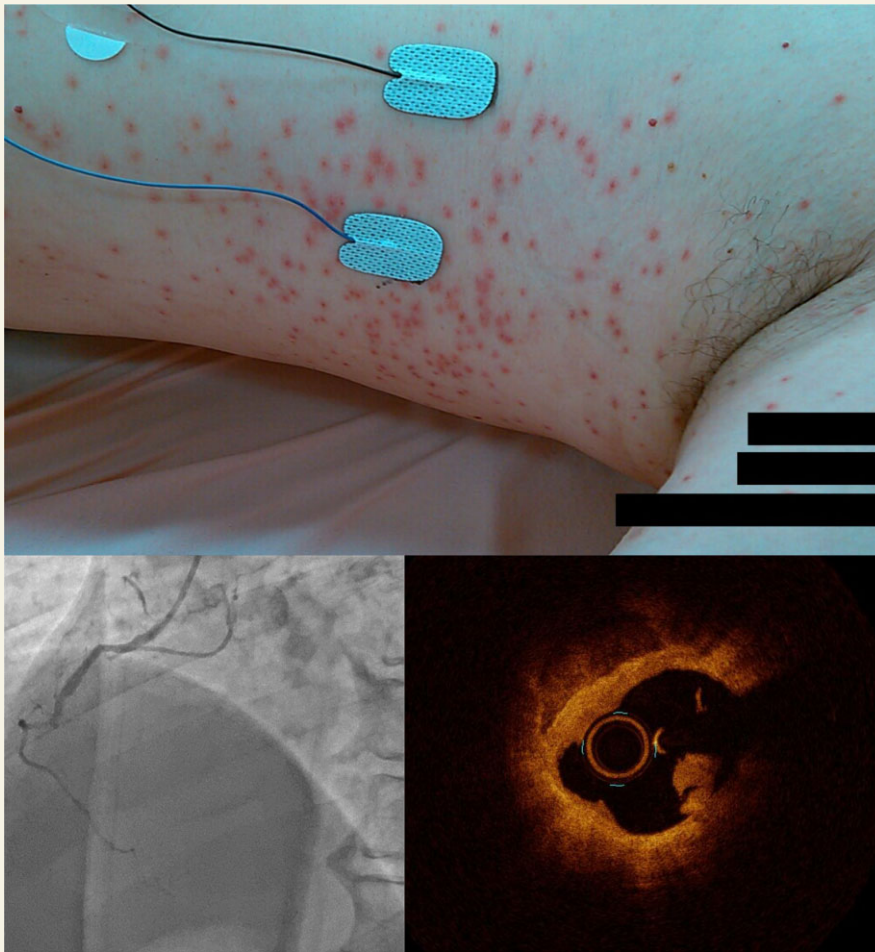
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Graphical Abstract



Keywords Acute myocardial infarction • Kounis syndrome • Optical coherence tomography • Plaque erosion • Case report

ESC Curriculum 3.1 Coronary artery disease • 3.2 Acute coronary syndrome • 3.4 Coronary angiography

Learning points

- Kounis syndrome is a rare and poorly recognized disease, but it is an important differential diagnosis in cases of ACS with allergic attacks.
- Kounis syndrome may take several days from antigen exposure to ACS onset.
- ACS due to plaque erosion may be associated with immunoglobulin E-mediated allergic response.

Introduction

Allergic angina syndrome, which is characterized by chest pain and an allergic skin reaction, was first reported by Kounis in 1991.¹ Kounis syndrome (KS) is defined as the occurrence of acute coronary syndrome (ACS), such as coronary spasm, acute myocardial infarction, and stent thrombosis due to allergy or hypersensitivity and anaphylactic or anaphylactoid insults. It is subdivided into three types: Type 1 results

from coronary spasm in normal arteries; Type 2 results from plaque instability in atherosclerotic coronary arteries; and Type 3 results from coronary stent thrombosis.² It is a very rare condition with a reported emergency department incidence of 0.0194% in all patients and 3.4% in patients with allergies.³ The KS is most commonly triggered by antibiotics (27.4%) and insect bites (23.4%).⁴ We present two cases of KS with plaque erosion likely triggered by insect bites, which were demonstrated using optical coherence tomography (OCT).

Timeline

Case 1	
Three days prior to presentation	The patient was bitten by a caterpillar and developed urticarial rashes throughout his chest and abdomen.
Presentation	The patient had chest pain and was diagnosed acute myocardial infarction due to plaque erosion with elevation of immunoglobulin E level.
Case 2	
Six days prior to presentation	The patient was stung by a paper wasp and developed an erythematous pruritic rash on the dorsum of his hand.
Presentation	The patient had chest pain and was diagnosed acute myocardial infarction due to plaque erosion with elevation of immunoglobulin E level.

Patient 1

A 67-year-old man was admitted to our hospital, complaining of chest pain radiating to the left arm. He had been bitten by a caterpillar 3 days prior to admission. He had a known history of hypertension, but was not taking any medications. He had no history of allergy, asthma, or addiction. His vital signs were as follows: blood pressure, 163/106 mmHg; heart rate, 78 beats/min, sinus rhythm; and respiratory rate 18 breaths/min. The patient developed urticarial rashes throughout his chest and abdomen ([Figure 1](#)).

Initial laboratory data revealed elevated levels of Troponin-I (19 382.2 pg/mL; normal: <34.2 pg/mL), lactate dehydrogenase (454 IU/L; normal: 124–222 IU/L), creatine phosphokinase (1093 IU/L; normal: 59–248 IU/L), and immunoglobulin E (IgE; 215.2 IU/mL; normal: <195 IU/mL). The patient's white blood cell count was elevated (13 300/ μ L; normal: 3300–8600/ μ L) and eosinophil percentage was normal (0.3%; normal: 0.6–5.4%). His lipid profile was as follows: serum cholesterol, 201 mg/dL (normal: 140–219 mg/dL); low-density lipoprotein (LDL)-cholesterol, 111 mg/dL (normal: 70–139 mg/dL); and high-density lipoprotein (HDL)-cholesterol, 73 mg/dL (normal: 40–69 mg/dL). His electrocardiogram (ECG) showed ST elevation in leads II, III, and aVF, suggestive of inferior wall infarction ([Figure 2](#)). The patient was treated with 200 mg aspirin and 20 mg prasugrel (the Ministry of Health, Labor and Welfare in Japan approves the loading dose of aspirin 162–200 mg and prasugrel 20 mg for patients with ACS) before emergency coronary angiography, which revealed total occlusion in the proximal portion of the right coronary artery and a left coronary artery atheroma with no flow limitation ([Figure 3A](#)).

After careful manual thrombectomy using an aspiration catheter (Thrombuster III®; Kaneka Medix, Osaka, Japan), OCT (Dragonfly OPSTAR; Abbot Vascular, Santa Clara, CA, USA) showed plaque erosion at the culprit lesion ([Figure 3B](#) and [see Supplementary material online, Video S1](#)). The minimum lumen area at the culprit lesion was 1.60 mm². Percutaneous coronary intervention was performed. An

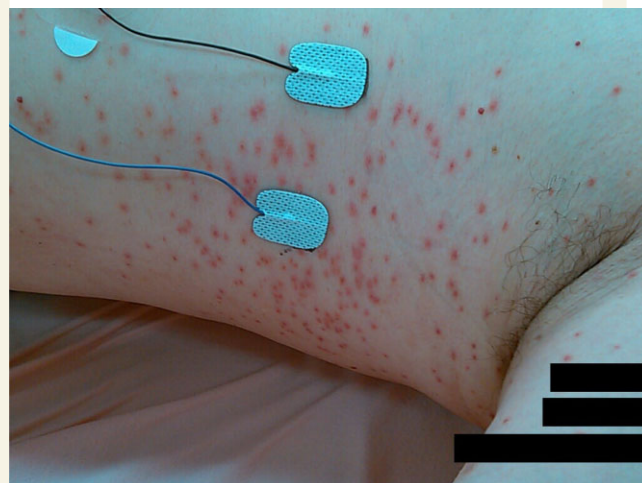


Figure 1 Skin assessment findings in Patient 1. Urticarial rashes throughout the chest and abdomen.

everolimus-eluting stent (3.25/38 mm) was successfully implanted after pre-dilatation with a 2.25/15 mm semi-compliant balloon. Post-dilatation with a 3.5/12 mm non-compliant balloon was performed at the proximal site within the stent. Final angiography and OCT revealed optimal stent expansion without stent-edge dissection. The patient was discharged 12 days later without any complications or exertional chest pain. He had no symptoms at the 9-month follow-up.

Patient 2

A 77-year-old man was admitted with complaints of chest pain. He had been stung by a paper wasp 6 days prior to admission. He had a history of hypertension, dyslipidaemia, and cedar pollen allergy. His vital signs were as follows: blood pressure, 147/88 mmHg; heart rate, 98 beats/min, sinus rhythm; and respiratory rate, 16 breaths/min. He developed an erythematous pruritic rash on the dorsum of his hand ([Figure 4](#)).

Cardiac biomarker level was slightly elevated (Troponin-I level, 218.3 pg/mL; normal: <34.2 pg/mL), with an increased IgE level (622.2 IU/L; normal: <195 IU/mL). The patient's white blood cell count was elevated (11 500/ μ L; normal: 3300–8600/ μ L) and eosinophil percentage was normal (2.2%; normal: 0.6–5.4%). His lipid profile was as follows: serum cholesterol level (260 mg/dL; normal: 140–219 mg/dL), LDL-cholesterol (171 mg/dL; normal: 70–139 mg/dL), and HDL-cholesterol (62 mg/dL; normal: 40–69 mg/dL). The ECG showed ST elevation in Leads V1–V4, suggestive of anterior infarction ([Figure 5](#)). He was treated with 200 mg aspirin and 20 mg prasugrel before emergency coronary angiography, which revealed diffuse atherosclerotic disease with severe stenosis involving the proximal left anterior descending artery (LAD; [Figure 6A](#)).

After coronary angiography, OCT showed plaque erosion at the culprit lesion, the ostium of the LAD ([Figure 6B](#) and [see Supplementary material online, Video S2](#)). The minimum lumen area of the lesion was 1.42 mm², which indicated that additional intervention at the proximal lesion might be required. An everolimus-eluting stent (3.0/16 mm) was successfully implanted after pre-dilatation with a 2.0/10 mm semi-compliant balloon. Final angiography and OCT revealed optimal stent expansion without stent-edge dissection. From the day after PCI,

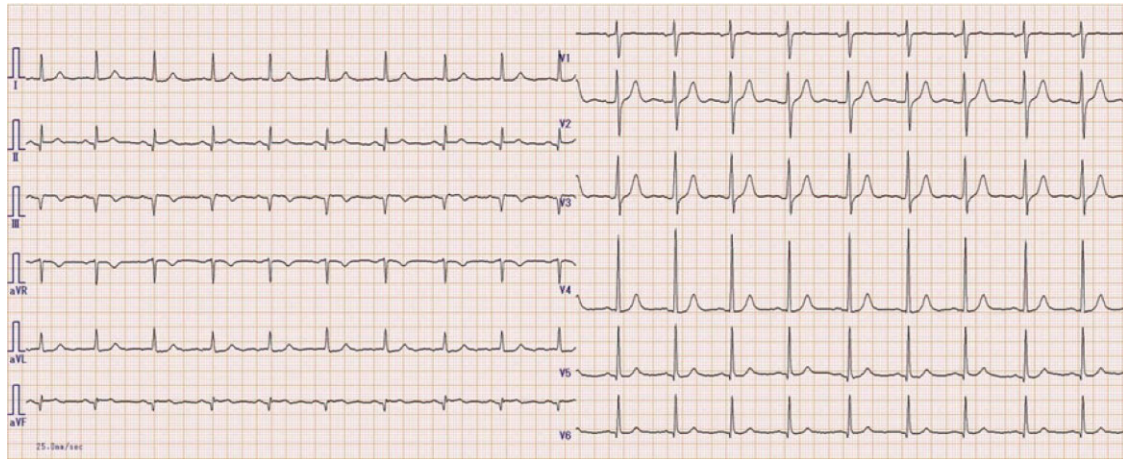


Figure 2 Electrocardiogram after chest pain in Patient 1. Electrocardiogram shows ST-segment elevation in Leads II, III, and aVF, with ST-segment depression in Leads I and aVL.

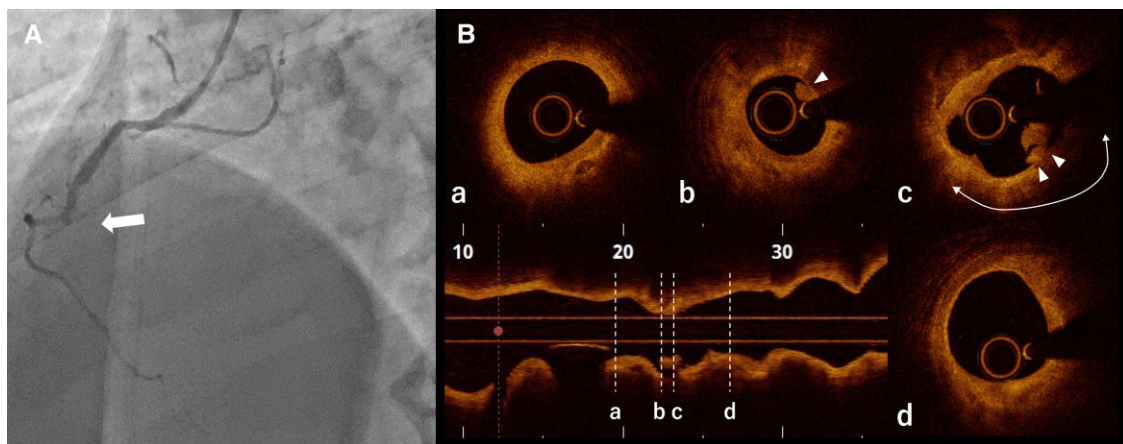


Figure 3 Coronary angiogram and optical coherence tomography image in Patient 1. (A) Pre-procedural coronary angiogram of the right coronary artery, revealing a complete occlusion (white arrow). (B) Points in longitudinal optical coherence tomography image marked (a)–(d) correspond to the cross-sectional images. (a) Distal reference of the culprit lesion. (b) and (c) The optical coherence tomography image after thrombectomy reveals an irregular luminal surface with white thrombus (white arrowheads) overlying a lipid-rich plaque characterized by the presence of a signal-poor lipid pool (white arc). (d) Proximal reference of the culprit lesion.

prednisolone 5 mg/day was administered for 3 days to reduce systemic allergic reactions. The patient was discharged 10 days later without any complications or exertional chest pain. He had no symptoms at the 4-month follow-up.

Discussion

Some drugs, foods, medical conditions, and environmental factors, including insect bites, have been associated with KS.⁵

Three common findings were derived from this case series. First, the patients developed a rash after an insect bite followed by ACS. Most reported cases of KS developed ACS immediately after antigen exposure.^{3,5} Our two cases are unique because of the duration from

antigen exposure to the development of ACS, suggesting that there may be more patients who develop ACS due to an allergic reaction. Second, IgE levels were increased. The mechanism of KS is still unclear and may be related to the release of inflammatory factors after the direct activation of mast cells mediated by IgE.⁶ Allergic reactions are mediated by IgE, which activates mast cells, causing degranulation and the release of mediators, such as histamine, leukotrienes, and cytokines. After insect stings, most people develop only minor local reactions, limited to local pain, tenderness, and swelling. These reactions last between 48 and 72 h. In contrast, the delayed reaction time is indicative of the most serious form of an IgE-mediated allergic reaction caused by insect stings.^{7,8} Finally, OCT identified the aetiology of ACS in this case series as erosion of the culprit lesions.

Plaque erosion is one of the most important pathological mechanisms underlying ACS. A previous study reported that mast-cell accumulation was observed in the shoulder regions of the atheroma, where erosion or rupture is most likely to occur.⁹ This suggests that mast-cell activation may be an important process in causing plaque erosion events but also in cases of an IgE-mediated allergic response, similar to what was observed in this case series.

The treatment of KS lacks consensus, and the most effective treatment is based on case reports. Previous case reports suggested that the management of KS should be performed as simultaneous treatment of myocardial revascularization and allergic manifestations. Myocardial revascularization for patients with KS should be performed according to the latest guidelines for ACS management. In both patients, since the culprit lesions had atherosclerotic changes

and small minimum lumen areas, stent implantations were needed. Furthermore, although opiates such as morphine are key players in the management of chest pain in acute myocardial infarction, they should be administered cautiously in patients with KS because they can induce mast-cell degranulation, which may further worsen the allergic reaction.² Corticosteroids and H1 and H2 antihistamines are commonly used to decrease systemic allergic reactions; however, we did not administer antiallergic therapy such as antihistamines in our patients at the time of diagnosis of ACS in the emergency department, because we did not recognize the presence of KS. On the other hand, glucocorticoids are associated with delayed healing, infarct size, left ventricular aneurysm, and left ventricular wall rupture.¹⁰ They should be used with precaution in patients with KS.

Conclusion

Although KS due to insect bites is a rare complication, KS itself is probably not uncommon and is underdiagnosed. In some cases, it may take several days from antigen exposure to ACS onset. It is important for physicians to consider the presence of KS, which will result in early diagnosis and appropriate treatment of KS. Furthermore, patients with a history of KS should avoid antigen exposure in order to prevent recurrence of KS.

Lead author biography



Yosuke Katayama, MD, PhD, graduated at Kinki University, Osaka, Japan, in 2011 and became a resident and medical staff in Cardiovascular Medicine in Wakayama Medical University, Wakayama. He specialized in cardiovascular intervention and invasive cardiovascular image assessment. His main research interests include clarifying the mechanism of coronary atherosclerosis progression.



Figure 4 Skin assessment findings in Patient 2. Erythematous pruritic rash on the dorsum of the patient's left hand.

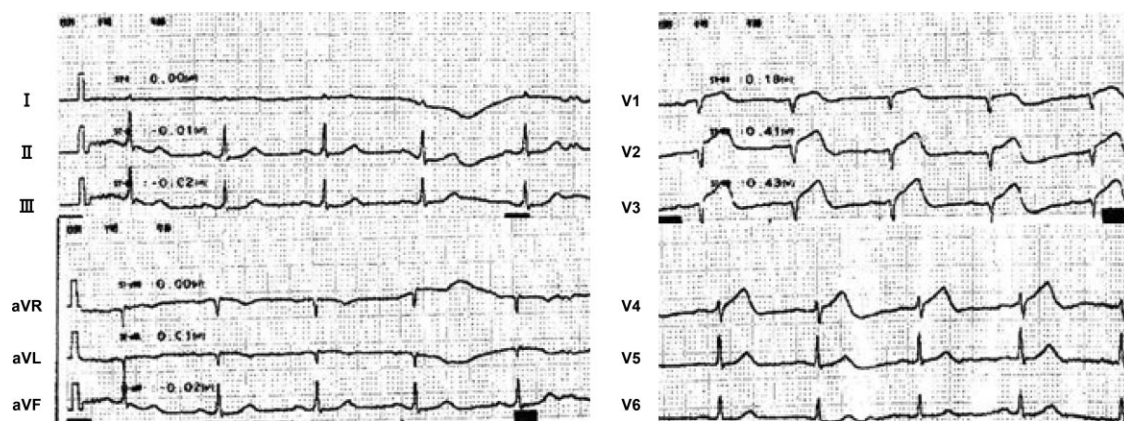


Figure 5 Electrocardiogram after chest pain in Patient 2. Electrocardiogram shows ST-segment elevation in Leads V1–V4.

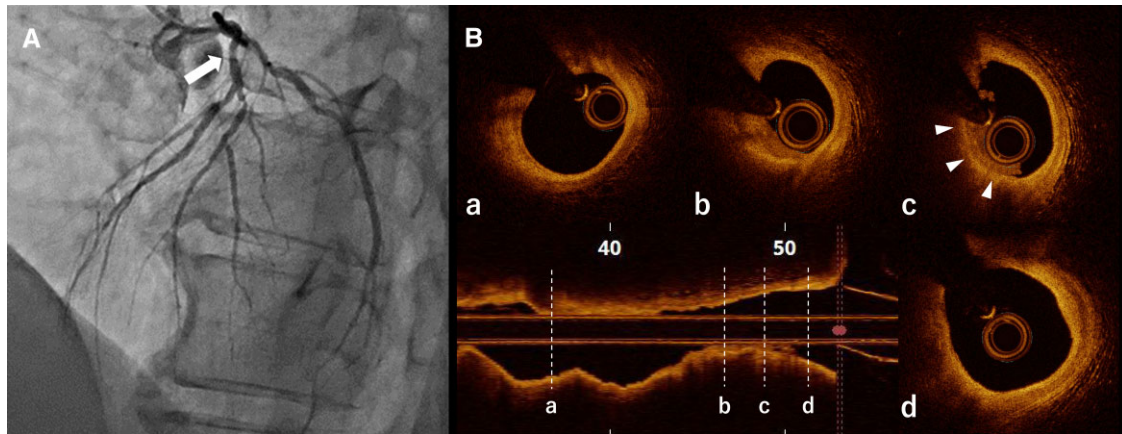


Figure 6 Coronary angiogram and optical coherence tomography image in Patient 2. (A) Pre-procedural coronary angiogram reveals moderate to severe stenosis (white arrow) at the proximal left anterior descending artery. (B) Points in longitudinal optical coherence tomography image marked (a)–(d) correspond to cross-sectional images. (a) Distal reference of the culprit lesion. (b) and (c) The optical coherence tomography image reveals a smooth luminal surface with a white thrombus (white arrowheads) overlying a lipid-rich plaque at the culprit lesion of the proximal left anterior descending artery. (d) Proximal reference of the culprit lesion.

Supplementary material

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

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

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

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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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