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CASE REPORT

# A case of repeated Kounis syndrome after anaphylactic shock: A note for disease management

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**Abstract**

**Background:** Kounis syndrome (KS) is an underdiagnosed disease. The management of the disease remains elusive because of its infrequency.

**Case Presentation:** A 78-year-old man with anaphylactic shock was admitted to our hospital 2 h after multiple bee stings. After recovering from an anaphylactic reaction, he presented with chest pain with ST elevation. We diagnosed him with KS. After a continuous intravenous infusion of vasodilators, his chest pain and ST elevation improved. However, chest pain with ST-segment elevation recurred the next day. Coronary angiography revealed severe stenosis in the middle left anterior descending coronary artery, and drug-eluting stents were implanted. The patient was discharged on foot after treatment for heart failure.

**Conclusion:** KS, in which anaphylaxis and acute coronary syndrome occur simultaneously, can recur repeatedly after an initial anaphylactic reaction; however, it could be delayed or it could present simultaneously with the anaphylactic reaction. Therefore, long-term observation is important.

**KEYWORDS**
acute myocardial infarction, allergy, anaphylactic shock, Kounis syndrome, spasm

## INTRODUCTION

Strong allergies, such as anaphylaxis or anaphylaxis-like reactions, induce hypersensitivity of the coronary arteries. Kounis syndrome (KS) is the combination of coronary artery spasms, acute myocardial infarction, and stent thrombosis following an allergic reaction.

KS is rarely diagnosed. Previous studies reported an incidence of KS in patients with strong allergic reactions of 1.1%–3.4%.[1,2] The lack of awareness of this disease makes its diagnosis and management difficult. We present an unusual case of multiple bee stings with recurrent anginal symptoms.

## CASE PRESENTATION

A 78-year-old man was admitted by ambulance with dyspnea 2 h after multiple bee stings. His medical history included diabetes and chronic renal failure but no history of any allergies or cardiac diseases. At the emergency room, he complained of dyspnea with wheezing and a generalized itchy rash. Two punctuated sting marks were observed on the back of his head and in his femoral region (Figure S1). On examination, his respiratory rate, oxygen saturation, blood pressure, and heart rate were 22 breaths/min, 100% (with oxygen 10 L/min), 90/42 mmHg, and 86 bpm, respectively.

We diagnosed the patient with anaphylactic shock; he was immediately treated with an intramuscular injection of 0.5 mg of adrenaline, intravenous injections of $H_1$ and $H_2$ antihistamine blockers, and steroids. Shortly after this treatment, his blood pressure increased to 116/43 mmHg, and symptoms of anaphylaxis disappeared. The first electrocardiogram (ECG) revealed no abnormality (Figure 1A), and echocardiography could not detect left ventricular asynergy immediately after the recovery of his vital signs. However, 10 min after the first ECG, he suddenly complained of chest

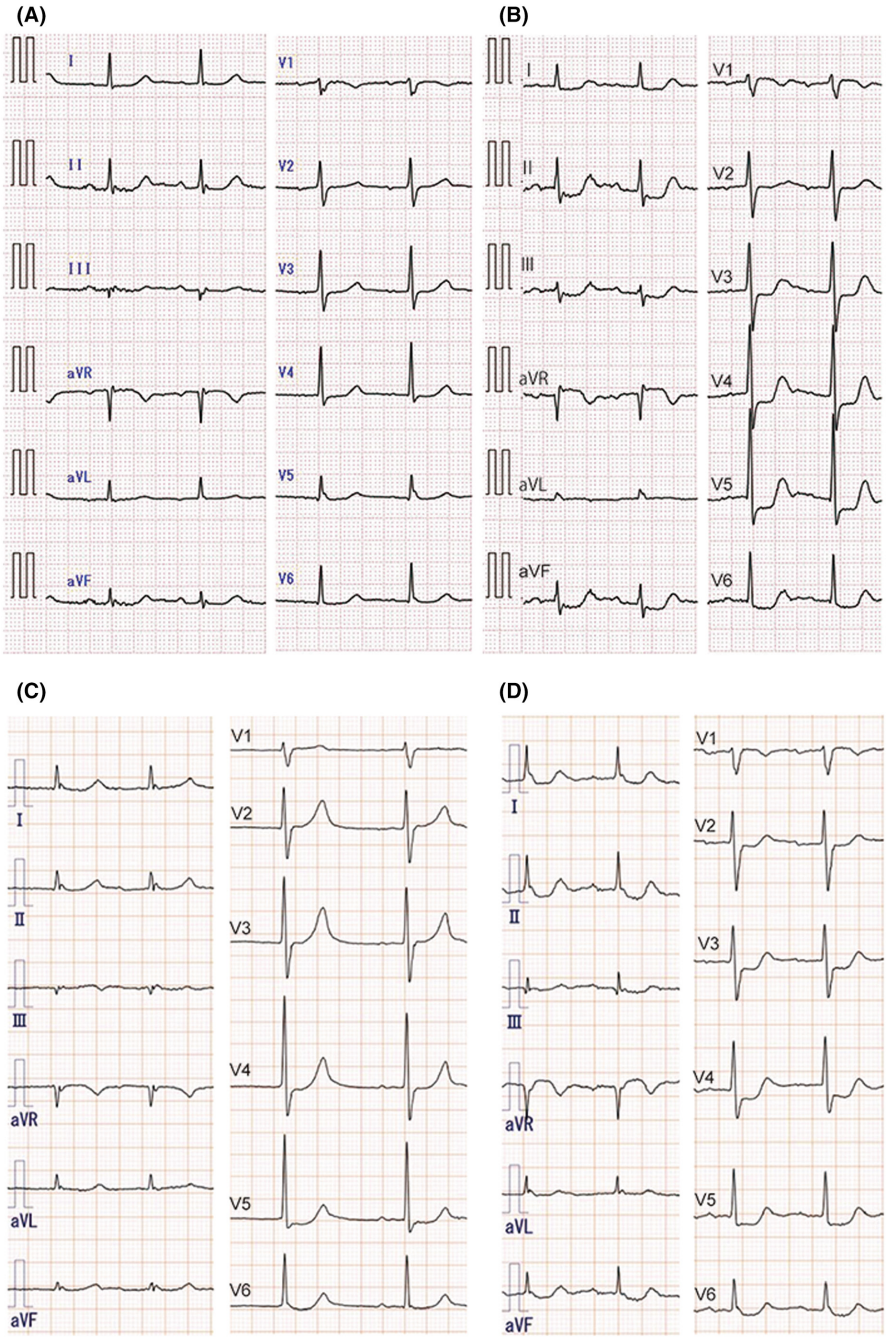


**FIGURE 1** Changes in the electrocardiogram (ECG) after the bee stings. (A) The first ECG at 2 h after the bee stings. (B) ST elevation in the aVR lead and ST depression in the II, III, aVF, and V2–V6 leads 10 min after the first ECG. (C) The ST shift was improved after a continuous intravenous injection of nicorandil. (D) Recurrent ST elevation in the aVR lead and ST depression in the II, III, aVF, and V2–V6 leads at 23 h after the bee stings.

oppression. ECG revealed ST elevation in the aVR lead and ST depression in leads II, III, aVF, and V2–V6 (Figure 1B). Echocardiography showed severe hypokinesis in the anteroseptal wall. We diagnosed the patient with KS and administered nicorandil via a continuous intravenous infusion for coronary artery spasms. This treatment immediately relieved his chest pain and improved the ST shift on ECG (Figure 1C). On blood examination, the patient's troponin I level was 12.9 pg/mL (reference range: 0–25.2 pg/mL), and his creatinine kinase MB (CK-MB) level was 6 U/dL (reference range: 0–14 U/dL). Blood examination at 1 h after nicorandil administration also revealed no leakage of cardiac enzymes (troponin I = 11.4 U/dL, CK-MB < 5 IU/dL; Table 1). Echocardiography indicated no abnormal wall motion. The unchanged cardiac enzyme levels and the history of chronic renal failure prevented our decision on emergent coronary angiography (CAG).

At 23 h after the bee stings, the patient suddenly complained of chest pain with hypotension, and ECG revealed ST elevation in the aVR lead and ST depression in the II, III, aVF,

and V2–V6 leads (Figure 1D). Blood examination disclosed increases in his troponin I (4,698.9 IU/dL) and CK-MB levels (20 U/dL; Table 1), and emergent CAG was performed. A coronary angiogram uncovered 99% stenosis at the middle left anterior descending artery (Figure 2A), and intravascular ultrasound revealed vulnerable attenuated plaques at the lesion (Figure 2B). Two drug-eluting stents were deployed at the lesion (Figure 2C). After the percutaneous coronary intervention, his heart failure and renal failure contributed to bilateral lung congestion on chest X-ray (Figure 2D and

**TABLE 1** Time course of ECG and evaluation of echocardiography, troponin I, and CK-MB levels.

| Evaluation | The first KS | | | The second KS |
|---|---|---|---|---|
| Time after the bee sting | 2 h 10 min | 3 h 10 min | 5 h | 23 h |
| ST shift on ECG | (+; Figure 1B) | (−; Figure 1C) | (−) | (+; Figure 1D) |
| Echocardiography | Hypokinesis | Normokinesis | Normokinesis | Hypokinesis |
| Troponin I (pg/mL) | 12.9 | 11.4 | 14.9 | 4698.9 |
| CK-MB (U/L) | 6 | <5 | <5 | 20 |

Abbreviations: CK-MB, creatinine kinase-MB; ECG, electrocardiogram; KS, Kounis syndrome.

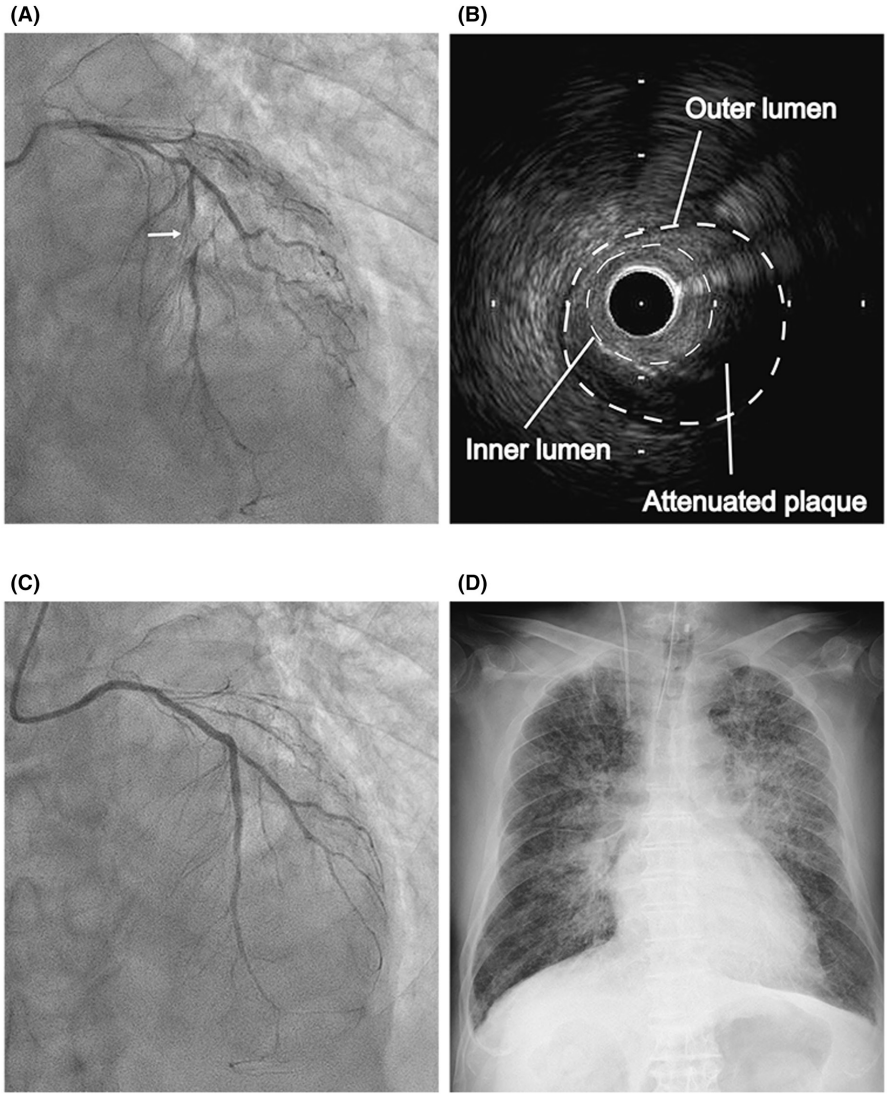


**FIGURE 2** Coronary angiogram and intravascular ultrasound of the stenosis lesion and a chest X-ray after stent implantation. (A) Emergency coronary artery angiography revealed 99% stenosis in the middle left anterior descending coronary artery (LAD). (B) Intravascular ultrasound after plain old balloon angioplasty revealed severe stenosis with vulnerable attenuated plaques at the LAD lesion. (C) LAD angiography revealed no stenosis after stent implantation. (D) A chest X-ray revealed severe lung congestion after percutaneous coronary intervention.

Figure S2). He was managed in the intensive care unit with mechanical ventilation and treatment with diuretic drugs, coronary vasodilators, and vasopressors. Finally, he was discharged on foot 19 days after arriving at our hospital.

## DISCUSSION

KS is classified into three types. In type I, inflammatory mediators from mast cells cause coronary artery spasms, leading to coronary ischemic symptoms. Type II is typified by plaque rupture attributable to coronary artery spasms, causing acute coronary syndrome. Type III is characterized by stent thrombosis attributable to allergic reactions in patients who previously underwent stent implantation.[3]

Here, we reported a case of repeated KS caused by bee stings. Although adrenaline is known to induce coronary artery spasms, we confirmed that a 1% xylocaine injection with adrenaline in the patient's local anesthesia did not cause any symptoms. In addition, the recovery of wall motion on echocardiography and ST elevation on electrocardiography after the first KS strongly suggests that the case had a repeat occurrence of KS.

This case highlights the need for three considerations. First, strong allergic reactions can induce coronary artery spasms, leading to myocardial injury. KS should always be anticipated in patients with strong allergic reactions. Second, KS might occur repeatedly during an allergic reaction. In general, mast cells release mediators both immediately and several hours after exposure to an allergen. Furthermore, the mediators affect the influx of other effector cells and trigger the late phase of the allergic reaction. Therefore, it is extremely important to prepare for KS in both the acute and late phases. To our knowledge, there are no reports of repeated KS from a single allergic reaction, but it is possible that either acute- or late-phase KS is missed in many patients. Our case clearly demonstrates that acute-phase type I KS was followed by type II KS several hours later. Third, KS might occur much later in the allergic reaction. Abdelghany et al[3] reported that 12 of 131 (9.2%) patients with allergy developed KS more than 6 h after the allergic reactions were induced. In fact, our patient developed type II KS 23 h after the bee stings.

Nittner-Marszalska et al[4] reported a case of type II KS with delayed onset after multiple bee stings. The patient presented with sudden ST-segment depression and elevated cardiac enzyme levels 9 h after bee stings. Emergency CAG revealed severe stenosis in the right and left coronary arteries, and coronary artery bypass surgery was performed. Yanagawa et al[5] reported repeated anaphylactic reactions with exercise-induced anaphylaxis after an intra-articular injection of diclofenac etalhyaluronate. In that case, the intra-articular injection caused the first anaphylactic shock, and negative T waves and a significant increase in troponin T levels appeared the following day.

Furthermore, Shrimanth et al reported a patient with very late-onset type II KS. The patient arrived at the hospital within 4 h after anaphylactic symptoms caused by the analgesic nimesulide, and the patient's condition stabilized after treatment. The next day, ST elevation appeared, and troponin T and CK-MB levels were elevated. Emergency CAG revealed severe stenosis with severe thrombus in the central part of the left anterior descending artery, and percutaneous coronary intervention was performed.[6]

These cases indicate that KS can occur repeatedly in the very late stages of an allergic reaction. Therefore, long-term management, including ECG monitoring and cardiac enzyme evaluation, is important to avoid overlooking repeated or late KS.

## CONCLUSION

Clinicians must remember that KS is an under-recognized disease that can be triggered by allergic reactions. In addition, KS can recur during an allergic reaction, even in the very late phase of the reaction. Therefore, long-term ECG monitoring and cardiac enzyme evaluations are critical for the management of patients with allergic reactions.

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### CONFLICT OF INTEREST STATEMENT

None declared.

### DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

### ETHICS STATEMENT

Approval of the research protocol: Not applicable.
Informed consent: Yes.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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