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Case Report

Resuscitation of a case of allergy, infarction, and ventricular fibrillation: Kounis syndrome type II and literature review

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Abstract: To study a case of Kounis syndrome (KS) type II, characterized by allergy, myocardial infarction, and ventricular fibrillation. A patient diagnosed with KS type II was admitted to Yangpu Hospital, School of Medicine, Tongji University in 2021. After systemic treatment, routine investigations, including blood tests, electrocardiography (ECG), and biochemical and coagulation analyses, were performed. The patient subsequently underwent coronary angiography and percutaneous coronary intervention, achieving a successful recovery. In patients with acute allergic reactions, particularly those presenting with severe manifestations or anaphylactic shock, timely ECG and cardiac enzyme testing are crucial to prevent misdiagnosis.

Keywords: Kounis syndrome, myocardial infarction, allergic reaction, ventricular fibrillation

Introduction

Kounis syndrome (KS) is a form of myocardial ischemia triggered by allergic reactions and characterized by electrocardiographic abnormalities, including ST-segment changes, tachycardia, or bradycardia, reflecting the cardiovascular system's hypersensitivity to allergic stimuli. KS is closely associated with the inflammatory response mediated by mast cells (MCs) [1]. MCs play a central role not only in allergic reactions but also in interacting with macrophages and T-lymphocytes, leading to degranulation and the release of diverse inflammatory mediators. These mediators exacerbate allergic symptoms and may provoke cardiovascular reactions [2].

The cardiovascular system serves as both a victim and a contributor in the progression of allergic reactions, highlighting its complex dual role [3]. KS shares overlapping clinical features with acute coronary syndrome (ACS), including chest tightness and myocardial ischemia [4]. Therefore, maintaining a high degree of clinical suspicion and ensuring early recognition of KS are crucial for timely and effective treatment. The similarities between KS and ACS can result in misdiagnosis or delayed management [5, 6]. Accurate diagnosis is critical to improving patient outcomes.

We presente a case of type II KS, in which prompt and precise diagnosis and treatment successfully saved the patient's life.

Case report

The patient was a 70-year-old male admitted to Yangpu Hospital, School of Medicine, Tongji University with a complaint of "skin rash for 4 days, worsening for 1 day". On December 10, 2021, after oral administration of "aloe vera pill", the patient developed widespread rashes and wheals accompanied by itching and increased skin temperature. One day before admission, the itching intensified, prompting him to seek care at our hospital.

On arrival, the patient's blood pressure was 81/53 mmHg, and he was diagnosed with anaphylactic shock. He was promptly treated with epinephrine and dexamethasone for anti-aller-

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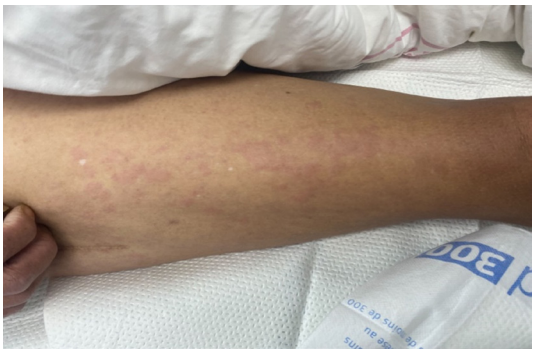

Figure 1. Lower extremity papules at admission.

gic management, sodium lactate Ringer's solution for fluid resuscitation, and supportive care. On December 14, 2021, the patient was admitted to the Emergency Intensive Care Unit. At the time of admission, his blood pressure had stabilized to 111/72 mmHg. Scattered red skin tinges were observed on his trunk and limbs (**Figure 1**).

Auxiliary examinations on December 14, 2021, revealed the following: Blood analysis: serum amyloid level, 86.36 mg/L; C-reactive protein, 28.94 mg/L; total white blood cell count, 13.1 × 10^9/L; platelets, 270 × 10^9/L; neutrophils, 89.5%. Biochemical tests: potassium, 3.87 mmol/L; creatinine, 150 μmol/L; high-sensitivity troponin T, 13.9 ng/L. Liver function tests and electrolytes were within normal limits. Coagulation analysis: D-dimer (FEU), 23.60 mg/L. Blood gas analysis: pH, 7.426; PCO_2, 3.73 kPa; PO_2, 14.5 kPa; K^+, 4.00 mmol/L; Na^+, 131 mmol/L; CL, 104 mmol/L; glucose, 13.20 mmol/L; lactate, 3.40 mmol/L; base excess, -4.0 mmol/L; HCO_3^-, 18.4 mmol/L.

The electrocardiogram (ECG) showed no abnormalities (**Figure 2A**).

Upon admission, the patient was treated with dexamethasone and ebastine for allergy management, glycerite lotion to relieve itching, cefoxitin to reduce inflammation, and rehydration therapy. By the second day of hospitalization, the rash had resolved.

At 09:46 on the third day, the patient experienced a recurrence of generalized rash (**Figure 3**), accompanied by chest tightness, chest pain, profuse sweating, hypotension (55/42 mmHg), bradycardia (42 bpm), and oxygen saturation of 90%. On December 16, 2021, the patient developed acute myocardial infarction (AMI).

Laboratory findings included: Blood analysis: serum amyloid A, 67.53 mg/L; C-reactive protein, 22.60 mg/L; leukocytes, 11.8 × 10^9/L; neutrophils, 94.4%. Coagulation analysis: D-dimer (FEU), 2.36 mg/L. Biochemistry: potassium, 3.96 mmol/L; interleukin-6 (IL-6), 15.14 pg/mL; procalcitonin (PCT), 0.12 ng/mL; high-sensitivity troponin T, 620.6 ng/L; myoglobin, 124.0 ng/mL; CK-MB, 10.12 ng/mL; B-type natriuretic peptide (BNP), 275 pg/mL. Blood gas analysis: pH, 7.529; PCO_2, 26.5 mmHg; PO_2, 87.8 mmHg; oxygen saturation, 87.38%; potassium, 3.7 mmol/L; lactate, 1.4 mmol/L; bicarbonate (HCO_3^-), 25.1 mmol/L.

The ECG revealed ST-segment elevation with upward convexity in leads II, III, and aVF (**Figure 2B**).

Management and resuscitation

Isoproterenol was administered to stabilize heart rate, norepinephrine (0.48 μg/kg/min) to raise blood pressure, and sodium lactate Ringer's solution for fluid resuscitation. Aspirin and clopidogrel were given as loading doses, and urgent coronary angiography was planned.

At 10:25, the patient experienced ventricular fibrillation, confusion, weak respiration, undetectable blood pressure, and fingertip oxygen saturation of 73%. Immediate measures included a single defibrillation (biphasic, 200J), chest compressions, and tracheal intubation with mechanical ventilation. After resuscitation, the patient's heart rate stabilized at 117 bpm, oxygen saturation improved to 92%, and he regained consciousness. ECG review showed resolution of ST-segment elevation (**Figure 2C**).

Aspirin and ticagrelor were continued for antiplatelet therapy, along with atorvastatin for plaque stabilization. On December 17, 2021, the patient successfully passed a spontaneous breathing trial (SBT) and was extubated.

Laboratory indicators at this stage included: Blood analysis: serum amyloid, 10.00 mg/L; C-reactive protein, 24.01 mg/L; leukocytes, 8.8 × 10^9/L; neutrophils, 85.5%. Coagulation analysis: D-dimer (FEU), 0.75 mg/L. Bioche-

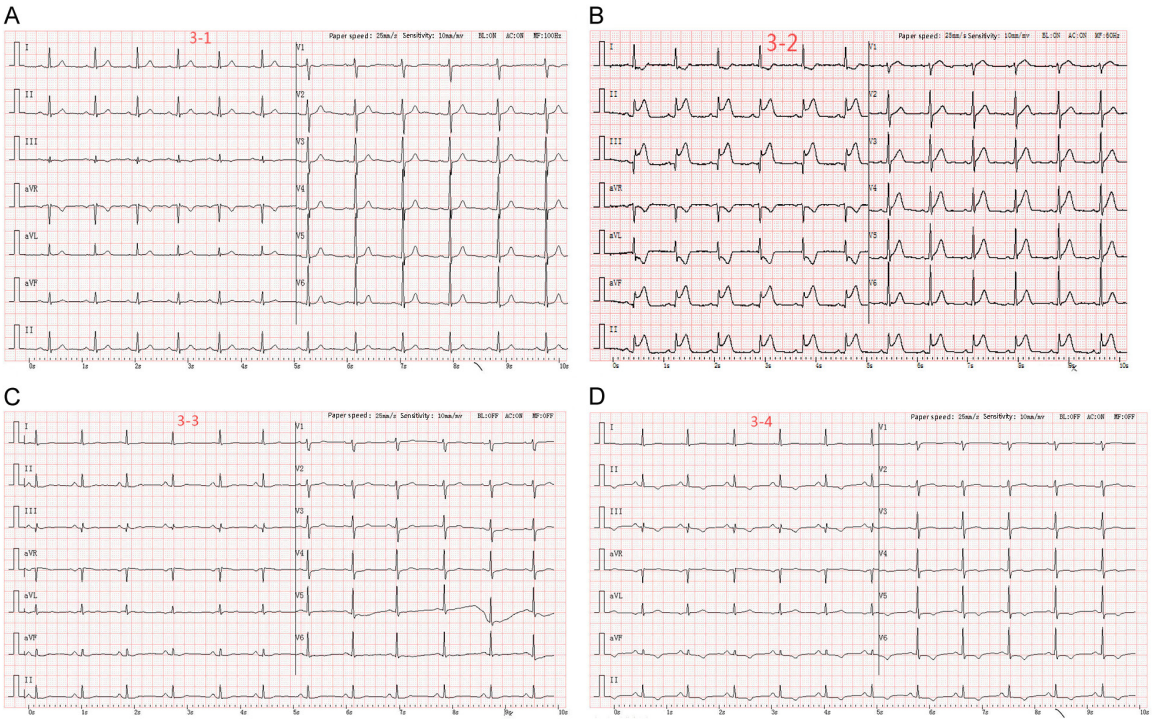

Figure 2. Electrocardiogram of the patient at different time points. A: Normal electrocardiogram at admission; B: ST segment elevation with an upward convexity in II, III, and avF leads on the 3rd day of admission; C: ST segment changes after resuscitation on the 3rd day of admission; D: Sinus rhythm, ST-T changes at discharge.

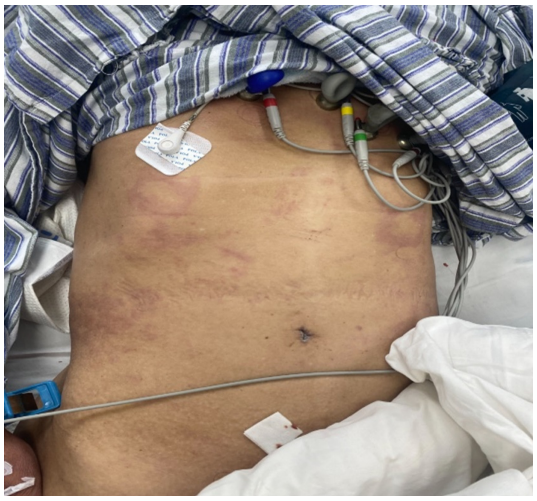

Figure 3. New rashes on the trunk on the 3rd day of hospitalization.

mistry: glutamic oxaloacetic transaminase (AST), 65 U/L; glutamic pyruvic transaminase (ALT), 56 U/L; potassium, 4.11 mmol/L; creatinine, 90 μmol/L; IL-6, 1.59 pg/mL; PCT, 0.30 ng/mL; high-sensitivity troponin T, 206.0 ng/L; BNP, 472 pg/mL.

The ECG showed sinus rhythm with ST-T changes (**Figure 2D**).

Definitive treatment

Following stabilization, coronary angiography and percutaneous coronary intervention (PCI) were performed on December 28, 2021. Angiography revealed an irregular wall in the distal left anterior descending artery (LAD), subtotal occlusion of the distal left circumflex artery (LCX), 30% stenosis in the mid-right coronary artery (RCA), and placement of one drug-eluting stent in the LCX (**Figure 4**).

The patient was discharged in stable condition.

Discussion

KS is an allergic myocardial ischemia condition triggered by drugs, food, environmental factors, or other stimuli. It is characterized by various cardiac electrophysiological abnormalities, including ST-segment elevation or depression and frequent T-wave inversions on ECG.

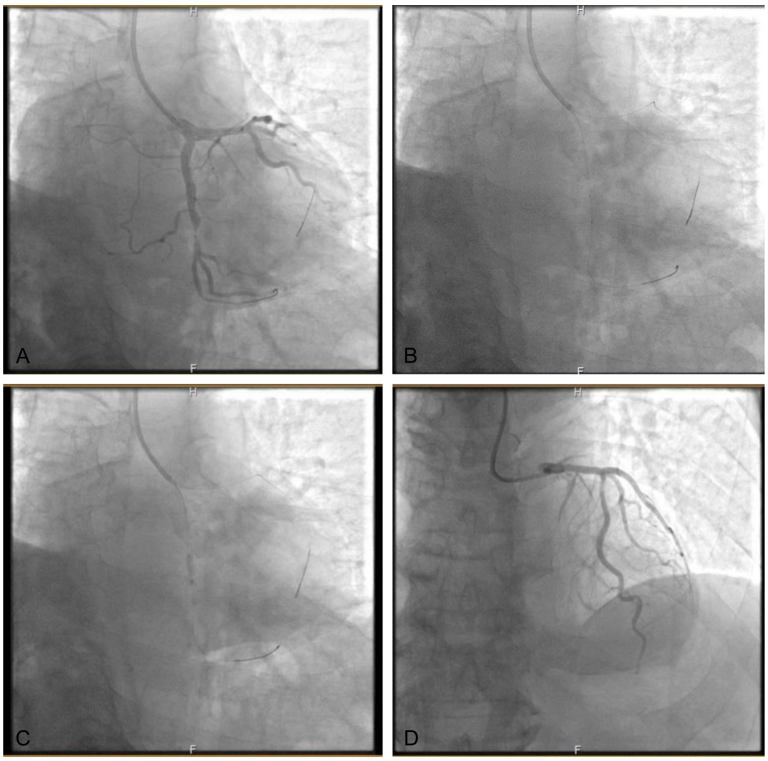

Figure 4. Coronary angiography of the left circumflex artery. A: LCX: Far segment subtotal closure; B: LCX: Guidewire in placement; C: LCX: Distal stent placement in progress; D: LCX: Good stent apposition after stent placement and re-contrast stenting. LCX: left circumflex artery.

Cardiac rhythm abnormalities such as sinus tachycardia, bradycardia, conduction block, atrial fibrillation, ventricular fibrillation, and ectopic beats may occur. Additionally, prolongation of the QRS complex duration and QT interval is common, often accompanied by clinical signs of myocardial ischemia or infarction [6, 7].

KS can be classified into three types. Type I: The most common form, accounting for 72.6% of cases, involves an acute allergic reaction causing coronary artery spasm. These patients typically have no coronary artery disease, and their cardiac enzyme and troponin levels remain normal. However, elevated levels may indicate progression to AMI [8]. Type II: Comprising 22.3% of cases, this type occurs in patients with coronary atherosclerosis, where an acute allergic reaction induces plaque erosion or rupture, leading to AMI. Type III: Rarely, KS occurs after coronary stent implantation due to an allergic reaction resulting in in-stent thrombosis [9].

The clinical presentation of KS includes two primary components: Acute coronary symptoms: These include chest pain, dyspnea, palpitations, syncope, profuse sweating, tachycardia, pallor, and cold extremities. Chest pain is the most common symptom, occurring in 86.6% of cases [10]. Severe cases may present with acute pulmonary edema or progress to hypotension and shock.

Acute allergic reactions: Symptoms include rash, pruritus, and nausea, with some patients experiencing severe systemic reactions.

Auxiliary examinations reflect these two aspects: Cardiac manifestations: ECG may show ST-segment depression or elevation, T-wave flattening or inversion, QT interval prolongation, and abnormal Q-waves. Elevations in cardiac enzymes (CK, CK-MB) and troponin (I or T) are also common.

Allergic response markers: Laboratory findings may include elevated IgE, eosinophils, histamine, peanut tetracene, arachidonic acid, thromboxane, leukotrienes, prostaglandins, tumor necrosis factor (TNF), interferon (INF), and interleukin-6 (IL-6) [10, 11].

The patient developed a persistent rash after allergen exposure, which gradually subsided following hospitalization. However, on December 16, 2021, the rash reappeared, followed by chest tightness, chest pain, profuse sweating, and loss of consciousness. ECG revealed ST-segment elevation in leads II, III, and aVF, along with upward bowing and ventricular fibrillation. High-sensitivity troponin levels were markedly elevated. After anti-allergic and anti-platelet therapy, the patient's condition improved. Coronary angiography, combined with the patient's history of coronary artery disease and prior PCI, confirmed a diagnosis of type II KS. The pathogenesis in this case

involved coronary atherosclerosis, with an allergic reaction activating mast cells, macrophages, and T lymphocytes. This triggered the release of cytokines and inflammatory mediators, leading to plaque rupture, coronary artery occlusion, and ventricular fibrillation. Peripheral vasodilation, hypotension, reduced coronary blood flow, and arrhythmias further contributed to the condition.

The management of KS comprises two key aspects: anti-allergic therapy and symptomatic treatment for acute coronary syndrome. In type II KS, the primary focus is on managing AMI, with concurrent use of glucocorticoids and antihistamines to alleviate allergic reactions [12]. However, KS presents unique therapeutic challenges necessitating cautious medication selection. β-blockers can exacerbate coronary artery spasm and should be avoided. Although epinephrine is the standard treatment for anaphylaxis, its use in KS may worsen myocardial ischemia, prolong the QTc interval, and induce coronary artery spasms and arrhythmias. Therefore, epinephrine should be administered with caution in KS patients [13, 14]. Similarly, opioids such as morphine and codeine, commonly used to alleviate acute chest pain, can induce mast cell degranulation and aggravate allergic reactions, warranting careful use [15].

Fluid management is crucial for patients with anaphylaxis to maintain hemodynamic stability, but it carries the risk of inducing or worsening heart failure symptoms. Central venous pressure monitoring can guide fluid management when necessary [16]. Thus, therapeutic drug selection must be carefully balanced, with close monitoring during treatment.

Prognostic factors for KS include the specific subtype, presence of complications, and allergen exposure. Among the three types, type I KS has the most favorable prognosis, while type III has the poorest, especially in cases complicated by AMI. Increased allergen exposure - both in duration and proximity - worsens the prognosis. Severe complications of KS are rare, with reported rates of cardiogenic shock (2.3%), cardiac arrest (6.3%), and mortality (2.9%) [17, 18].

The literature consistently highlights the dual presentation of KS, encompassing allergic reactions (e.g., rashes, elevated immune markers) and cardiac events (e.g., chest pain, ST-segment elevations, and T-wave inversions on ECG) [19, 20]. The current case aligns with this pattern, as the patient exhibited both allergic symptoms and ischemic cardiac events, evidenced by elevated troponin levels and ECG abnormalities. Type II KS, as in this case, is typically linked to pre-existing coronary atherosclerosis, where an allergic trigger causes plaque rupture or erosion, leading to AMI [21, 22]. Inflammatory mediators such as IgE, eosinophils, and cytokines play pivotal roles in this process, contributing to vasodilation, hypotension, and ultimately ventricular fibrillation, as observed in the patient [23].

Managing KS requires careful therapeutic balancing, particularly in avoiding medications like β-blockers and epinephrine, which may exacerbate coronary spasms and myocardial ischemia [24, 25]. Prognosis varies based on KS subtype and associated complications. Type I KS, driven purely by allergic mechanisms, generally has a favorable prognosis, while type II KS, complicated by AMI, presents greater challenges [26]. Repeated or prolonged allergen exposure further worsens long-term outcomes, increasing the risk of severe episodes [27]. Relevant literature is summarized in **Table 1**.

This case underscores critical therapeutic considerations for KS, particularly the importance of medication selection. The patient received anti-allergic therapy and antiplatelet treatment for AMI; however, caution must be exercised with commonly used drugs such as β-blockers, epinephrine, and opioids, as they can aggravate coronary spasms and allergic reactions. These insights are crucial for guiding clinical decisions, ensuring tailored therapy to minimize risks.

The dual nature of KS, spanning cardiology and allergy/immunology, emphasizes the need for a multidisciplinary approach. Effective management requires collaboration between cardiologists, allergists, and emergency physicians, particularly in acute settings where prompt diagnosis and treatment are essential to improve patient outcomes.

In conclusion, KS is a rare but complex condition characterized by diverse clinical manifestations that combine acute allergic and isch-

Table 1. Summarization of the similar literature to the case in this study

Study	Key Findings	Relevance to KS
[19] Koivula K. (2023)	ECG abnormalities in KS, including ST elevation and T-wave inversion; emphasis on ischemic manifestations.	Highlights the key electrocardiographic features of KS, confirming its relationship with allergic myocardial ischemia.
[20] Karunarathna et al. (2024)	Chest pain and allergic symptoms as predominant clinical manifestations of KS.	Reinforces the importance of recognizing both allergic and ischemic symptoms for timely diagnosis.
[21] Yamamoto et al. (2022)	Classifies KS into three types: coronary spasm, plaque rupture, and stent thrombosis.	Essential for understanding the pathophysiological variations and treatment implications of the different KS types.
[22] Hu et al. (2022)	Investigated the prevalence of type II KS in patients with coronary atherosclerosis and allergic reactions.	Relevant to this case study, where coronary atherosclerosis played a significant role in the patient's KS episode.
[23] Kheshtchin et al. (2024)	Explores immune responses in KS, such as elevated IgE and eosinophil levels.	Supports the immunological and allergic components contributing to coronary spasm and acute myocardial events in KS.
[24] Parichatikanond et al. (2024)	Highlights potential risks of using β-blockers and epinephrine in KS patients.	Cautions against the inappropriate use of medications that could worsen coronary spasm, offering critical therapeutic guidance.
[25] Celeski et al. (2024)	Examines the paradoxical effects of epinephrine in KS patients, particularly in triggering coronary vasospasms.	Emphasizes the careful management of typical anaphylactic treatments, such as epinephrine, which may complicate KS management.
[26] Kyriakopoulos et al. (2024)	Reports on prognosis and complications in KS, with a focus on cardiogenic shock and mortality.	Provides valuable prognostic data, showing the mortality rate and severe complications that influence long-term outcomes in KS patients.
[27] Roumeliotis et al. (2021)	Analyzes the role of allergen exposure in the recurrence and prognosis of KS.	Suggests that increased allergen exposure worsens the prognosis, emphasizing the need for preventive strategies in KS management.

emic cardiac features. Its diagnosis is often delayed or missed due to a lack of systematic understanding among clinicians. Furthermore, there is no robust evidence-based research on KS, highlighting the need for accumulating more clinical cases to explore its pathogenesis and treatment strategies. In patients presenting with acute allergic reactions, particularly those with severe symptoms or anaphylactic shock, prompt assessment of ECG and cardiac enzymes are critical to avoid missed diagnoses.

Disclosure of conflict of interest

None.

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