CASE REPORT

Nagoya J. Med. Sci. **87**. 163–167, 2025
doi:10.18999/nagjms.87.1.163

Rifampicin-induced type 1 Kounis syndrome: a rare case

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ABSTRACT

Kounis syndrome (KS) manifests as an acute coronary syndrome triggered by allergy, hypersensitivity, or anaphylaxis. It is believed that mast cells and histamine can potentially induce acute cardiac events by activating various inflammatory pathways. Here, we present a case of KS triggered by rifampicin administered during empyema drainage in a young male patient with no history of coronary artery disease. To the best of our knowledge, our case is the first report of rifampicin-induced KS documented in the literature. The wide range of etiological factors complicates the diagnosis of KS. Healthcare professionals should consider KS as a potential diagnosis in patients experiencing angina or similar pain alongside suspected allergic reactions.

Keywords: acute coronary syndrome, allergic reaction, coronary vasospasm, Kounis syndrome

Abbreviation:
KS: Kounis syndrome

BACKGROUND

Acute coronary syndrome (ACS) triggered by a hypersensitivity reaction is known as Kounis syndrome (KS). KS was first described as allergic angina by Kounis and Zavras[1] in 1991. The theory suggests that immune mediators such as platelet-activating factor, histamine, arachidonic acid products, neutral proteases, cytokines, and chemokines released during hypersensitivity reactions can induce coronary vasospasm, atheroma plaque erosion, or rupture, ultimately resulting in ACS.[2] Reports have shown that many drugs have the potential to induce this syndrome.[3] However, based on our research, no cases of rifampicin-induced KS have been reported previously.

CASE PRESENTATION

A 35-year-old man with schizophrenia visited an external clinic 45 days ago, complaining of chest pain and breathlessness. Following examinations, pneumonia was diagnosed, leading

Received: July 29, 2024; Accepted: August 30, 2024
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to the initiation of antibiotic treatment. During follow-up, the patient developed parapneumonic effusion and was subsequently diagnosed with empyema. A chest tube was inserted, and antibiotic treatment continued. Unfortunately, the specific antibiotic protocol utilized at the external center remains unknown as the information could not be retrieved. The chest tube was removed after completing the treatment. However, the symptoms persisted, prompting a referral to our center and admission to the Thoracic Surgery Clinic. Due to lung empyema, a decision was made to re-insert a chest tube for drainage in our institution. The patient's medication regimen included aripiprazole, valproic acid, and clonazepam. The patient had a 20-year history of smoking, no known allergies or asthma, and no family history of allergies or atherosclerosis. In addition, intravenous ceftriaxone therapy was initiated. To treat the empyema, 50 milliliters of 0.09% sodium chloride solution mixed with rifampicin (125 milligrams, 1.5 milliliters) was administered through the tube. Within the first minute of rifampin administration, the patient developed tachycardia, chest pain, and syncope but regained consciousness as a result of fluid support and Trendelenburg position. An electrocardiogram (ECG) revealed ST segment elevation in leads V1-6, D1, and aVL, as well as reciprocal ST segment depressions in leads D3 and AVF (Figure 1A). The patient's arterial blood pressure was 110/60 mmHg, with a fingertip oxygen saturation of 96% and a pulse of 85 beats/min. A transthoracic echocardiogram indicated a left ventricular ejection fraction of 50%. A decline in systolic function was observed, along with mild hypokinesia at the apex and anterior segments. No additional sounds or murmurs were detected on auscultation. Rales were present in the basal segments during the respiratory system evaluation. The heart team urgently transferred the patient to the catheterization laboratory after diagnosing acute anterior myocardial infarction and KS. No nitrate or any vasodilator treatment was administered before the procedure. Diagnostic angiography revealed no obstructive lesions in either the left or right coronary arteries (Figure 2). The patient reported that his pain had resolved. Before the completion of the procedure, an ECG showed that the precordial ST-segment elevation had returned to the isoelectric line (Figure 1B). A follow-up transthoracic echocardiography performed after the procedure indicated a left ventricular ejection fraction of 69% with no segmental wall motion defect (Figure 3). The diagnosis was confirmed as type 1 KS triggered by rifampicin. Before the coronary angiography, the patient's high-sensitivity cardiac troponin test (hs-cTnT) was negative, but it increased to 1000 ng/L after 3 hours. The hs-cTnT peak value was measured the next day as 3000 ng/L. As the hs-cTnT levels gradually decreased during follow-up and no further symptoms were reported, the patient was discharged with acetylsalicylic acid and diltiazem.

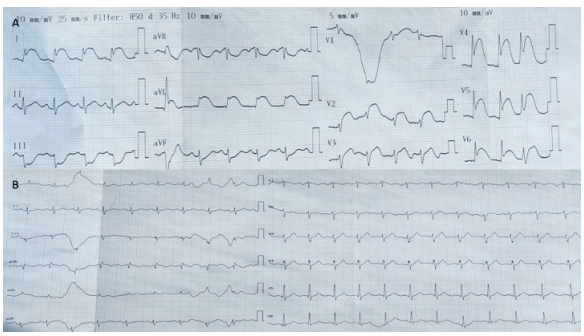

Fig. 1 12-lead electrocardiography of the patient
Fig. 1A: Before coronary angiography.
Fig. 1B: After coronary angiography.

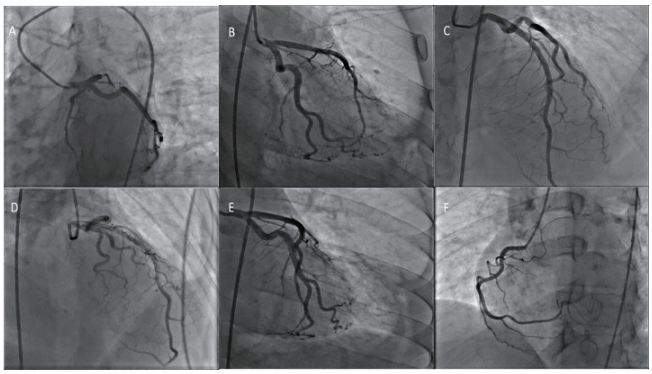

Fig. 2 Coronary angiography images of the patient

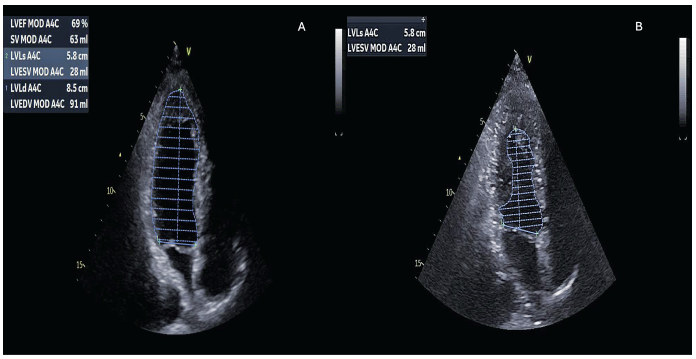

Fig. 3 Transthoracic echocardiography of the patient after coronary angiography

Fig. 3A: Left ventricular end-diastolic volume obtained by the Modified Simpson method from the transthoracic echocardiographic apical four-chamber view.

Fig. 3B: Left ventricular end-systolic volume obtained by the Modified Simpson method from the transthoracic echocardiographic apical four-chamber view.

DISCUSSION AND CONCLUSION

KS can affect individuals of all ages. Medications such as antibiotics, non-steroidal anti-inflammatories, chemotherapeutics, and allergens like food and insect bites can trigger KS. Individuals with a history of atopy, asthma, smoking, and atherosclerosis may be affected more frequently.[4] A recent epidemiological study suggested that KS was detected in approximately 1.1% of individuals hospitalized for hypersensitivity. In patients diagnosed with KS, hospital stays were longer, with higher rates of thromboembolic events, arrhythmias, and mortality.[5] Symptoms of this condition include flushing, nausea, vomiting, shortness of breath, and chest pain, and in severe cases, it can lead to shock and sudden death. In 1991, KS was initially identified as allergic angina syndrome and categorized into three types.[1] The most common form is type 1, which responds well to pharmacological treatment.[6] The type 2 variant can develop due to an allergic event that leads to the rupture of a pre-existing atheroma plaque, resulting in a myocardial infarction. Myocardial infarction caused by stent thrombosis in the coronary artery due to an allergic reaction is known as the type 3 variant.[7] Serum histamine, tryptase, immunoglobulin E, and troponin are laboratory parameters that can assist in making a diagnosis. Additionally, ECG, transthoracic echocardiography, and coronary angiography support the diagnosis.[8] The particular

case described here was compatible with type 1 KS, as no lesions were detected in the coronary arteries. The resolution of chest pain during coronary angiography suggests the possibility of coronary vasospasm. Research has shown that various antibiotics can lead to the development of KS.[4] However, to our knowledge, no case of rifampicin-induced KS has been reported to date. KS treatment varies depending on the type. Approaches can range from managing allergic reactions to coronary revascularization.[9] Misdiagnosis can lead to inappropriate treatments, which may worsen the patient's condition. For KS patients, morphine, although effective for ACS, should be avoided due to its potential to trigger histamine release. Beta-blockers and epinephrine can exacerbate coronary vasospasm by disrupting adrenergic balance.[7] The recommended therapy for type 1 KS allergic reactions includes hydrocortisone and antihistamines, while nitrates and calcium channel blockers help control coronary vasospasm.[9,10] Types 2 and 3 KS require both coronary revascularization and management of allergic reactions.

In conclusion, the wide range of etiological factors makes diagnosing KS challenging. It is vital to establish a differential diagnosis for prompt identification and intervention. Treatment approaches may vary between KS and anaphylaxis, and incorrect medical management can exacerbate the condition, leading to severe consequences. Therefore, medical professionals should consider KS as a possible diagnosis in patients presenting with angina or similar pain alongside suspected allergic reactions.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This manuscript adheres to the Declaration of Helsinki, and the patient provided informed consent.

CONSENT FOR PUBLICATION

Written consent was obtained from the patient to publish.

AUTHOR CONTRIBUTIONS

All authors contributed to the preparation of this case report article. The authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

No funding was provided for the preparation of this paper.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

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