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CASE REPORT

Sudden Cardiac Arrest Associated with Widespread Coronary Vasospasm After Oral Amoxicillin/Clavulanic Acid Intake: A Rare Case of Kounis Syndrome

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Abstract

Kounis syndrome is known as a type of acute coronary syndrome that occurs secondary to hypersensitivity reactions and constitutes a life-threatening medical emergency. Although multiple etiologies of KS have been elucidated, pharmacological agents are the most prevalent. Antimicrobial agents and nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently utilized medications. KS is not rare, and its frequency has been reported to increase since it was first described in 1950. However, it is often underdiagnosed owing to its wide range of clinical manifestations. Diagnostic evaluation should encompass laboratory, electrocardiographic, echocardiographic, and angiographic evidence in addition to clinical symptoms and signs. In this case study, we presented a 56 year old patient without any chronic disease who presented with sudden cardiac arrest after taking oral amoxicillin/clavulanic acid.

Key words: Oral antibiotic use, cardiac arrest, coronary vasospasm, Kounis syndrome

INTRODUCTION

Kounis syndrome (KS) is defined as a hypersensitivity reaction triggered by an allergic event leading to acute coronary syndrome (ACS). Also known as "allergic myocardial infarction", this condition can lead to coronary artery vasospasm and subsequent myocardial ischemia via allergic mediators (1).This phenomenon may occur as a result of various pharmaceutical agents, including nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics, antibiotics, anti-neoplastics, proton pump inhibitors, contrast agents, corticosteroids, anti-hypertensive drugs, and other medications, particularly those frequently used in routine clinical practice. Environmental exposure, insect bites, food and stents can also be causative agents of KS (2).

KS was first described in 1950 as a reaction to penicillin and has been increasingly described in the literature. Desai et al reported a 1.1% incidence of Kounis syndrome-associated ACS among patients admitting to hospitals in the USA with hypersensitivity, allergic, or anaphylactic reactions (3). Three different subtypes of KS have been described:

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Type 1: This variant arises from coronary blockage and spasm, representing the most prevalent mechanism at approximately 72.6% of all cases. It is predominantly seen in younger individuals who lack cardiovascular risk factors. Endothelial dysfunction and microvascular angina serve as the underlying causes of this condition, which is characterized by electrocardiographic evidence of ischemia induced by coronary spasm. Elevated or normal cardiac enzyme levels may serve as a potential indicator of progression towards acute myocardial infarction.

Type 2: Manifests in individuals with atherosclerotic conditions, where a sudden surge of inflammatory agents can trigger either isolated coronary artery spasms or plaque rupture or erosion, resulting in acute myocardial infarction. This form represents approximately 22.3% of all KS instances.

Type 3: Seen in patients with prior coronary stent implantation. These patients may experience an allergic response leading to in-stent thrombosis, which is characterized by an eosinophil-rich thrombus. This can result in ischemia owing to platelet activation, adhesion, and aggregation induced by inflammatory mediators. This type constitutes approximately 5.1% of all cases of Kounis syndrome. (4).

CASE REPORT

A 56-year-old male patient with no past medical history was administered oral 1000 mg amoxicillin/clavulanic acid for a dental abscess. It has been confirmed that the patient did not receive any other medical treatment other than this treatment. The patient developed sudden severe chest pain after receiving the first dose of medication. Within 10 minutes of the onset of the pain, the patient lost consciousness and fainted. The emergency health services team called to the house, determined that the patient was in cardiac arrest and started cardiopulmonary resuscitation. The patient's first intervention was successful. After intubation and hemodynamic stabilization, the electrocardiogram (ECG) of the patient revealed sinus tachycardia with the heart rate of 130beats/minute and ST elevation in leads DII, DIII, and aVF and 3 mm ST depression in leads V2-6 (ECG 1). The patient underwent immediate coronary angiography with the diagnose of ST segment elevation myocardial infarction

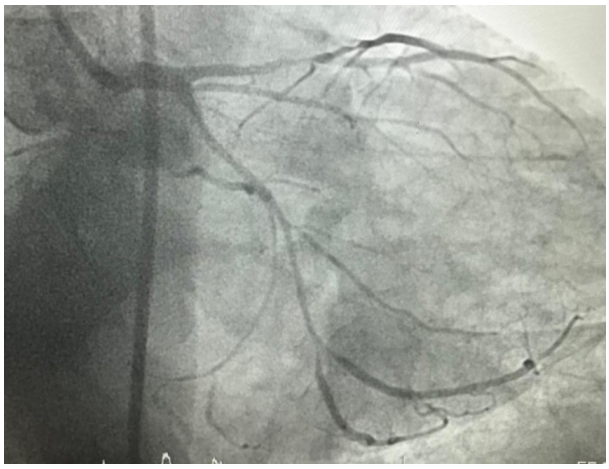

Figure 1. The first image of the patient's left coronary system in the presence of spasm on coronary angiography

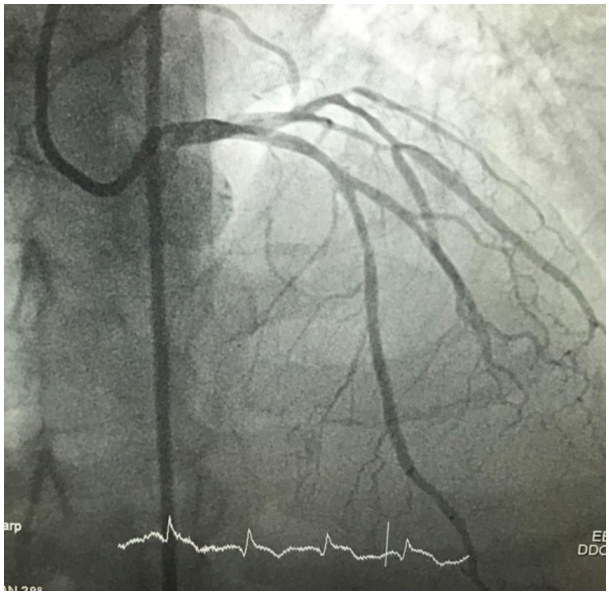

Figure 2. The second image of the patient's left coronary system in the presence of spasm in coronary angiography.

(STEMI). On coronary angiography, the left main coronary artery (LMCA) was normal. In the left anterior descending coronary artery (LAD) there was a long segment obstruction that was critically restricting the coronary blood flow (Figure 1) In circumflex artery (Cx), long segment obstruction throughout the main artery was observed (Figure 2).

The right coronary artery (RCA) was non-dominant, and we detected a critical osteal lesion (Figure 3).

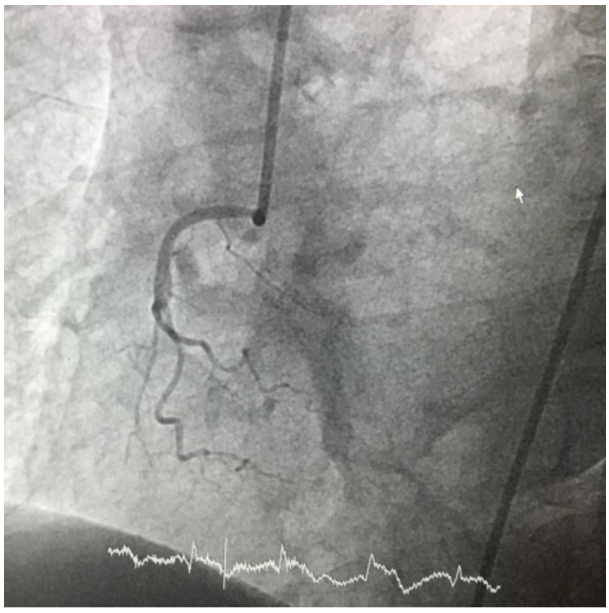

Figure 3. The patient's right coronary system in the presence of spasm on coronary angiography.

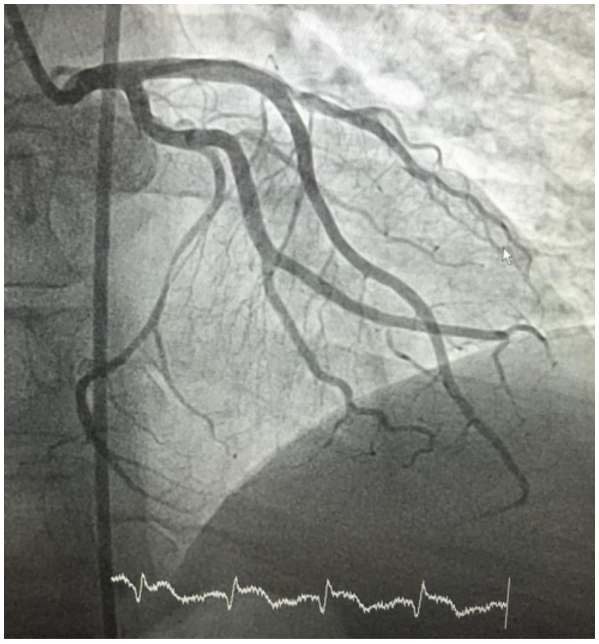

Figure 4. The first image of the patient's left coronary system on coronary angiography when the coronary spasm begins to resolve.

Ventricular tachycardia developed simultaneously while intracoronary nitrate was applied through the left guiding catheter. During the coronary angiography procedure, 300mg intravenous amiodarone were administered to the patient, who was hemodynamically stable.

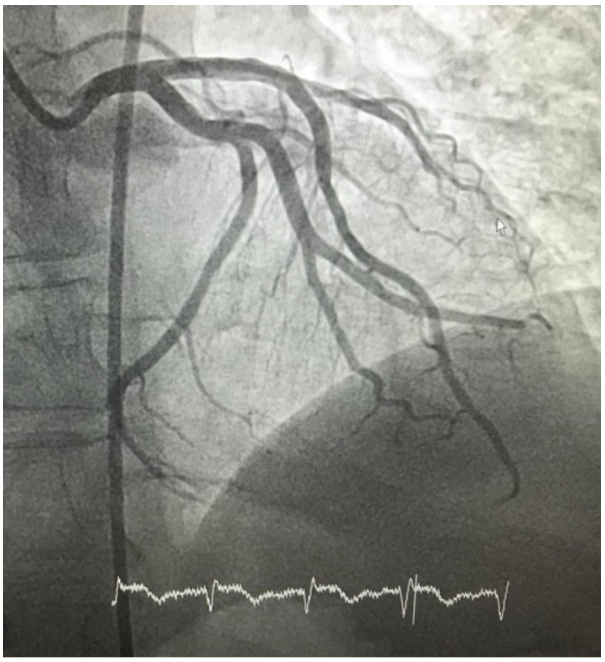

Figure 5. The last image of the patient's left coronary system on coronary angiography after the coronary spasm had completely resolved.

Normal sinus rhythm was achieved without the need for electrical cardioversion (ECG 2). In the images taken after intracoronary 200 μg nitrate, the LAD (Figure 4) and then the CX coronary spasms were completely resolved. In the final images of the coronary angiography, a myocardial bridge was seen in a short segment of the LAD mid-region, causing 40% stenosis (Figure 5).

The transthoracic echocardiography of the patient, who was taken to the coronary intensive care unit after hemodynamic stabilization, revealed a left ventricular ejection fraction (LVEF) of 55%, no significant wall motion abnormality, and mild mitral and tricuspid valve regurgitation. Laboratory parameters at the time of admission to the emergency department are presented in the table (Table 1). The patient was followed up under coronary intensive care unit for a day and then transferred to the anesthesiology and reanimation department. The patient, who was evaluated as hypoxic brain after neurological examinations and whose spontaneous breathing did not return despite all efforts and could not be extubated, died due to resistant pneumonia after 34 days of intensive care follow-up.

DISCUSSION

In this case report we present a 56-year-old patient without any chronic disease who presented with sudden cardiac arrest after taking oral amoxicillin/clavulanic acid. As it was seen in our case, Kounis syndrome is prevalent in 40–70-year-old male individuals and is mostly accompanied by chest pain (5)

Kounis syndrome (KS) is a clinical condition that precipitates acute coronary syndrome (ACS) due to hypersensitivity reactions. Within 60 minutes of exposure to the etiological agent, symptom onset occurs in 80% of cases. A recent investigation revealed that the predominant cardiac manifestations were chest discomfort (60%) and reduced blood pressure (75%). The study also documented dermatological, respiratory, and gastrointestinal involvement in 70%, 30%, and 20% of individuals, respectively. The study also found that electrocardiographic changes, such as ST-segment elevation or depression, were present in 85% of cases. Elevated cardiac biomarkers, particularly troponin levels, were detected in 70% of the patients, indicating myocardial damage. These findings underscore the importance of prompt recognition and management of Kounis syndrome to prevent potentially fatal complications (6).

The primary mechanism of KS pathogenesis involves the activation and degranulation of mast cells through various processes, leading to an increase and release of inflammatory mediators in both cardiac tissue and systemic circulation. This activation can result in coronary vasoconstriction, trigger platelet activation, cause plaque rupture, or initiate the coagulation cascade. Acute myocardial injury or sudden coronary or stent thrombosis may develop from coronary artery spasm (7). In the current case we present, there was no known ischemic coronary artery disease in the patients past medical history. Immediate coronary angiography did not show any atherosclerotic lesion or thrombus formation other than the noncritical muscular bridge in the mid-LAD region, but widespread severe coronary spasm was detected.

In a case report presented by Ralapanawa et al. a 74-year-old male patient with a history of diabetes and hyperlipidemia was admitted to the emergency room with anginal chest pain after taking oral amoxicillin. The patient, whose laboratory tests were stable, was discharged after relief of the chest pain from the emergency department (8). However, in our case, although there was no risk factor, unfortunately the patient had a sudden cardiac arrest at home and died despite all interventions due to prolonged hypoxia. This shows us that the severity of coronary vasospasm may vary and that the clinical condition of the patient before the first medical contact is very important for survival.

In the management of anaphylaxis, epinephrine remains the gold standard treatment. Timely administration is crucial, as it enhances patient survival. Nevertheless, caution is warranted in cases of acute coronary syndrome, where epinephrine may potentially aggravate ischemia, extend the QT interval, and trigger coronary vasospasm and cardiac arrhythmias. Because adrenaline can increase the production of thromboxane B2 synthesized by platelets and have a triggering effect on platelet aggregation (9,10). Although the use of adrenaline in the treatment of Kounis syndrome seems controversial. In the current case, adrenaline was compulsorily administered during the intervention of sudden cardiac arrest. However, its effect could not be evaluated due to ongoing hemodynamic instability.

In the management of acute coronary syndrome, acetylsalicylic acid (ASA) is commonly employed. Nevertheless, this medication carries the risk of inducing allergic reactions, which may manifest as anaphylactoid symptoms. Furthermore, ASA has the potential to aggravate pre-existing anaphylaxis in affected individuals. Its benefit in KS is unclear because, while it may provide benefits, it may also potentially worsen anaphylaxis. In the treatment of KS, calcium channel antagonists are regarded as the optimal anti-ischemic therapy, owing to their efficacy in counteracting the vasospastic pathophysiological mechanism commonly associated with this condition (11).

Kounis syndrome (KS) is an acute coronary syndrome triggered by hypersensitivity reactions. This case study demonstrates the importance of considering KS in patients with cardiac symptoms after allergen exposure, particularly antibiotics. The patient's cardiac arrest following amoxicillin/clavulanic acid administration and angiographic evidence of coronary vasospasm are consistent with KS. Prompt diagnosis and tailored treatment are crucial for improved outcomes. Management involves balancing allergic and cardiac manifestations. The case underscores the need for increased awareness among healthcare providers. Future research should focus on standardized diagnostic criteria, treatment protocols, long-term prognosis, and preventive strategies for KS patients.

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Abbreviations List

ACS: Acute coronary syndrome
Cx: Circumflex artery
ECG: Electrocardiogram
KS: Kounis syndrome
LAD: Left anterior descending coronary artery
LMCA: Left main coronary artery
LVEF: Left ventricular ejection fraction
RCA: Right coronary artery
STEMI: ST elevation myocardial infarction

Ethics approval and consent to participate

Ethical committee approval is not required because of the article is a case report. Informed consent was obtained from patient.

Consent for Publication

Although the personal information of the patient presented in the case was kept confidential, consent to share data was obtained from the patient and her relatives. This case study was conducted in accordance with the principles of the Declaration of Helsinki.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declaration of Conflicting Interests

The author declares that he has no conflicts of interest.

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