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Remember Kounis in the Emergency Department: A Case Report

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ABSTRACT

Background: Anaphylaxis is a life-threatening allergic reaction. Epinephrine is the first-line treatment of this condition. Kounis syndrome indicates the occurrence of acute coronary syndrome in a patient of hypersensitivity, allergy, or anaphylaxis associated with mast cells and platelets activation. Epinephrine can be the etiology of myocardial infarction in this setting.

Cases report: This report represents a case of a 58-year-old female who had myocardial infarction while being treated of anaphylaxis in response to cefuroxime intake.

Conclusion: Emergency physicians should be aware of the possibility of myocardial infarction in anaphylactic patients to properly manage it.

Keywords: Anaphylaxis, Kounis syndrome, Hypersensitivity, Case report.

INTRODUCTION

Anaphylaxis is an acute, serious, systemic allergic reaction related to a variety of triggers, mechanisms, clinical presentations, and grades of severity [(1)]. Several risk factors have been recognized for myocardial infarction (MI); however, the differential diagnosis of this condition in an anaphylactic patient is either an allergic acute coronary syndrome (ACS) known as Kounis syndrome or the effect of epinephrine treatment [(2,3)]. Kounis syndrome refers to the occurrence of ACS including coronary spasm, acute myocardial infarction, and stent thrombosis with mast cells and platelets activation in a patient experiencing hypersensitivity, allergy, or anaphylaxis [(4)].

The pathophysiology behind Kounis syndrome involves mediators as histamine causing coronary vasoconstriction, platelet activation, inflammatory cell activity modulation, and cytokine production. Another suggested mechanism is activation of matrix-degrading metalloproteinases by chymase and tryptase enzymes eventually leading to atherosclerotic plaques. There are three described variants of Kounis syndrome: Type I that involves coronary vasospasm in patients without pre-existing coronary problems, type II that includes patients with pre-existing coronary plaques, and type III that involves coronary stent thrombosis [(5)].

Kounis syndrome diagnosis is based on symptoms, laboratory findings, electrocardiography (ECG), echocardiography, and coronary angiography. It should be suspected in patients who present with chest pain or angina-like symptoms in the presence of symptoms of systemic allergic reaction [(5)].

Elevation of serum tryptase, histamine, cardiac biomarkers, and troponins is a clue for diagnosis [(6)]. Till now, there are no guidelines for its management [(7,8)].

The second possible etiology behind MI in the setting of anaphylaxis is epinephrine. It is considered the first line of treatment in anaphylaxis [(9)]. The different mechanisms suggested included coronary vasospasm, promotion of platelet aggregation, and increase of thrombin-induced platelet fibrinogen binding [(3)].

The time interval between epinephrine administration and the occurrence of acute MI is the main determining factor in the differential diagnosis. If the cardiac symptoms occur at the same time or shortly after epinephrine administration, an epinephrine-related etiology is highly suspected. Kounis syndrome is more likely if MI symptoms and ECG changes happened before epinephrine administration [(3)].

The challenging aspect of Kounis syndrome is that managing ACS in the setting of anaphylaxis differs from that of a standard acute MI. Treatment requires harmonizing the management of coronary vasospasm or thrombosis with allergy at the same time [(8)].

CASE REPORT

A 58-year-old female attended the emergency room complaining of sudden itching all over her body, dizziness, vomiting and a fainting episode, one hour following cefuroxime intake.

The patient had type 2 diabetes mellitus and hypertension. On examination, the patient was sweaty, dyspneic, and with urticarial rash. Her vital data were as follows: blood pressure 80/50 mmHg, pulse 105 beats/minute, oxygen saturation 96% on room air, and temperature 36.8 ºC. Anaphylaxis was suspected, and the patient was given intramuscular epinephrine (0.5 mg), intravenous hydrocortisone (200 mg), and one liter of intravenous normal saline. The initial ECG showed nonspecific changes (**Figure 1**).

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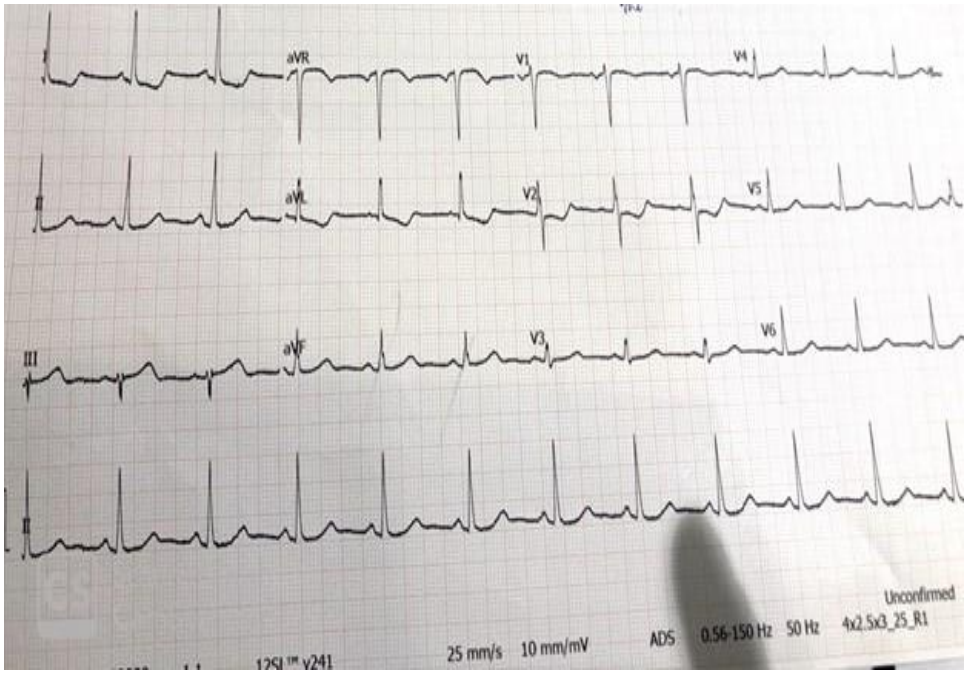

Figure 1. Electrocardiography showing nonspecific changes.

The symptoms improved, and the patient became stable. Her initial troponin was normal; 30 minutes later, the patient started complaining of throat pain and chest tightness. Therefore, the ECG was repeated, and it showed dynamic changes with AVR ST elevation and ST depression in the anterolateral leads (**Figure 2**).

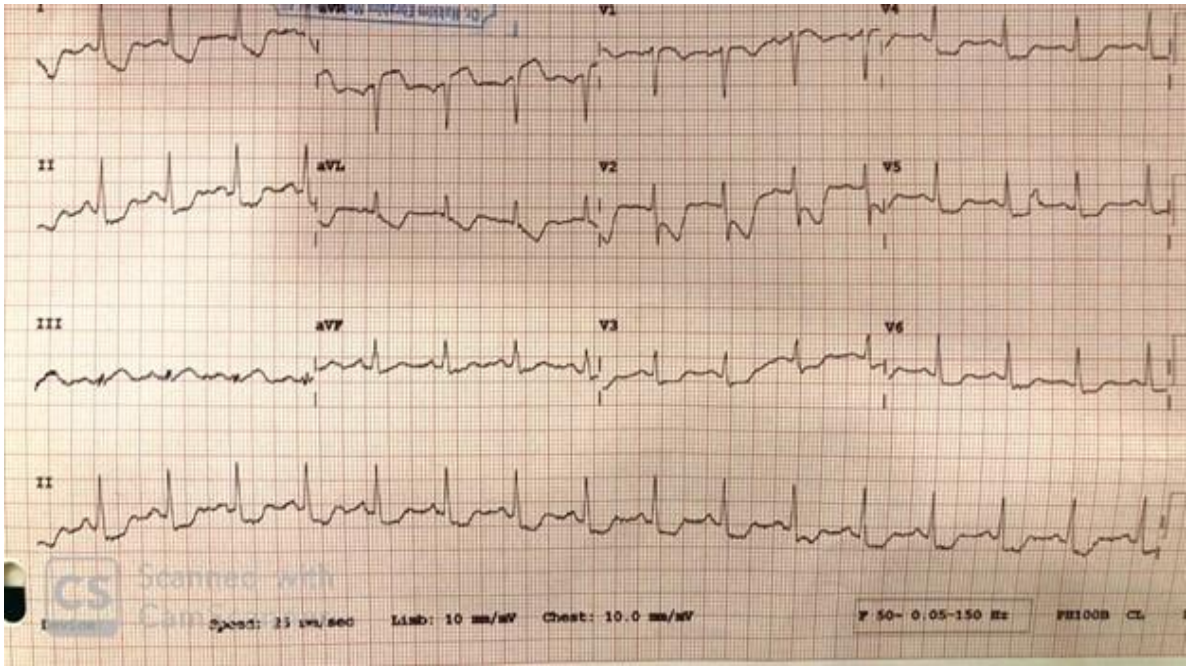

Figure 2. Electrocardiography showing AVR ST elevation and ST depression in the anterolateral leads.

An urgent cardiac consultation was sought. Troponin level was repeated, and it was found elevated. Emergency angiography showed severe left main coronary and left circumflex disease without thrombosis (**Figure 3**).

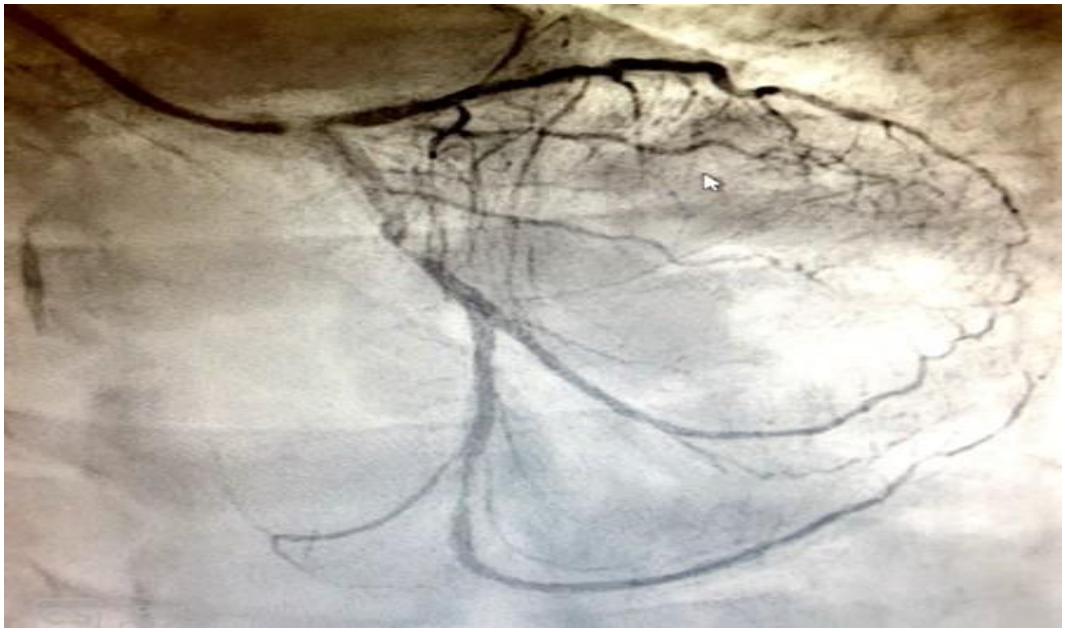

Figure 3. Coronary angiography showing severe left main coronary and left circumflex disease without thrombosis.

The patient was treated conservatively with antiplatelets and enoxaparin, and was discharged from the Cardiology Care Unit after 72 hours.

Ethical Approval

An approval of the study was obtained from our local IRB. The patient and her relatives were informed that the case would be published as case report, and this was accepted. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

DISCUSSION

We report a case of MI that occurred in an anaphylactic patient. The 58-year-old female suffered from an anaphylactic reaction one hour following cefuroxime intake. The patient was given intramuscular epinephrine. Shortly after, the patient started complaining of chest pain. Follow-up ECG and repeated troponin levels confirmed the presence of ACS. Further confirmation was established by coronary angiography.

In the setting of ACS in an anaphylactic patient, the cause could either be Kounis syndrome or adrenaline therapy. Several clinical reports suggested that the cardiovascular system can be a target of anaphylaxis [6,10]. According to **Guedeney *et al.*** [11], there was a frequent persistence of high residual inflammatory risk after percutaneous coronary intervention, which was associated with worse outcomes of the patients. Reduction of inflammation, using canakinumab, improved the long-term cardiovascular outcomes in the Canakinumab Anti-inflammatory Thrombosis Outcome Study (CANTOS) [12]. Therefore, cardiac troponins should be measured in all patients with anaphylaxis. This could help early diagnose and appropriately manage ACS [6].

The triggering agents for Kounis syndrome reported in the literature are widely variable. Cefuroxime was reported by **Kounis** [5] as one of the xenobiotics capable of causing Kounis syndrome. Our patient's age and medical history (hypertension and diabetes) were consistent with the literature reports regarding the risk factors of developing Kounis syndrome [3].

The possibility that epinephrine could have caused MI in our patient is supported by the onset of chest pain, which started after the therapy. It is worth mentioning that most MI cases of with epinephrine use were reported to have received high intravenous doses. On the other hand, there are rare, reported cases of MI after receiving low doses or intramuscular epinephrine [13-17]. **Campbell *et al.*** [18] concluded that intramuscular epinephrine is safer than intravenous administration in anaphylaxis that needs extreme caution and vigilance.

Unfortunately, there are no established clinical guidelines for the management of Kounis syndrome [8]. Antihistamines and steroids can be given in type I Kounis syndrome. Intramuscular epinephrine may worsen ischemia, especially in old cardiac patients [3]. Vasodilators can be given for coronary spasm; however, meticulous observation is required as hypotension can be worsened due to the anaphylaxis [8]. In types II and III Kounis syndrome, the ACS is managed by the established guidelines using antiplatelets, aspirin, and P2Y12 receptor inhibitor, which can be followed by

revascularization, if necessary [19]. Beta blockers should not be used. The unopposed α-adrenergic receptor activity can worsen the existing coronary vasospasm. Opioids may aggravate the allergy through induction of mast cell degranulation [4].

CONCLUSION

We reported a case of an elderly female with silent preexisting coronary artery disease. Her condition showed progression to MI after an anaphylactic reaction and adrenaline therapy. This has been assumed to be due to coronary vasospasm induced by alpha receptor stimulation. The role of adrenaline in managing anaphylaxis is undoubtedly important, and may even be life-saving. However, emergency physicians should be aware of the possibility of occurrence of ACS in this setting, especially with pre-existing cardiac illness, old age, or intake of beta-blockers. Patient monitoring using ECG and cardiac troponins can help in early diagnosis. There is a need to establish guidelines for management of Kounis syndrome.

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