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BMH Med. J. 2021;8(4):138-142. **Case Report**

Kounis Syndrome with Atrial Fibrillation and Seizures Following Intake of Diclofenac Sodium

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Abstract:

Kounis syndrome refers to the coexistence of acute coronary syndromes with allergic, hypersensitivity, and anaphylactic reactions due to mast cell activation. The patient being described developed myocardial infarction with atrial fibrillation and seizures following intake of diclofenac sodium.

Keywords: Kounis syndrome, acute coronary syndrome, atrial fibrillation, anaphylaxis, seizures, mast cell

Introduction

Kounis syndrome represents the concurrence of acute coronary syndrome due to mast cell activation as a result of allergic and anaphylactic reactions. It was first described by Kounis and Zarvas in the year 1991.[1] It may be triggered by certain foods, drugs, and environmental factors like insect bites, pollens, or latex contact. Though the condition is not rare, it is often overlooked; probably because the focus remains mainly on angina. This is the case of a middle aged male who developed anaphylactic shock with seizures followed by ST segment elevation with atrial fibrillation (AF) and seizures after taking diclofenac sodium.

Case report

A middle aged male with no prior comorbidities was taken to a local hospital with complaints of urticarial rash and seizures. He was not on any regular medications. He did not have any food allergies. On evaluation he was found to be in shock with blood pressure 80/40 mm Hg. His electrocardiography (ECG) showed ST elevation in II, III, aVF, ST depression in V2-6 and AF with fast ventricular rate (**Figure 1**). Random blood glucose was 122 mg/dL. He was given loading doses of aspirin, clopidogrel and atorvastatin along with intravenous normal saline and immediately referred to our hospital.

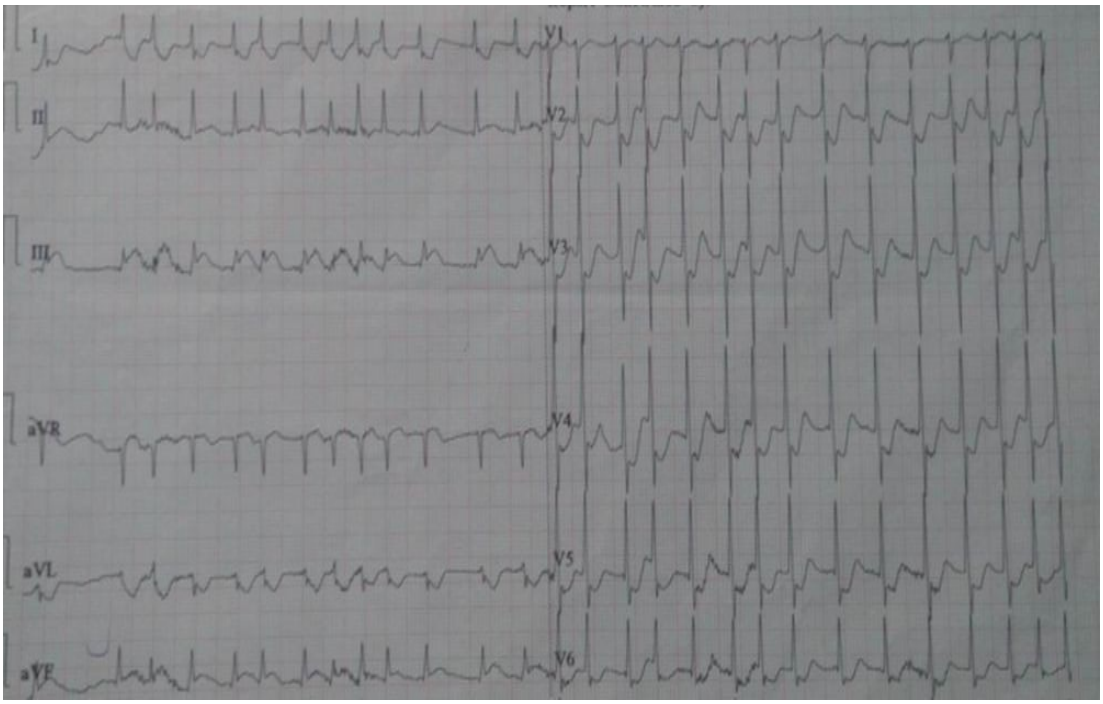

Figure 1: ECG at the time of presentation, with ST elevation in II, III, aVF, ST depression in V2-6 and AF with fast ventricular rate.

On arrival to our hospital, he was conscious, oriented and afebrile. His pulse rate was 80/minute and blood pressure 110/70 mmHg. Urticarial rashes were present all over his body. His systemic examinations were normal. There were no signs of meningeal irritation. His repeat ECG taken about 2 hours after the initial one was normal [**Figure 2**]. Magnetic resonance imaging (MRI) of brain was normal and electroencephalogram (EEG) did not show any epileptic changes. His complete blood counts showed eosinophilia (12%). Other blood investigations like renal and liver functions, electrolytes, random blood glucose, calcium, magnesium and thyroid stimulating hormone were normal. CK-MB and Troponin I levels were also normal. Serum tryptase could not be done due to lack of availability. Absolute eosinophil count was elevated (620/mm^3) and serum IgE levels were normal. Antinuclear antibody profile, anti-cyclic citrullinated peptide and antineutrophil cytoplasmic antibodies (p and c) were negative. Echocardiography showed concentric left ventricular hypertrophy with no regional wall motion abnormality and ejection fraction was 70%.

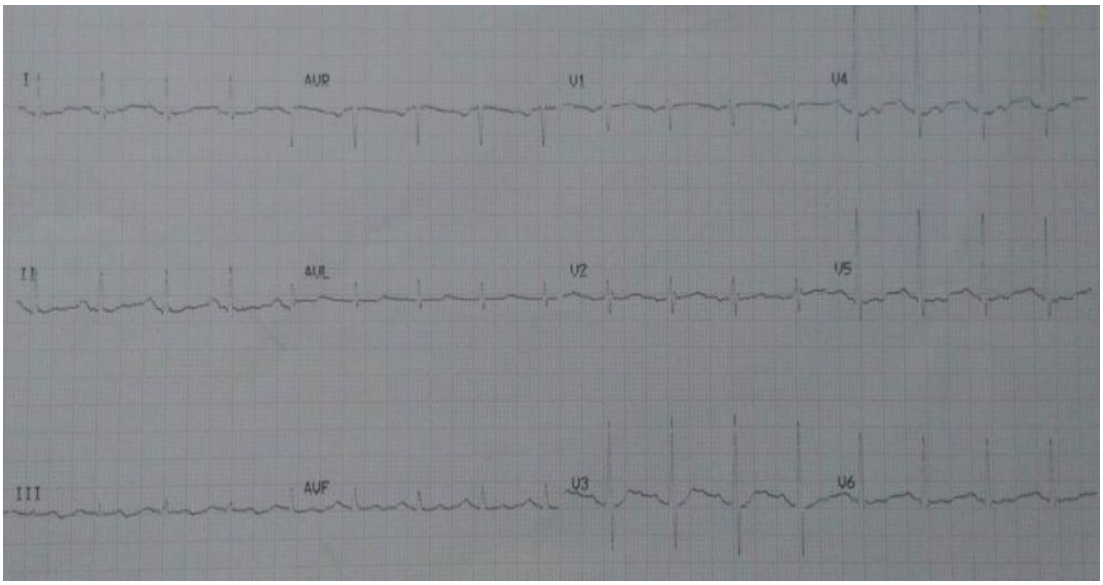

Figure 2: Repeat ECG taken about 2 hours after the initial ECG, in sinus rhythm

On detailed history taking, the patient had mild back pain for which he had taken a tablet of diclofenac sodium before going to bed. About 3 hours later, he woke up with urticarial rashes all over the body, facial puffiness and dyspnoea. A few minutes later, he dropped down with generalised tonic clonic seizures as noted by his wife. There was frothing from the mouth and tongue bite, with no bowel or bladder incontinence. The seizure episode lasted for about 1 minute, followed by about 15 minutes of postictal state. About 8 months ago, there was a similar episode of urticarial rash with seizure when the patient had taken a tablet for neck pain. At that time he was evaluated for seizure disorder; and investigations like MRI brain, EEG and cerebrospinal fluid analysis were normal. The details of ECG during that episode was not available.

On the basis of history, clinical presentation and investigations, the diagnosis of Kounis syndrome was considered. He was given intravenous methylprednisolone, intramuscular pheniramine and intravenous ranitidine; following which he became stable. His coronary angiogram was normal. Holter monitoring showed few atrial ectopics with no significant arrhythmias. By day 3 of admission, he was perfectly fine with pulse rate of 80/ minute and blood pressure 140/90 mm Hg. His rashes had disappeared. Over the next 8 months follow up, there were no similar episodes.

Discussion

Kounis syndrome has been attributed to the activation of mast cells and platelets in the setting of allergy and anaphylaxis. The triggering factors include various drugs, environmental exposures, and conditions like asthma, idiopathic anaphylaxis and mastocytosis. The degranulation of mast cells, which occurs during allergic reactions, releases inflammatory mediators like histamine into the systemic circulation; which in turn causes coronary vasoconstriction. Histamine induces tissue factor expression and activates the platelets leading to thrombosis.[2,3] Eosinophils cause vasoactive smooth muscle contraction by synthesizing leukotriene C4. Moreover, eosinophils also activate mast cells and basophils to produce vasoactive substances.[4]

Three variants of Kounis syndrome have been described:

*Type I: Normal or near normal coronary arteries without risk factors for coronary artery disease. The inflammatory mediators may either induce coronary vasospasm without increasing the cardiac enzymes and troponins or coronary vasospasm progressing to acute myocardial infarction with raised cardiac enzymes and troponins.

*Type II: In the setting of pre-existing atheromatous disease, the release of inflammatory mediators may induce either coronary vasospasm alone or along with plaque erosion or rupture manifesting as acute myocardial infarction.

*Type III: Coronary artery stent thrombosis.[5]

The treatment of Kounis syndrome is mainly aimed at coronary vasodilation and amelioration of allergic reaction. Calcium channel blockers and nitrates are the first-line management drugs. Since histamine induces tissue expression through H1 receptors, the use of H1 receptor blockers may be useful in the management. H2 receptor blockers have also been found to be effective. The efficacy of mast cell stabilizers is unclear.[6] Corticosteroids are effective in treating angina symptoms as well as normalizing the eosinophil count.[7]

The potential effect of certain medications is debatable. Aspirin may aggravate allergic

reactions. Beta-blockers may induce further vasospasm due to unopposed effect on alpha-adrenergic receptors. Nitroglycerine may cause tachycardia and hypotension. Epinephrine, used in anaphylaxis, may aggravate ischemia and worsen coronary vasospasm. Morphine may induce mast cell degranulation and aggravate allergic reaction.[8]

A handful of cases of Kounis syndrome have been reported with usage of diclofenac.[9-11] Our patient had type I Kounis syndrome with AF, transient ST segment elevation and seizures. Seizures are infrequent presentation of anaphylaxis.[12] The scenario faced by our patient, to the best of our knowledge, has not been reported earlier.

Conclusion

Kounis syndrome is an under recognised condition, and needs to be considered especially in young individuals presenting with acute coronary syndrome. These patients can have ECG changes with normal cardiac biomarkers. Coronary vasodilators form the mainstay of treatment. Corticosteroids, H1 and H2 receptor blockers also provide symptomatic relief. The routine medications for myocardial infarction like aspirin, beta blockers and morphine may be avoided in these patients.

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