ABSTRACT

Kounis syndrome (KS) is an acute coronary syndrome secondary to allergic reactions and can be triggered by many factors. It is a rare condition that is difficult to diagnose, which delays the prognosis of the disease. KS can be classified into three subtypes. In this study, we report a 57-year-old patient with a history of anaphylaxis three times, one after using Moxifloxacin and the other two following a physical activity and an application of hair dye, which were released by an intramuscular adrenaline injection. The two different types of KS occurred at different times due to different causes in the same patient. Our patient was consistent with type 2 KS at the first attack and type 1 KS at the second attack. Therefore, clinicians should not misdiagnose myocardial ischaemia in patients who present with an allergy complaint.

Keywords: Kounis syndrome, anaphylaxis, allergic angina

ÖZ


Anahtar Kelimeler: Kounis sendromu, anafilaksi, alerjik anjina

Introduction

Kounis syndrome (KS) was defined by Kounis and Zavras (1) in 1991 as a chest pain in the course of an anaphylactic reaction related to mast cell activation. It may be seen as angina pectoris or myocardial infarction (MI) with normal coronary arteries (1,2). The KS can be classified into three subtypes: type 1 patients suffer from chest pain associated with an acute allergic reaction and have no predisposing factors for coronary heart disease (3); type 2 presents in patient with primary coronary artery disease (CAD) and may cause plaque erosion or rupture (2,3) and type 3 patients suffer stent thrombosis (4). The various clinical manifestations of KS are chest pain, nausea, vomiting, syncope, pruritus, urticaria, palpitations and almost half of the patients suffer from respiratory manifestations including wheezing, stridor, rhinitis and dyspnoea (5). KS may be initiated by drugs, foreign bodies, diseases caused as a result of release of chemical mediators such as histamine, leukotrienes, chemokines and cytokines (6,7). Immunoglobulin E (IgE) and tryptase may be elevated in KS. An early diagnosis of KS is important for the prognosis and treatment of it.

Case Report

A 57-year-old woman presented with chest pain, palpitations, sweating, cough, weakness and near syncope. She had taken amoxicillin for pneumonia. She had a previous history of allergy but not of any CAD. Her history also included anaphylaxis three times, one after using Moxifloxacin and the other two following a physical activity and an application of hair dye, which were released by intramuscular adrenaline injection. Furthermore, she was allergic to Moxifloxacin, diazepam, iodine, Benzydamine oral spray, cinnamon, pistachio and peanut. Her medication included levothyroxine for the treatment of Hashimoto’s thyroiditis. She was a tobacco smoker for 25 pack-years. She had a family history of Parkinson’s disease, diabetes mellitus, bladder and colon cancer. Her vital signs were stable when she presented to the emergency
room. She was presented with acute-onset chest pain, accompanied by allergic symptoms. Cardiac enzymes (Troponin, creatine kinase-MB) were normal. Antinuclear antibodies, anti-dsDNA, complete blood count, brain natriuretic peptide urea/creatinine, aspartate aminotransferase/alanine aminotransferase, lactate dehydrogenase/creatine phosphokinase, tryptase, antithrombin III, thyroid stimulating hormone, C3, C4 and D-dimer were normal. The abnormal test results were LDL: 157 mg/dL and IgE: 384 (n<100). Anthelmintic treatment was administered to eradicate any other possible cause of IgE elevation. Hepatitis B virus and hepatitis C virus serology were also negative. Abdominal ultrasonography and computerized tomography (CT) were normal. Thorax CT was performed showing bronchiectasis in small region.

Electrocardiography (ECG): Normal (Figure 1), echocardiography showed segmental left ventricular motion abnormality, but ejection fraction was normal, coronary angiography also revealed right coronary artery (RCA) spasm in the midportion and plaques in the left anterior descending (35%-50%) and circumflex arteries (Figures 2, 3). The RCA diameter was expanded after intravenous nitrate injection. Diltiazem, clopidogrel, statin, isosorbide dinitrate and, if necessary, isosorbide mononitrate were started as a maintenance therapy. After 15 months, the patient was readmitted with anaphylaxis-associated chest pain, amaurosis fugax and filiform pulse while dyeing her hair. She had taken nitroglycerine spray and acetylsalicylic acid when chest pain began prior to being admitted. Cardiac enzymes and transthoracic echocardiography were normal, ejection fraction was calculated as 55%. ECG: Normal (Figure 4), IgE: 322. Coronary angiography was performed showing no abnormal pathology. At that time, it was thought that the patient might have KS.

Parenteral H1 blocker and steroid were added to the treatment. No additional complaint was reported by the patient after being followed-up for three days. Drugs were adjusted and the patient was referred to the allergy department for allergic MI.

The patient gave a verbal and written consent before participating in the study.

Discussion

We present an interesting case of KS in a patient with an uncommon clinical presentation, which is significant for the awareness of KS. First, despite the recurrent anaphylaxis, there were no abnormalities in ECG and cardiac enzymes. Second, while using anti-ischaemic and anti-lipemic therapies, Kounis attacks reoccurred due to the allergic reactions

![Figure 1. Normal electrocardiography of the patient when she was first admitted to the emergency service](image1)

![Figure 2. Coronary angiography shows non-critical plaques in the LAD (35%-50%) and Cx](image2)

LAD: left anterior descending

![Figure 3. Coronary angiography revealed right coronary artery spasm in the midportion](image3)

RCA: right coronary artery
even when narrowing disappeared. Briefly, the patient experienced two different types of KS at different times due to different causes - the consistent type 2 KS at the first attack and type 1 KS at the second.

The plaques were seen in the coronary arteries at the first coronary angiography, normal troponin but abnormal echo findings were observed, and the patient had used an antibiotic that had caused the KS. The second coronary angiography was normal when the patient had used a hair dye.

KS refers to varying degrees from myocardial ischaemia to infarction as a result of allergic and anaphylactic reactions. It could be presented as a broad clinical spectrum differing from only chest pain to ST segment elevated MI. Allergic reactions may be subclinical, acute or chronic. KS may develop for many reasons; antibiotics and other drugs (8).

Nitrates, calcium blockers, anti-histaminic and steroids are used to treat type 1 KS, whereas antithrombotic drugs are required for type 2 KS (9). Clinicians should not misdiagnose myocardial ischaemia in patients who present with an allergy complaint.

In our case, there were changes in echocardiogram (ECHO) and clinical findings considering ischaemic heart disease, however, no change in enzymes or ECG were seen. Coronary angiography was performed. Ischaemic coronary arteries and vasospasm were seen. Fifteen months later, second coronary angiography was performed due to the chest pain and anaphylaxis, but the coronary arteries were normal.

**Conclusion**

To conclude, we suggest that clinicians should always consider KS as a differential diagnosis if there are any signs and symptoms of allergy and ischaemic heart disease such as changes in ECG, ECHO or enzymes.

**Ethics**

**Informed Consent:** Verbal and Written informed consent was obtained from the patient.

**Peer-review:** Internally peer-reviewed.

**Authorship Contributions:** Surgical and Medical Practices- Y.F., T.G.; Concept- Y.F., B.M., F.F.B.; Design- Y.F., B.M., C.B.; Data Collection or Processing- Y.F., B.M., T.G., C.B.; Analysis or Interpretation- Y.F., F.F.B., T.G.; Literature Search- Y.F., B.M.; Writing- Y.F., B.M., F.F.B.

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