CASE REPORT / *Olgu Sunumu*
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Kounis Syndrome Following Metamizole Infusion

Metamizol infüzyonu sonrası Kounis Sendromu

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Abstract

Objective Kounis Syndrome (KS) is described as temporary vasospasm of coronary arteries after exposure to an allergen. It may present as severe chest pain, ST elevated or non-ST elevated myocardial infarction. Among factors causing KS are bee stings, all kinds of medications and food.

Case A 25-year-old female patient developed dyspnea and syncope following metamizole infusion. During follow-up in Emergency department, she developed severe chest pain and blood results revealed Troponin I elevation. She underwent coronary angiogram and any narrowing in coronary arteries was not determined. After hospitalization in the Intensive Care Unit with supportive therapy, levels of Troponin I decreased and the patient was discharged with a total recovery.

Conclusion Emergency physicians must be aware of this rare entity in order to prevent mortality and morbidity.
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Keywords Kounis syndrome, allergy, Emergency department

Öz

Amaç *Kounis Sendromu (KS) allerjenle temas sonrası koroner arterlerde geçici vazospazm gelişmesi olarak tarif edilir. Şiddetli göğüs ağrısı, ST eleve ya da non-ST eleve miyokardiyal infarkt şeklinde kendini gösterebilir. KS nedenleri arasında arı sokmaları, her türlü ilaçlar ve yiyecekler sayılabilir.*

Olgu *25 yaşındaki bayan hastada metamizol infüzyonu sonrası dispne ve senkop gelişmiştir. Acil servisteki takibi esnasında, şiddetli göğüs ağrısı oldu ve kan sonuçlarında Troponin I seviyesi yüksekliği saptandı. Koroner anjiyograma alındı ve koroner arterlerinde darlık saptanmadı. Yoğun bakıma yatırılıp destek tedavisi aldıktan sonra Troponin I seviyesi düştü ve hasta tam iyilik haliyle taburcu edildi.*
(Sakarya Tıp Dergisi 2016, 6(3):170-174)

Sonuç *Mortalite ve morbiditeyi azaltmak için acil doktorları bu nadir hastalık için dikkatli olmalıdırlar.*

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INTRODUCTION

Kounis Syndrome (KS) is described as the concurrence of acute coronary syndromes and allergic reactions. In the etiology, mast cell over activation plays a role[1]. Characteristics of the syndrome are known to be unstable angina or acute myocardial infarction (MI) confirmed by clinical or laboratory findings. Following an allergic reaction, patients may develop ST elevation or depression in electrocardiography (ECG) or increases in serum cardiac biomarkers and typical chest pain[2].

Among the possible triggering factors of KS are hymenoptera stings, drugs, food, environmental exposure, and diverse conditions such as bronchial asthma, mastocytosis, etc. Any medication can cause this syndrome, but most cases have been reported in relation to beta-lactam antibiotics and non-steroidal anti-inflammatory drugs[3].

In this report, we present you a rare cause of KS, metamizole infusion, and aim to emphasize importance of this syndrome in the light of current literature.

CASE REPORT

A 25-year-old female patient was administered fluid containing metamizole sodium for high fever and generalised pain due to upper respiratory tract infection in a primary healthcare facility.

After a short while, the patient developed bruising, severe dyspnea and syncope. Clinical findings had been linked to a possible allergic reaction. After quick airway maintanance, methyl prednisolone (40 mg) infusion was initiated.

Meanwhile, the patient vomitted.

Patient was brought to our Emergency department (ED) by ambulance. From history, it was determined that cardiopulmonary arrest has not develop and cardiopulmonary resuscitation was not performed.

The patient was alert and conscious on arrival to the ED. Her only complaint was dizziness. Her vital signs were as follows: TA: 70/50 mmHg, heart rate: 105/minute, sO2: 98%. The physical examination did not reveal any findings of allergic reaction such as uvula edema, wheezing or urticarial lesions.

An ECG was performed and ST depressions in anterior leads were determined (fig 1). Patient was administered methyl prednisolone (40 mg) and 0,9% saline infusion, and monitored in the ED observation room. Blood samples for cardiac enzymes and routine laboratory studies were obtained. In the observation room, antihistamine and steroid therapy was continued.

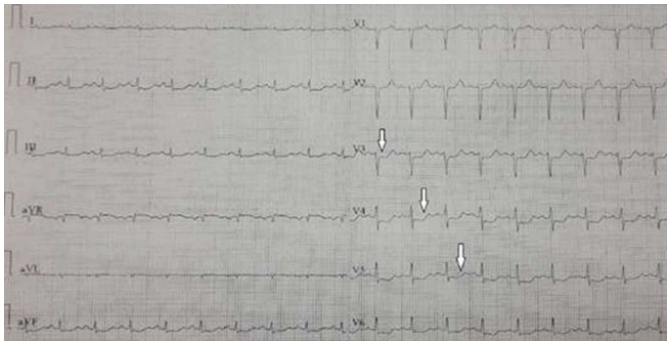

Figure1: Initial ECG of the patient. Arrows show widespread ST depression in anterior leads

On follow-up, the patient developed severe chest pain and an ECG was repeated.

The patient was stil hypotensive and tachycardic (80/50, 120-140 beats/minute).

Results of the blood tests revealed increased troponin level (8,96 ng/ml), so the patient was consulted with cardiology and an echocardiography was performed. Echocardiography of the patient did not reveal any regional wall motion abnormality or systolic dysfunction (ejection fraction: 60%).

An acute coronary syndrome was not considered.

The cardiologist suggested control ECG and troponin measurement after 3 hours.

In the follow-up, dyspnea developed and sO2 level reduced to 75 mmHg. On auscultation, widespread rales were determined and the patient's complaint of chest pain increased.

Elevated cardiac troponin levels was determined in control markers (trop: 11,3 ng/ml). Then, the patient was administered 300 mg acetylsalicylic acid, clopidogrel bisulfate, B-blocker, nitrate and furasemide therapy. Simultaneously, non-invasive

respiratory support was initiated with oxygen mask.

In PA chest X-ray, widespread infiltrations and fluid extravasation were determined.

Then the patient has undergone angiographic intervention. Any narrowing in the coronary arteries was not determined (fig 2a left main coronary artery, left anterior descending coronary artery and circumflex coronary artery and fig 2b right coronary artery). With initial diagnosis of KS, patient was hospitalized in intensive care unit (ICU). After 3 days of supportive therapy in the ICU, her troponin level decreased to normal range and the patient was discharged with total recovery.

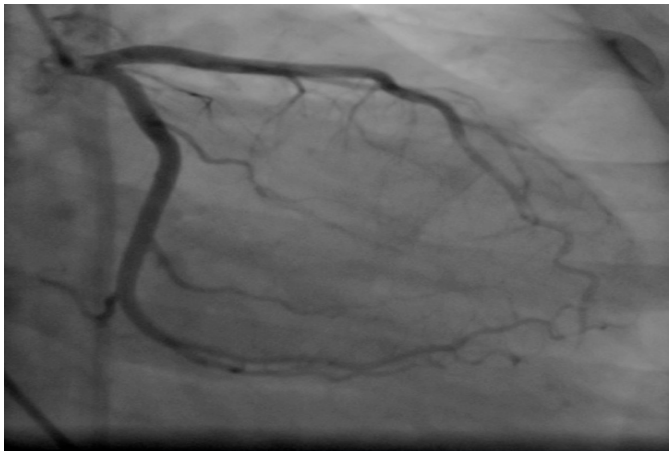

Figure 2a: Photograph of normal left main coronary, left anterior descending and circumflex coronary arteries during angiography

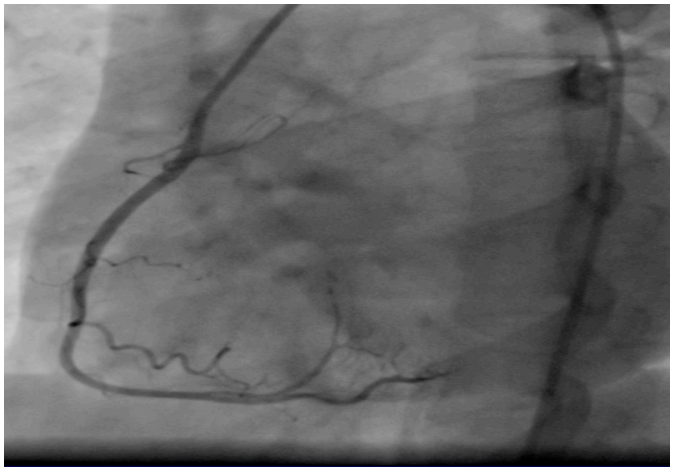

Figure 2a: Photograph of normal left main coronary, left anterior descending and circumflex coronary arteries during angiography

DISCUSSION

Kounis syndrome (allergic angina and allergic myocardial infarction) has been described as coincidental occurrence of acute coronary syndromes with conditions associated with mast cell activation, such as allergies or hypersensitivity and anaphylactoid insults. It is caused by inflammatory mediators such as histamine, neutral proteases, arachidonic acid products such as leukotrienes, platelet activating factor and a variety of cytokines and chemokines released during the activation process[4].

The released mediators can induce either coronary artery spasm which can progress to acute myocardial infarction or atheromatous plaque erosion or rupture culminating to coronary thrombosis.[5]

Justle et al reported a case of a patient who suffered KS with cardiogenic shock and asystole after intravenous infusion of metamizole, and in which no lesions were observed in coronary angiography[6]. Similarly, our patient possibly developed temporary cardiac ischemia due to metamizaole infusion. Our findings were ST depression and elevated troponins instead of shock and asystole. Coronary angiography of our patient was also found to be normal.

There are three variants of KS. Type 1 variant includes patients with normal coronary arteries without predisposing factors for coronary artery disease, in whom the acute allergic insult induces either coronary artery spasm with normal cardiac enzymes and troponins or coronary artery spasm progressing to acute myocardial infarction with raised cardiac enzymes and troponins. This variant might represent a manifestation of endothelial dysfunction or micro vascular angina. Type II variant includes patients with quiescent pre-existing atheromatous disease in whom acute allergic episode can induce plaque erosion or rupture manifesting as an acute myocardial infarction. Several reports have shown that type I variant of KS has better prognosis than type II variant. However, in both types prognosis depends on the magnitude of the initial allergic response, the patient's sensitivity, co-morbidity, the site of antibody antigen reaction, the allergen concentration and the route of allergen entrance. A type III variant has been described as coincidence of hypersensitivity reactions following

implantation of drug-eluting stents, causing stent thrombosis. In a report of a 60-year-old patient with type 2 diabetes mellitus has been stunk by a bee. She has developed widespread ST segments depressions and inverted T waves. She had no previous history of angina and her echocardiogram and exercise ECG were normal. A coronary angiography could not have been performed. In the report, it was underlined that, without coronary angiogram it was difficult to say which type of KS she actually had[7].

In our report, patient was a young female without comorbidities, so, elevation of troponin is likely to occur due to temporary vasospasm of coronary arteries either by metamizaole or sultamisilin infusion. Kounis Syndrome determined in our patient was compatible with Type-1.

It should be noted that every serious allergic reaction that causes hypotension, tachycardia and sometimes severe hypoxygenaemia (anaphylactic shock), can cause myocardial ischaemia in patients with subclinical coronary artery disease[8]. We performed coronary angiography and could not determine narrowing in coronary arteries. It may be considered that cardiac ischemia has occured due to general hypoxygenaemia since angiography was found to be normal. However, reason for normal coronary arteries may be a result of nitrates given in the ED.

Gunawardena et al. reported a 38-year-old man who presented with anterior ST elevation myocardial infarction and peripheral blood eosinophilia. It was reported that he had rhinitis and malaise for several days prior to presentation. There were no signs of hypersensitivity such as urticarial rash or pruritus. Coronary angiogram revealed only mild plaque disease. Blood investigations revealed moderate eosinophilia and elevated IgE levels. Computerized Tomography of the thorax revealed fluid extravasation at multiple sites. Screening for a possible secondary cause for eosinophilia revealed hypersensitivity to multiple antigens. A diagnosis of KS was made. Within days of starting steroids and antihistamines, the patient's eosinophil count has returned to normal range with improvement of clinical picture. They also reported that their case differed from classical KS as there was no acute allergic reaction except atopic rhinitis. They reported that fluid extravasation at multiple sites has not been described in previous cases.[9] Accordingly, in our case, fluid extravasation was determined in chest X-ray. This finding may be confusing and mistaken by pneumonia. Clinicians must be careful of this unexpected finding.

With regards to the therapeutic approach of coronary spasms following an allergic reaction, the medications should include vasodilators, such as nitrates, and calcium channel inhibitors, which are in any case the treatment of choice in every case of coronary spasm[7]. Our case was treated with supportive therapy with no additional medication and discharged with total recovery after 3-day follow-up.

CONCLUSION

Mast cell activation in allergic diseases may cause KS. It may develop due to many factors regardless of age and previous coronary disease. Emergency medicine specialists must be aware of this entity to prevent morbidity and mortality.

References

1. Kounis, N.G, Zavras, G.M. Histamine-induced coronary artery spasm: the concept of allergic angina. Br J Clin Pract 1991;45:121–128.
2. Buturak A, Norgaz T, Gorgulu S. Brivudine induced coronary vasospasm as a manifestation of Kounis syndrome: First report. Int J Cardiol 2015;185:4-6.
3. Garcipérez de Vargas FJ, Mendoza J, Sánchez-Calderón P, Ortiz C, Porro R, Mogollón-Jiménez MV. Cardiogenic shock secondary to metamizole-induced type II Kounis syndrome. Rev Esp Cardiol (Engl Ed). 2012;65:1138-9.
4. Ralapanawa DM, Kularatne SA. Kounis syndrome secondary to amoxicillin/clavulanic acid administration: a case report and review of literature. BMC Res Notes 2015:26;8:97.
5. Kounis NG, Soufras GD, Davlouros P, Tsigkas G, Hahalis G. Combined etiology of anaphylactic cardiogenic shock: Amiodarone, epinephrine, cardioverter defibrillator, left ventricular assist devices and the Kounis syndrome. Ann Card Anaesth 2015; 18:261-4.
6. Juste JF, Garces TR, Enguita RG, Blasco PC, Trallero JA. [Cardiac complications in a metamizole-induced type I Kounis syndrome.] [Article in Portuguese] Rev Bras Anestesiol. 2015 Mar 5. pii: S0034-7094(13)00103-7.
7. Ralapanawa DM, Kularatne SA. A case of Kounis syndrome after a hornet sting and literature review. BMC Res Notes 2014,3; 7:867.
8. Hamilos MI, Kochiadakis GE, Skalidis EI, Igoumenidis NE, Zaharaki A, Vardas PE. Acute myocardial infarction ina patient with normal coronary arteries after an allergic reaction. Hellenic J Cardiol 2005; 46:79-82.
9. Gunawardena MD, Weerasinghe A, Herath J, Amarasena N.Myocardial infarction associated with eosinophilia and plasma extravasation at multiple sites. A variant of Kounis syndrome. BMJ Case Rep. 2015 Jan 21; 2015. pii: bcr2014207987.