ACUTE MYOCARDIAL INFARCTION AFTER THE USE OF AMOXICILLIN/CLAVULANIC ACID: TYPE I KOUNIS SYNDROME

Case Report

AMOKSİSİLİN KULLANIMI SONRASI GELİŞEN AKUT MİYOKARD İNFARKTÜSÜ TİP 1 KOUNİS SENDROMU

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ABSTRACT

In 1991, Kounis and Zavras described the syndrome of allergic angina that can progress to allergic myocardial infarction accompanied by the clinical manifestation, laboratory and electrocardiographic findings of classic angina and myocardial infarction. This report discusses a patient who recieved amoxicillin/clavulanic acid treatment for a flu-like ilness after which he started to develop manifestation of ACS with ST elevation. All other etiologies were appropriately ruled out.

***Key words*:** *Kounis syndrome; allergic myocardial angina; amoxicillin/clavulanic acid.*

ÖZET

Kounis ve Zavras 1991 yılında, klasik anjina ve miyokard enfarktüsünün klinik, elektrokardiografik ve laboratuar bulgularını içeren alerjik myokard enfarktüsüne ilerleyebilen, alerjik anjina sendromunu tanımladılar. Bu olgu sunumunda grip benzeri semptomlar sonrasında amoksisilin/klavulanik asit tedavisi alan bir hastada ST elevasyonlu akut koroner sendrom gelişimi tartışılmıştır. Diğer etyolojik nedenler dışlanmıştır.

Anahtar sözcükler: *Kounis sendromu; alerjik miyokardial anjina; amoksisilin/klavulanik asid.*

INTRODUCTION

Amoxicillin/clavulanic acid (ACA) is a frequently used antimicrobial agent. Hypersensitivity reactions have been rarely reported. Allergic or hypersensitivity reactions are associated with mast cell activation and release of the mediators including leukotrienes, histamine, and neutral proteases (tryptase, chymase). The concurrence of ACSs (ACS) with hypersensitivity reactions have been described as Kounis syndrome (1,2). Two variants of this syndrome are recognized. Type I variant which includes patients with

normal coronary arteries in whom the acute allergic episode induces coronary artery spasm which might represent a manifestation of endothelial dysfunction or microvascular angina. Type II variant of Kounis syndrome includes patients with coronary spasm occuring in the preexisting atheromatous coronary artery disease in whom acute allergic episode can induce plaque erosion or rupture with coronary spasm (2).

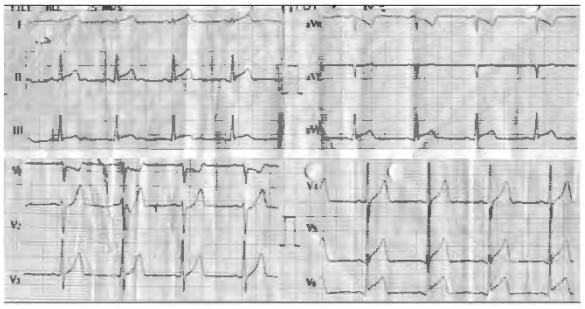
In this report, we present a patient who developed ACS following an allergic reaction after ACA administration and we describe the pathophysiology and clinical implications of this syndrome.

CASE REPORT

A 25-year-old male patient was admitted to the emergency department (ED) complaining from a chest pain radiating to his back and both of the upper limbs typical for angina pectoris. The patient reported that he previously suffered from a flu-like illness and amoxicillin/clavulanic acid was prescribed for him in the primary health care center. The complaints of the patient started approximately 20 min after the first oral dose of 1000 mg of ACA. After the first dose of ACA, the patient developed 1-2 hours lasting retrosternal heaviness with radiation to the back and both of the upper limbs which resolved spontaneously. After the second dose, the pain of the patient became more severe and lasted for more than 3 hours after drug ingestion upon which he visited the emergency department.

On admission, his electrocardiogram (ECG) showed 2mm ST elevation in leads II, III, aVF, V5-6, 1 mm ST elevation in leads I, ST depression in leads V1-2 indicating acute inferio-lateral ischemia **(Fig 1).**

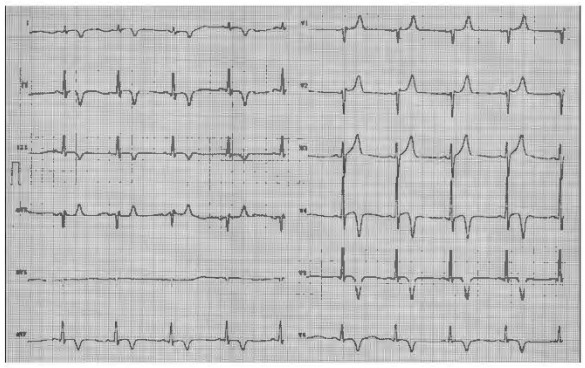
Figure 1A:



A) Electrocardiogram showing ST elevation in I, II, III, aVF, V5-6 leads, ST depression in V1-2 leads compatible with acute inferolateral myocardial ischemia on admission.

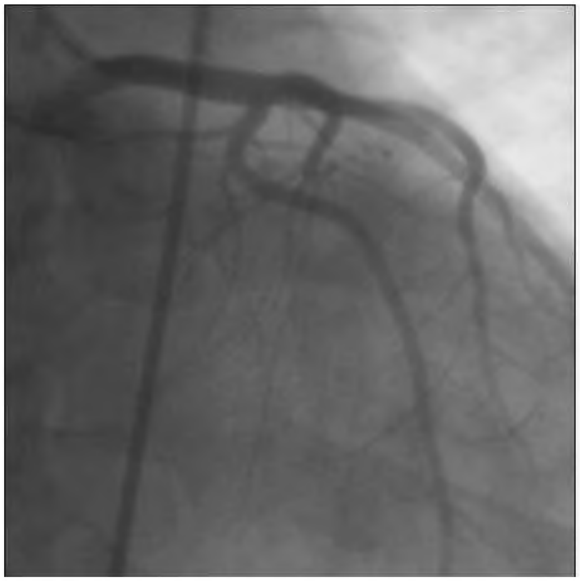
Chest pain and ST elevation resolved following intravenous administration of the nitroglycerine and T wave inversion developed in the affected leads I, aVL, II,III, aVF, V4-6 **(Fig 2).**

Figure 1B:

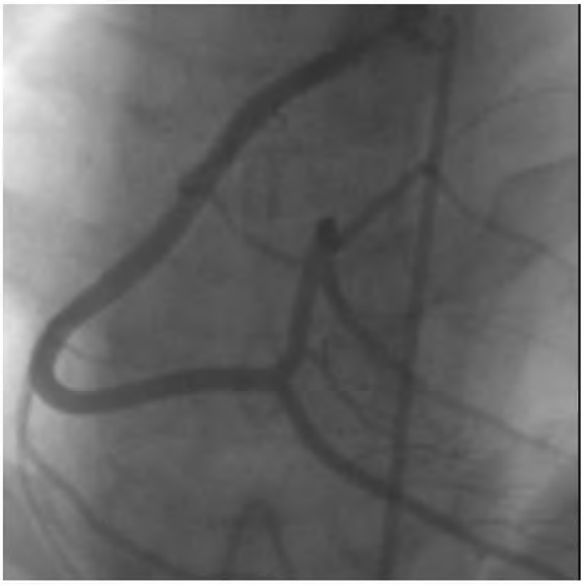


B) Electrocardiogram showing complete ST segment resolution after intravenous administration of the nitroglycerine.

Figure 2A:



A) Left cranial view of the left coronary artery on the coronary angiography image showing normal coronary artery.



B) Right anterior oblique view of the right coronary artery on the coronary angiography image showing normal coronary artery.

The physical examination of the patient was normal, and the laboratory investigations were as follows:

Complete blood count revealed a moderate eosinophila, whereas biochemistry levels were completely normal. The level of Troponin T was: 2,40 ng/ml (ref. 0-0,1), CK-MB: 79u/l (ref. 0-25), CRP 39 mg/l, ESR 62 mm.

The patient was diagnosed to have an ST elevation ACS and was admitted to the Coronary Care Unit (CCU).

In the CCU anti-ischemic and anti-platelet drugs were started while thrombolytic drugs were not administered because of relief of his symptoms.

An echocardiography that was performed within the first hour of the patient's admission revealed hypokinesia, in the inferor and the lateral walls associated with mildly reduced left ventriculer systolic function. The coronary artery angiography, that was preformed one day after the admission, revealed normal coronary arteries. Two days later, the patient experienced a maculopapular rash which subsided spontaneously after three days.

To exclude vasculitis and other rheumatological diseases fundoscopy was performed and rheumatic markers were investigated and found to be normal. The history of the patient did not involve the use of any illegal drugs. The elevated level of eosinophiles raised the suspicion of allergic myocardial infarction for which the amoxycillin skin allergy test, was performed and was found to be positive. The patient was diagnosed to have allergic myocardial infarction due to amoxicillin/clavulanic acid, type I variant of Kounis syndrome.

No complications were reported in the daily observations and the patient was discharged from the hospital. Three weeks after his discharge the patient was called for follow up in which the physical examination and laboratory investigations were normal. The echocardiographic examination was within normal limits and no wall motion defects were observed. Currently the patient is under follow up with medical theraphy.

DISCUSSION

We describe a patient who developed ACS after receving ACA in this case report. ACSs associated with acute allergic reactions, although seldomly reported, are increasingly encountered in clinical practice. Previous reports have suggested association between allergic reactions and ACS, which has been described as Kounis syndrome (1-3). The mechanism of its' onset is characterized by coronary artery spasm due to mast cell degranulation and the subsequent release of vasoactive mediators. The mast cells are found in most parts of the human body, including heart tissue and adventitia of coronary arteries. Several vasoconstricting and collagen degrading compounds are released locally and in the peripheral circulation (1). Released mediators can be preformed mediators such as histamine, neutral proteases (chymase and tryptase), platelet activating factor and newly synthesized mediators such as cytokines, chemokines, arachidonic acid products-leukotrienes, prostoglandins (1-3). Histamine and leukotrienes are powerful coronary vasocontrictors, neutral proteases and metalloproteinase activators initialize degradation of collagen and induce plaque erosion or rupture, which may trigger an ACS (1).

We believe that the abnormalities observed in the ECG and cardiac markers were attributed to ACA use for several reasons; chest pain episodes started just after taking ACA, and resolved after withdrawal of the drug, without recurrence. The development of the acute allergic reaction, following the chest pain and ECG changes manifested in skin rash for which amoxicillin skin allergy test was performed and found to be positive. Vasculitis, other rheumatological diseases, previous usage of any illegal drugs were excluded. And finally, atheromatous coronary artery disease was appropriately ruled out by angiography.

In the previous reports, only two ACA induced type-I Kounis syndrome were reported. Vivas et al. reported a patient allergic to amoxicillin who had three episodes of severe coronary spasm, but only in two of these three episodes amoxillin was previously given, and the patient demonstrated severe metabolic acidosis in all these three episodes. Metabolic acidosis producing tissue hypoxia may have played a more significant role in the onset of these angina attacks (4).

Soufras et al. reported a patient with type I Kounis syndrome. However the penicillin allergy has not been proven by skin testing, and the cause of the rapid deterioation of the condition and finally death of the patient three weeks later was unclear despite stopping the administration of penicilin (5). However, we believe that the diagnosis of the Kounis syndrome was more definite in the present case, since the penicilin allergy was clear, the coronary artery angiography findings were completely normal, and the other causes of MI were also excluded.

CONCLUSION

The manifestations of ACS secondary to acute allergic reactions may be atypical, causing diagnostic confusions. This case is reported to emphasize the importance of careful medical history taking and the thorough investigation in clinical practice to determine the possible non-atherosclerotic causes of acute myocardial infarction in young patients. This report also highlights the importance of drug allergy tests before drug administration and call attention to the avoidance of unnecessary use of drugs.

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