

## Interesting presentation of Kounis syndrome secondary to amoxicillin/clavulanate use: Coronary vasospasm and simultaneous appropriate implantable defibrillator shock

### Amoksisilin/klavulonat kullanımına ikincil gelişen Kounis sendromunun ilginç başvurusu: Koroner vazospazmına eşlik eden uygun implante edilebilir defibrilatör şoklaması

Uğur Canpolat, M.D., Duygu Koçyiğit, M.D., Kudret Aytemir, M.D.

Department of Cardiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

**Summary**– Kounis syndrome (KS) is defined as concurrent acute coronary syndrome and allergic or hypersensitivity reactions. Despite being increasingly reported, it is still an underdiagnosed entity. Several medications are already known to result in KS. Amoxicillin/clavulanic acid is a frequently used antibiotic, and its use has been linked with KS. The aim of the present report was to draw attention to rare clinical manifestation of KS following peroral amoxicillin/clavulanate use.

Kounis syndrome (KS) was described for the first time in 1991 by Kounis and Zavras as a syndrome of allergic angina and allergic myocardial infarction.<sup>[1]</sup> Today, it is defined as concurrent acute coronary syndrome and allergic or hypersensitivity reactions. It may occur in patients without predisposing factors for coronary artery disease (CAD) due to coronary vasospasm (type 1), as well as patients with angiographic evidence of CAD as a result of plaque erosion or rupture (type 2) or drug-eluting stent thrombosis (type 3).<sup>[2,3]</sup> These acute coronary events are caused by pro-inflammatory mediator release from mast cells during an allergic response; however, determinants of the magnitude of detrimental effects are not yet explicit.<sup>[4]</sup>

A wide variety of medical conditions, environmental exposures, and medications are known to result in KS. Beta-lactam antibiotic use has been found to be

**Özet**– Kounis sendromu (KS), akut koroner sendrom ve alerjik ya da aşırı duyarlılık reaksiyonlarının bir arada görülmesi şeklinde tanımlanmaktadır. Bildirilme sıklığı her ne kadar artış göstermiş olsa da tanı konulması güç olan bir klinik durumdur. Çeşitli ilaçların KS'ye neden olduğu bilinmektedir. Sık tercih edilen antibiyotiklerden amoksisilin/klavulonik asit'in, KS ile ilişkisi öne sürülmüştür. Bu olgu sunumunda, ağız yoluyla amoksisilin/klavulonik asit kullanımına ikincil gözlenen KS'nin nadir bir başvuru şekline dikkat çekilmek istenmiştir.

associated with KS.<sup>[5]</sup> Among beta-lactams, amoxicillin/clavulanic acid use has been linked with KS occurrence in previous case reports<sup>[6–8]</sup> and analysis of pharmacovigilance databases.<sup>[9]</sup>

The aim of this report was to draw attention to rare clinical manifestation of KS just after peroral amoxicillin/clavulanate use.

#### Abbreviations:

CAD	Coronary artery disease
ECG	Electrocardiogram
ICD	Implantable cardioverter defibrillator
KS	Kounis syndrome
VF	Ventricular fibrillation

#### CASE REPORT

A 54-year-old male patient was admitted to emergency room with implantable cardioverter defibrillator (ICD) shock. In 30-minute interval after administration of 1000 mg peroral amoxicillin/clavulanate

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Correspondence: Dr. Uğur Canpolat, Hacettepe Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, 06100 Ankara, Turkey.

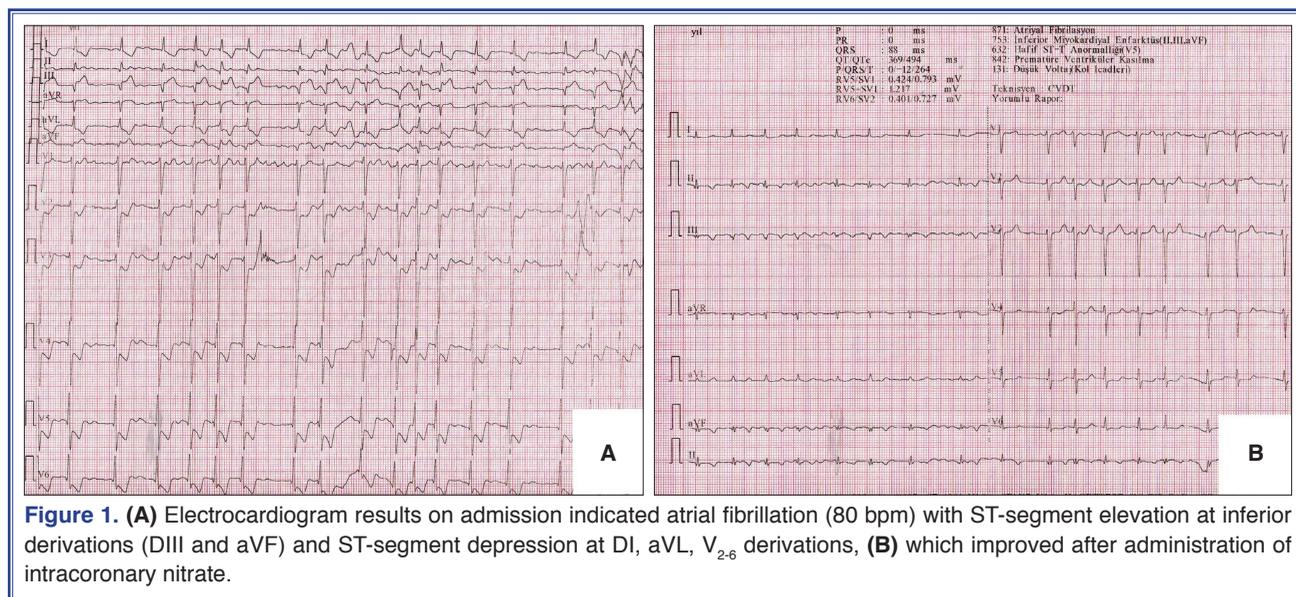
Tel: +90 312 - 305 17 80 e-mail: dru\_canpolat@yahoo.com

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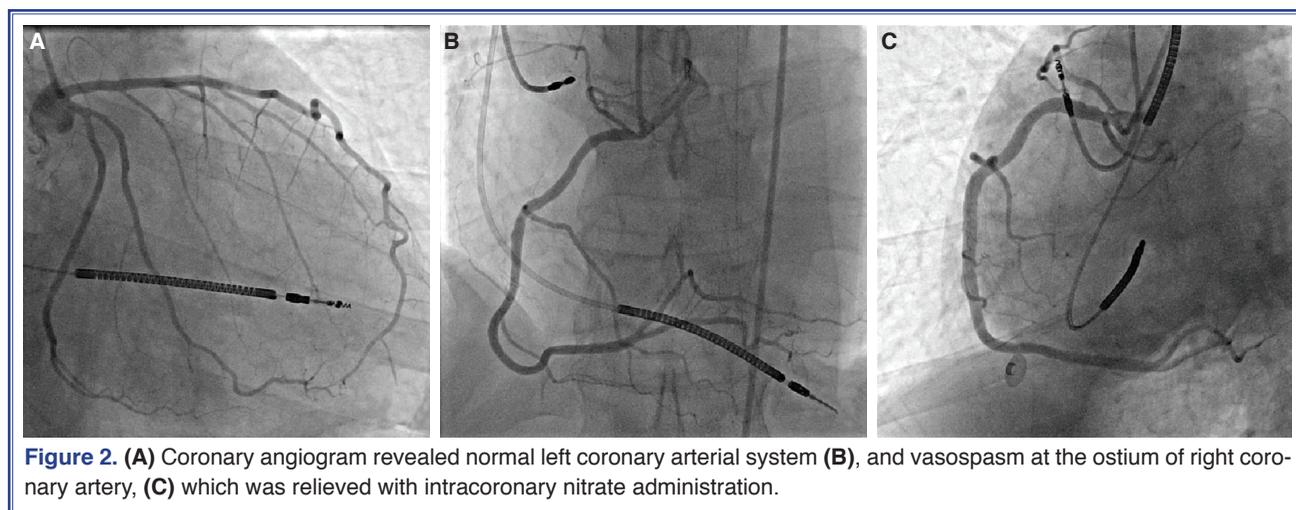


(Croxilex 1000 mg; Ibrahim Etem Ulagay İlaç Sanayi Türk A.Ş.–Menarini Group, Istanbul, Turkey) for upper respiratory tract infection, he had suddenly developed itching, nausea, and retrosternal chest pain. Subsequently, presyncope and ICD shock were observed. Medical history included ICD implantation as primary prophylaxis for non-ischemic dilated cardiomyopathy 3 years earlier with no history of appropriate or inappropriate ICD shock. Patient history was unremarkable for any allergic reaction, smoking, hypertension, diabetes mellitus, or dyslipidemia. Physical examination revealed blood pressure of 120/70 mmHg, irregular pulse of 80 bpm, oxygen saturation of 94% and erythematous rash over the whole body without angioedema. Electrocardiogram (ECG) on

admission revealed atrial fibrillation (80 bpm) with ST-segment elevation at inferior derivations (DIII and aVF) and ST-segment depression at DI, aVL, and V<sub>2-6</sub> derivations (Figure 1a, Video 1\*). Aspirin 300 mg, clopidogrel 600 mg, and unfractionated heparin 4000 IU were administered in emergency room. Due to ongoing chest pain, he was transferred to catheterization lab for coronary angiography. Angiogram demonstrated normal left coronary arterial system, and vasospasm at the ostium of right coronary artery, which was relieved with intracoronary nitrate administration (Figure 2, Video 1\*). Follow-up ECG in catheterization lab showed normalization of ST-segment changes at all derivations (Figure 1b, Video 1\*). The patient was hospitalized in coronary care unit. Echocardiog-



**Figure 1.** (A) Electrocardiogram results on admission indicated atrial fibrillation (80 bpm) with ST-segment elevation at inferior derivations (DIII and aVF) and ST-segment depression at DI, aVL, V<sub>2-6</sub> derivations, (B) which improved after administration of intracoronary nitrate.



**Figure 2.** (A) Coronary angiogram revealed normal left coronary arterial system (B), and vasospasm at the ostium of right coronary artery, (C) which was relieved with intracoronary nitrate administration.



assessment, most frequently reported antibiotic suspected for KS was combination of amoxicillin/clavulanate.<sup>[9]</sup> But other drug classes and even coronary stents may also be cause of development of KS.<sup>[14–16]</sup> Although no specific, logical explanation was provided as to why amoxicillin/clavulanate was antibiotic most commonly responsible for KS, frequent use of amoxicillin/clavulanate combination all over the world may be the exact reason.

We suspected KS in our patient due to prodromal allergic reactions just before chest pain, presyncope, and subsequent ICD shock. During coronary angiogram, occurrence of vasospasm at the ostium of right coronary artery directed us to diagnose our patient as type 1 KS. Retrospective assessment of ICD records at beginning of patient symptoms also confirmed coronary vasospasm-induced VF and appropriate ICD shock. Therefore, in patients with acute coronary syndrome who experienced prodromal allergic reactions following triggering factor like use of antibiotics, physicians should suspect possible diagnosis of KS.

**Conflict-of-interest issues regarding the authorship or article: None declared.**

**\*Supplementary video file associated with this article can be found in the online version of the journal.**

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**Keywords:** Amoxicillin/clavulanate; Kounis syndrome; vasospasm.

**Anahtar sözcükler:** Amoksisilin/klavulonat; Kounis sendromu; vazospazm.