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Case Report

Kounis syndrome triggered by diclofenac sodium injection which leads to myocardial infarction and cardiac arrest

Caglar Emre Cagliyan (MD)^{a,*}, Mehmet Balli (MD)^b, Kamuran Tekin (MD)^c,
Serdar Turkmen (MD)^d, İbrahim Halil Tanboga (MD)^e

^a Department of Cardiology, Adana Numune Training and Research Hospital, Adana, Turkey

^b Department of Cardiology, Adiyaman State Hospital, Adiyaman, Turkey

^c Department of Cardiology, Batman State Hospital, Batman, Turkey

^d Department of Cardiology, Sani Konukoglu Research Hospital, Gaziantep, Turkey

^e Department of Cardiology, Ataturk University Faculty of Medicine, Erzurum, Turkey

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ABSTRACT

Allergic reactions due to drugs may lead to different clinical conditions. Acute coronary syndromes triggered by Type 1 hypersensitivity reactions due to drug intake are known as “Kounis syndrome.” Vasospasm occurring in normal coronary arteries (Type 1) and plaque rupture (Type 2) are two variants of this syndrome; both caused by vasoactive and inflammatory mediators due to hypersensitivity reaction. In this case report, we will present Type 2 Kounis syndrome leading to acute anterior myocardial infarction and cardiac arrest in a healthy male after diclofenac sodium injection via intramuscular route. **<Learning objective:** Incidence of Kounis syndrome due to diclofenac is higher than reported. Some of the myocardial infarction events referred to in the studies might be due to Kounis syndrome. The risk of myocardial infarction probability due to allergic reactions after intake of these drugs must be kept in mind when prescribing.>

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Introduction

Allergic reactions due to drug administration may cause myocardial infarction (MI) besides chest pain [1]. Diclofenac sodium, which is in wide use as a non-steroidal anti-inflammatory drug (NSAID), may lead to allergic reactions besides gastrointestinal, hepatic, hematologic, and renal adverse effects [2]. Allergic angina and MI may be triggered by various drugs and is known as “Kounis syndrome” [3]. The exact prevalence of this syndrome has not been determined since it is not always reported in the medical literature, and it may lead to life-threatening cardiovascular events [4].

Case report

A 49-year-old male was admitted to a secondary medical center with complaints of sore throat, generalized pain, and fatigue. He had diabetes mellitus, hyperlipidemia, and tobacco usage as cardiovascular risk factors. He did not have any information in his past medical history except for appendectomy performed 9 years previously. Slight hyperemia in the pharynx was observed

on physical examination. Cardiac examination was normal. Since his electrocardiogram (ECG) was normal at that time, acute coronary syndrome (ACS) was excluded (Fig. 1). Diclofenac sodium via intramuscular route was administered to the patient. Cardiac arrest due to ventricular fibrillation occurred five minutes after diclofenac injection. After successful defibrillation and cardiopulmonary resuscitation, an emergent ECG was taken which was compatible with acute anterior MI (Fig. 2). The patient was transferred to our department.

He was unconscious and had pulmonary edema. His blood pressure was 80/40 mmHg. He had been emergently taken to the catheter laboratory. His left anterior descending (LAD) was occluded just distal to the first diagonal branch (Fig. 3a). Intracoronary nitroglycerin (0.25 mg) was administered, which showed no benefit. After placement of a floppy guidewire in the LAD, grade 2–3 thrombolysis in myocardial infarction flow was achieved. Successful primary percutaneous coronary intervention (PCI) was performed (Fig. 3b) by direct stenting of the vessel. He was transferred to the coronary care unit. Fourth hour control ECG showed resolution of ST segment elevation (Fig. 4) and the patient started to gain consciousness at 6 h from onset.

There was neutrophilia in his complete blood count. Biochemical tests showed hyperglycemia (359 mg/dl), hyperlipidemia (low-density lipoprotein cholesterol, 248 mg/dl), marked elevation of cardiac enzymes, and a slight elevation of creatinine (1.6 mg/dl).

* Corresponding author. Tel.: +90 505 3850959; fax: +90 322 2394128.

E-mail address: cemrec76@hotmail.com (C.E. Cagliyan).



Fig. 1. Normal electrocardiogram before diclofenac injection.

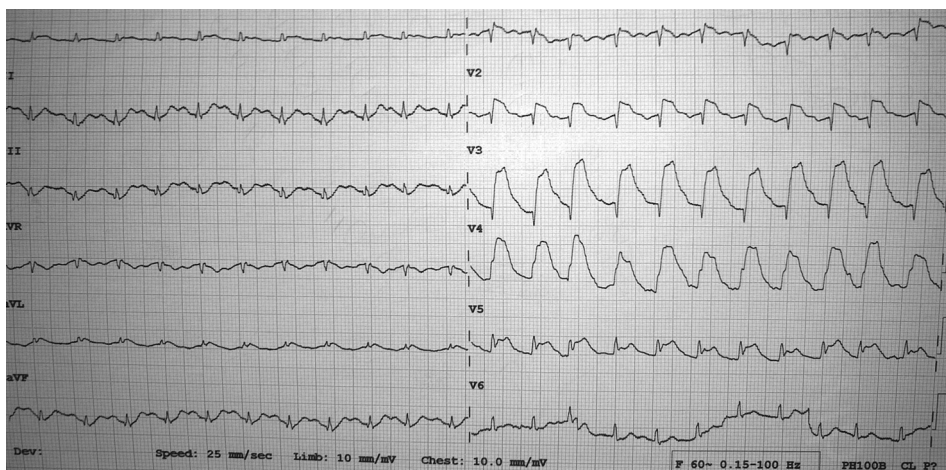


Fig. 2. Electrocardiogram after diclofenac injection; compatible with acute anterior myocardial infarction.

His serum IgE levels were found to be 1300 IU/mL (normal range: 0–165 IU/dl). The patient was diagnosed as having Kounis Syndrome leading to acute anterior MI. Since he was stable during his follow-up, he was discharged on day 5.

Discussion

Administration of NSAIDs has been blamed for development of ACS in recent decades. Since they alter the balance between thromboxane-prostacyclin equilibrium, they may lead to vasospasm and development of small platelet thrombi [5]. Diclofenac has been found to be associated with ACS in some

studies [6,7]. However, NSAIDs are usually associated with increased risk of non-ST elevation ACS instead of ST elevation MI [5].

Type 1 hypersensitivity reaction occurring by vasoactive amines such as histamine and serotonin plays a role in the pathophysiology of MI cases developing after drug administration [3]. Two types of Kounis syndrome have been described by Kounis and colleagues. Type 1 develops in normal coronary arteries and vasospasm due to endothelial dysfunction is the main mechanism. However, Type 2 variant occurs in the coronary atherosclerotic plaques and rupture triggered by allergic reaction leading to MI is the main mechanism. Although many drugs are thought to be associated with Kounis

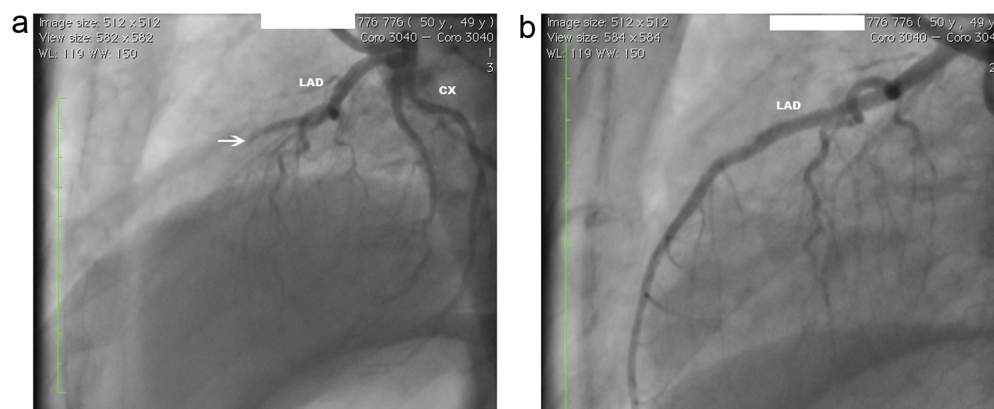


Fig. 3. (a) Coronary angiography showing complete occlusion of the mid segment of the LAD (white arrow). (b) Coronary flow is maintained after successful stent implantation. LAD, left anterior descending; CX, circumflex.

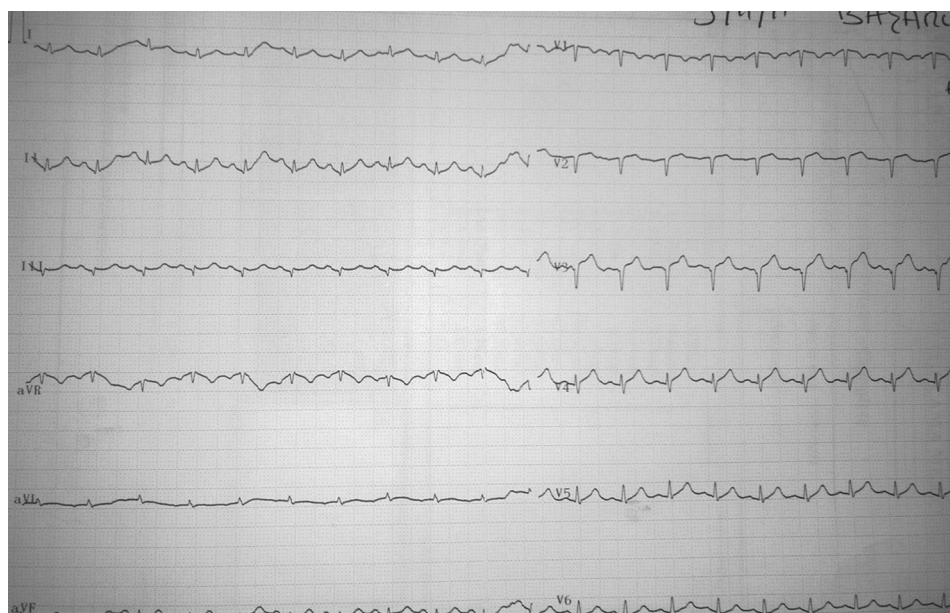


Fig. 4. ST elevations partially resolve after successful percutaneous coronary intervention. Abnormal Q waves are present in leads V1–3.

syndrome, anti-inflammatory, antihistaminic, and antibiotic drugs are the most frequently responsible agents; especially when administered to atopic individuals [3].

In the studies investigating the adverse effects of NSAIDs, the cardiovascular ones such as ACS and MI are attributed to the anti-prostacyclin effects of these drugs [6–8]. There are only two reported cases of MI due to Kounis syndrome triggered by the diclofenac molecule [9,10]. Abrupt onset after intake of the drug and high IgE levels are typical supportive clinical features. We think that the incidence of Kounis syndrome due to diclofenac is higher than reported. Some of the MI events referred to in the studies might be due to Kounis syndrome. The risk of MI probability due to allergic reactions after intake of these drugs must be kept in mind when prescribing.

Conflict of interest

None of the authors have any conflicts of interest that should be disclosed.

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