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CLINICAL SPOTLIGHT

An Extraordinary Case Associated with an Allergic Reaction to Clopidogrel: Coronary Artery Spasm or Kounis Syndrome?

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Kounis syndrome is the concurrence of acute coronary syndrome with allergic reactions, such as anaphylaxis or anaphylactoid reactions. Here, we describe a unique case: CASs (coronary artery spasms) with both non-hypersensitivity and hypersensitivity aetiology (associated with clopidogrel hypersensitivity) were observed in a 61 year-old patient. Herein, the mechanism and clinical implications of this association are discussed.

Keywords Allergic reaction • Clopidogrel • Kounis syndrome • Coronary artery spasm

Introduction

Kounis syndrome was described in 1991 by Kounis and Zavras as the coincidental occurrence of acute coronary syndromes (ACS) with allergic reactions (anaphylactic or anaphylactoid) [1]. Multiple causes of Kounis syndrome have been described, including drugs, insect stings, foods, environmental exposures and medical conditions, among others [2].

There are two variants of Kounis syndrome. Patients with the type I variant have normal or nearly normal coronary arteries without predisposing factors for coronary artery disease, and in those patients, acute allergic attacks can induce either CAS alone without raised cardiac enzymes and troponins or coronary artery spasm leading to acute myocardial infarction with raised cardiac enzymes and troponins. Patients with the type II variant have a quiescent pre-existing atheromatous disease that makes them susceptible to induction by acute allergic attacks of CAS or plaque erosion or rupture manifesting as acute myocardial infarction [3]. In recent years a third variant of Kounis syndrome has been proposed in patients with drug-eluting stent thrombosis [4].

In the following report, we describe a case of Kounis syndrome associated with an allergic reaction to clopidogrel.

Case Report

A 61 year-old man was recently admitted to our hospital for worsening chest pain. He had a 10-year history of recurrent episodes of crushing chest pain at rest and during ordinary activity and ST changes on ECG. The patient's chest pain could be spontaneously relieved within 10 mins or within a few minutes after administration of sublingual nitro-glycerine. He was a heavy smoker who had smoked 20 cigarettes per day for nearly 30 years. Furthermore, he had a past history of hypertension and atopic eczema and allergic reactions.

On admission, his blood pressure was 130/70 mmHg, and his heart rate was 70 beats/min; electrocardiography and all other related tests were normal. Transthoracic echocardiography did not show any regional wall motion abnormality.

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Clopidogrel was administered in preparation for coronary angiography. He had not taken clopidogrel previously. After one hour, he complained of generalised itching and a widespread erythematous rash without any other discomfort. The patient's symptoms seemed to subside after he was treated with 10 mg of dexamethasone. However, after another hour, the patient suddenly fainted while on the toilet; this episode included a loss of consciousness and profuse sweating. The electrocardiogram revealed ST segment elevation in the inferior leads with complete atrioventricular block (Fig. 1). The patient was given 0.5 mg atropine, 3 mg dopamine, and 10 mg dexamethasone intravenously. The patient's cardiac rhythm reverted to a sinus rhythm, and his BP and HR were recovered at 90/60 mmHg and 80 beats/min, respectively. An emergency coronary angiography was immediately performed, and it initially showed approximately 80% stenosis of the midportion and 100% occlusion of the distal segments of the right coronary artery (Fig. 2A, arrow). The vasospasm was relieved after intracoronary administration of 200 µg isosorbide dinitrate, and the patient did not have significant lesions (Fig. 2B). The results of the blood examination revealed normal levels of cardiac enzymes, troponin, and blood eosinophils. However, total IgE was elevated to 245 IU/ml (normal value: 110 IU/ml), the tryptase level was elevated to 19.6 µg/l (normal range: 5.6–13.5 µm/l). The patient was diagnosed with type I Kounis syndrome secondary to an allergic reaction to clopidogrel. The patient was admitted to the coronary care unit and was orally administered 30 mg of altiazem every 8 h. Subsequently, nuclear myocardial imaging showed a small area of a partially reversible perfusion abnormality involving the apex. The patient's remaining stay at the hospital was uneventful, and he was discharged on the fourth day of hospitalisation and advised to avoid taking clopidogrel.

Discussion

Kounis syndrome is defined as the concurrence of acute coronary syndromes with conditions associated with mast cell activation involving interrelated and interacting inflammatory cells and including allergic or hypersensitivity and anaphylactic or anaphylactoid attacks. It is caused by inflammatory mediators, such as histamine, neutral proteases, arachidonic acid products, platelet activating factors and a variety of cytokines and chemokines released during the activation process [2,5,6].

We believe this is an extraordinary case. The patient developed a generalised urticarial rash after taking clopidogrel. The patient then presented with symptoms and signs of CAS confirmed by ECG changes and coronary angiography; he had concurrently raised levels of tryptase and IgE but normal levels of cardiac enzymes and troponins. This is a characteristic case of type I Kounis syndrome. To our knowledge, this is the second case of clopidogrel-induced Kounis syndrome, and some unique clinical characteristics of this case are discussed here. The previous case of clopidogrel-induced Kounis syndrome was a patient who developed recurrent stent thrombosis following an allergic reaction to clopidogrel.

Previously, patients with type I Kounis syndrome were considered to lack predisposing factors for coronary artery disease. However, the current patient had a past history of

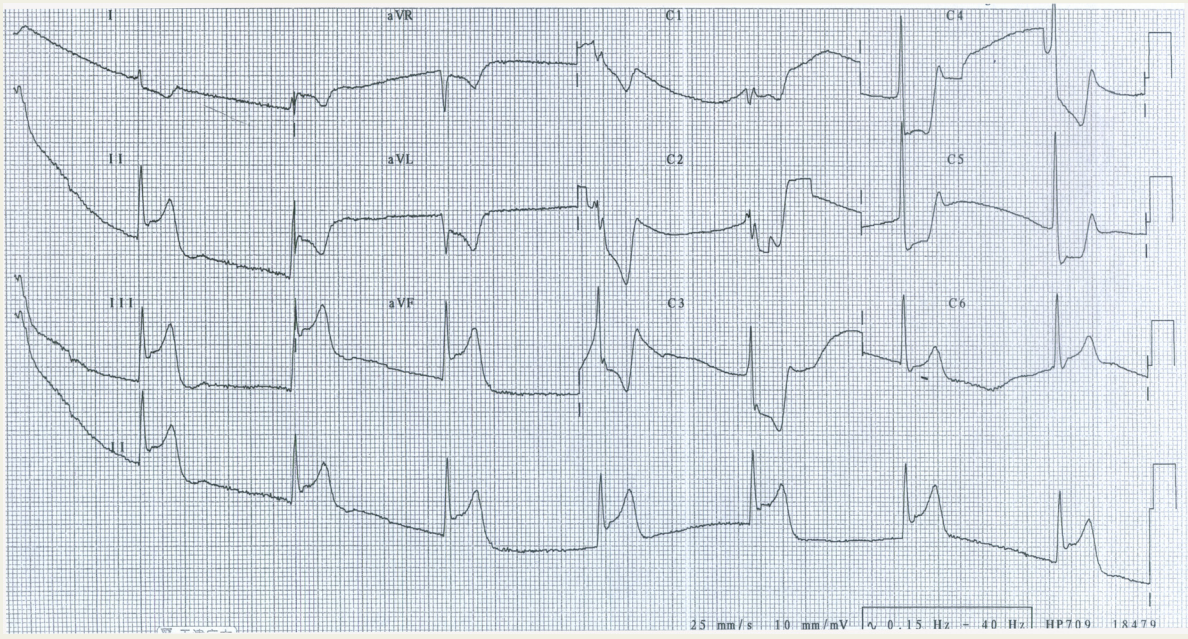

Figure 1 Electrocardiogram showing ST segment elevation in inferior leads with complete atrioventricular block.