Case Report

# Chlorpheniramine and phenylephrine induced coronary vasospasm manifesting as Kounis syndrome in a patient with moderate mitral stenosis

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## ABSTRACT

We report a case of Kounis syndrome (allergic angina) documented with normal coronary arteries on angiography and echocardiographically proved moderate mitral stenosis in a patient with severe chest pain and electrocardiographic ST-segment elevations but with normal troponin levels.

**Keywords:** Acute hypersensitivity coronary syndrome, allergic angina, chlorpheniramine kounis phenylephrine

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## Introduction

Kounis syndrome (KS) is the concurrence of acute coronary syndromes with conditions of hypersensitivity reactions involving activation of inflammatory cells and including allergic or hypersensitivity and anaphylactic or anaphylactoid insults.[1]

Chlorpheniramine and phenylephrine are commonly used drugs for the relief of symptoms in patients with upper respiratory tract infections. Due to these drugs, cardiac side effects especially arrhythmias have been reported previously.[2] The simultaneous occurrence of chest pain and allergic reaction caused by inflammatory mediators such as histamine or leukotrienes released during allergic insult can mimic the diagnosis of the acute coronary syndrome. We wish to present a case of coronary vasospasm induced by the concomitant usage of chlorpheniramine and phenylephrine.

## Case Report

A 50-year-old male patient admitted to an emergency department with typical retrosternal chest pain. The symptoms had started 1 h after the patient's first ever intake of drug (650 mg paracetamol, phenylephrine hydrochloride 10 mg, and, chlorpheniramine maleate 4 mg) which had been prescribed for relieving symptoms of upper respiratory tract infection by his general practitioner. On his history, he had no risk factors other than smoking. Because of



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prehospital electrocardiogram-(ECG) revealed ST-elevations in the anterior leads [Figure 1], he admitted to the coronary care unit diagnosed as acute anteroseptal myocardial infarction and immediately taken to catheterization laboratory for primary percutaneous coronary intervention. Coronary angiography revealed normal coronary arteries [Figures 2 and 3]. Echocardiography showed normal systolic functions, the left atrial enlargement and moderate rheumatic mitral stenosis with a mitral valve area of 1.3 cm². There was no increase in troponin levels at follow-up. He was enrolled again to the coronary care unit, and nitroglycerin infusion was started. Chest pain resolved completely after 30 min. The follow-up ECG on the 2nd day of admission showed complete resolution of ST elevations [Figure 4]. The patient did not develop any allergic symptoms on arrival and follow-up, on the 1st day of admission we assessed immunoglobulin E and serum complement levels (C3, C4) on laboratory and found in normal limits. We could not perform allergic skin prick test on ethical grounds.

As a result, the patient was considered as drug-induced transient coronary vasospasm.

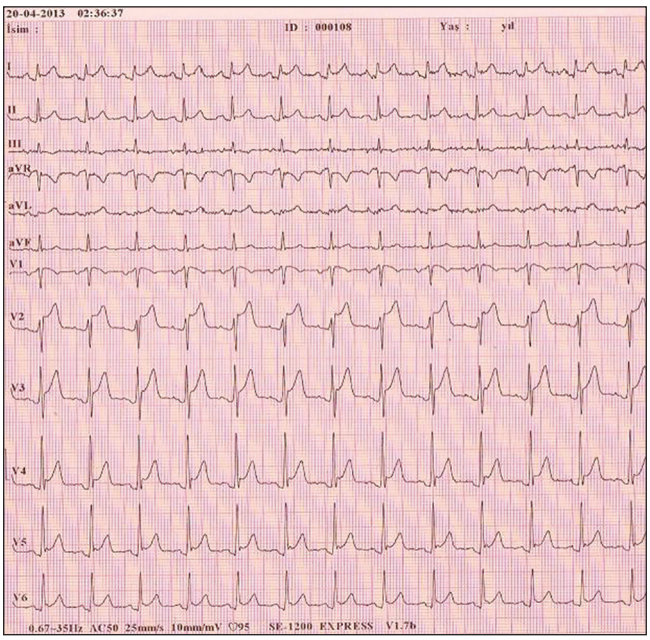


**Figure 1:** Admission electrocardiogram consistent with ST elevation on anterior leads

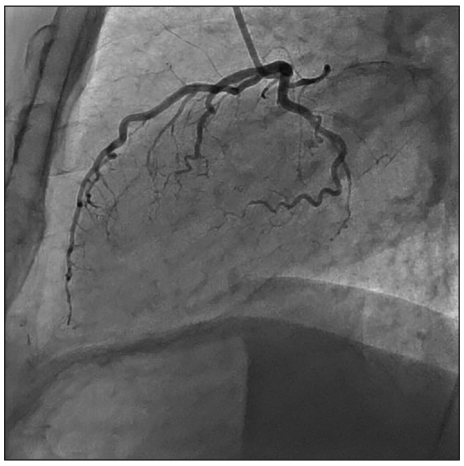

**Figure 3:** Normal left coronary system on emergency coronary angiography

## Discussion

KS is characterized by a group of symptoms that manifest as unstable vasospastic or nonvasospastic angina secondary to the hypersensitivity reaction. It is caused by inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet activating factor and, a variety of cytokines and chemokines released during the activation process. Kounis and Zavras described the "syndrome of allergic angina" as the coincidental occurrence of chest pain and allergic reactions accompanied by clinical and laboratory findings of classical angina pectoris caused by inflammatory mediators released during the allergic insult.[1] Allergic angina can progress to acute myocardial infarction which was named "allergic myocardial infarction."

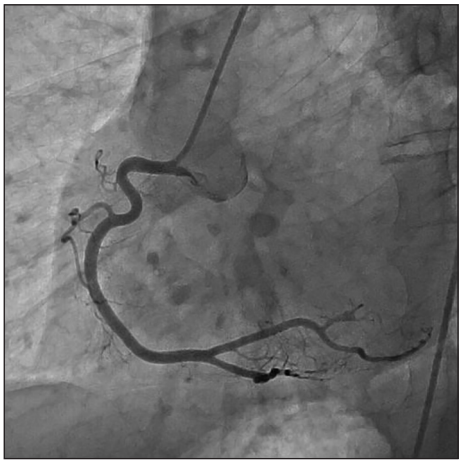

**Figure 2:** Normal right coronary artery on emergency coronary angiography

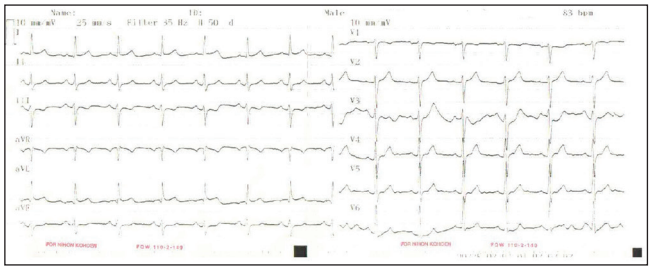

**Figure 4:** Complete resolutions of ST elevations on the follow-up electrocardiogram

There are two variants of this syndrome that have been described recently. Type I variant include 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 microvascular angina. Type II variant include patients with culprit but quiescent preexisting atheromatous disease in whom acute allergic episode can induce plaque erosion or rupture manifesting as an acute myocardial infarction.[3]

A Type III variant has been described recently and includes the patients with stent thrombosis in whom thrombus aspiration shows eosinophilic infiltration and/or mast cell presence.[4]

However, allergy-induced acute coronary events in the absence of anaphylaxis are increasingly encountered in clinical practice, suggesting mast cell-based vasospasm as the principal mechanism. The management of KS may be challenging for clinicians, and unfortunately guidelines have not been established yet. Patients with KS need treatment with steroids, antihistamines, fluid resuscitation, possibly epinephrine, oxygen, and antithrombotics before transfer to the cardiac catheterization laboratory.[5]

Demirel *et al.* report a systemic reaction to chlorpheniramine maleate that was found through skin tests.[6] Furthermore, Madsen and Andersen claimed that phenylephrine may cause allergic contact dermatitis.[7]

In our patient, the myocardial injury occurred in the absence of an anaphylactic reaction, strengthening the suspicion of mast cell-based pathophysiology. On the other hand, his chest pain developed suddenly without any apparent allergic reaction, suggesting a possible local effect of chlorpheniramine and phenylephrine, individually or in combination, directly on the coronary mast cells.

To the best of our knowledge, this is the first case in literature describing the association between this syndrome and chlorpheniramine and phenylephrine simultaneously administered orally.

## Conclusion

When there is no underlying coronary heart disease, cardiac symptoms due to drug-induced allergic reactions should be kept in mind.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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