HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

e-ISSN: 2687-4717 Cilt|Volume: 8 • Sayı|Issue: 1 - Şubat|February 2026

# From Anaphylaxis to Acute Myocardial Infaction: Type II Kounis Syndrome Caused by Ceftriaxone

Anafilaksiden Akut Miyokard İnfarktüsüne: Seftriakson Kaynaklı Tip II Kounis Sendromu

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**Makale Bilgisi | Article Information**
**Makale Türü | Article Type:** Olgu Sunumu | Case Report
**Doi:** https://doi.org/10.52827/hititmedj.1823345
**Geliş Tarihi | Received:** 14.11.2025
**Kabul Tarihi | Accepted:** 26.01.2026
**Yayım Tarihi | Published:** 27.02.2026

**Atıf | Cite As**
Yasak İH, Uysal MH, Hamallar E. From Anaphylaxis to Acute Myocardial Infarction: Type II Kounis Syndrome Caused by Ceftriaxone. Hitit Medical Journal 2026;8(1):205-210. https://doi.org/10.52827/hititmedj.1823345

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Gerek yoktur.
**İntihal Kontrolleri:** Evet (iThenticate)
**Çıkar Çatışması:** Yazarlar çalışma ile ilgili çıkar çatışması beyan etmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: İHY; Tasarım: İHY, MHU; Veri Toplama/Veri İşleme: MHU, EH; Veri Analizi: İHY, EH; Makalenin Hazırlanması: İHY, MHU, EH
**Hasta Onamı:** Tüm hastalardan yazılı bilgilendirilmiş onam ve yayın için izin alınmıştır.
**Finansal Destek:** Çalışma için finansal destek alınmamıştır.


**Peer Review:** Evaluated by independent reviewers working in at least two different institutions appointed by the field editor.
**Ethical Statement:** Not applicable
**Plagiarism Check:** Yes (iThenticate)
**Conflict of Interest:** The authors declared that they have no conflict of interest.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: İHY; Design: İHY, MHU; Data Collection/Data Gathering: MHU, EH; Data Analysis: İHY, EH; Manuscript Preparation: İHY, MHU, EH
**Informed Consent:** Written informed consent and consent for publication was obtained from the patients.
**Financial Disclosure:** No financial support was received for the conduct of this study.

## From Anaphylaxis to Acute Myocardial Infarction: Type II Kounis Syndrome Caused by Ceftriaxone


### ABSTRACT

A 70-year-old male patient with a history of hypertension and previous non-ST-elevation myocardial infarction (NSTEMI) presented to the emergency department with throat pain. Physical examination revealed pharyngeal hyperemia, and ceftriaxone therapy was initiated based on suspected cryptic tonsillitis. During the initial dose administration, the patient developed sudden altered consciousness and hypotension. Electrocardiogram (ECG) showed widespread ST depression in leads V2-V6 and elevated troponin-I (1928.3 ng/L). Coronary angiography performed after anaphylaxis treatment revealed critical stenoses of 80% in the left main coronary artery, 90% in the left anterior descending artery (LAD), 80% in the circumflex artery, and 99-100% in the right coronary artery. The acute myocardial infarction secondary to the allergic reaction was classified as Kounis syndrome Type II. The patient underwent successful percutaneous coronary intervention and was discharged in stable condition. This case demonstrates that antibiotic allergy can lead to life-threatening cardiac complications in the presence of underlying coronary artery disease. Written informed consent was obtained from the patient for publication of this case report.



**Keywords:** Anaphylaxis, Ceftriaxone, Kounis Syndrome, Myocardial Infarction.


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## Anafilaksiden Akut Miyokard İnfarktüsüne: Seftriakson Kaynaklı Tip II Kounis Sendromu


### ÖZ

Yetmiş yaşında, hipertansiyon ve geçirilmiş ST elevasyonsuz miyokard infarktüsü (NSTEMI) öyküsü olan erkek hasta, boğaz ağrısı nedeniyle acil servise başvurdu. Fizik muayenin kriptik tonsilit ile uyumlu olması nedeniyle seftriakson tedavisi başlandı. İlacın ilk doz uygulaması sırasında hastada ani bilinç değişikliği ve hipotansiyon gelişti. Elektrokardiyogramda (EKG) V2-V6 derivasyonlarında yaygın ST depresyonu ve Troponin-I yüksekliği (1928,3 ng/L) saptandı. Anafilaksi tedavisi sonrası yapılan koroner anjiyografide sol ana koroner arterde %80, sol ön inen arterde (LAD) %90, sirkumfleks arterde %80, sağ koroner arterde %99-100 kritik darlıklar tespit edildi. Alerjik reaksiyona sekonder gelişen akut miyokard infarktüsü, Kounis sendromu Tip II olarak değerlendirildi. Hastaya başarılı perkütan koroner girişim uygulandı ve stabil seyrederek taburcu edildi. Bu olgu, antibiyotik alerjisinin mevcut koroner arter hastalığı zemininde hayatı tehdit eden kardiyak komplikasyonlara yol açabileceğini göstermektedir.



**Anahtar Sözcükler:** Anafilaksi, Kounis Sendromu, Miyokard İnfarktüsü, Seftriakson

## Introduction

Kounis syndrome is defined as an acute coronary syndrome (ACS) triggered by an allergic reaction. First described in 1991 by Kounis and Zavras as "allergic angina," this syndrome occurs as a result of the effect of vasoactive mediators (histamine, tryptase, leukotrienes, thromboxane, etc.) released by the degranulation of inflammatory cells such as mast cells, platelets, and eosinophils on the coronary arteries (1, 2). These mediators can cause spasm in the coronary arteries and trigger thrombosis by causing erosion or rupture in existing atherosclerotic plaques. Tryptase, released particularly from mast cells, is thought to have a direct vasoactive effect and to destabilize the plaque by activating metalloproteinases within the atheromatous plaque (3).

Kounis syndrome is classified into three main types and various subtypes based on the underlying coronary artery pathology (4). Type I: Myocardial ischemia due to coronary artery spasm following an allergic reaction in patients with normal coronary arteries. Type II: Acute thrombus formation in patients with pre-existing but not always symptomatic atherosclerotic lesions, caused by allergic mediators rupturing or eroding the plaque. This is the most common form. Type III: This type is associated with coronary stent thrombosis and is characterized by the allergic reaction triggering thrombus formation within the stent.

This case presentation discusses a patient diagnosed with Type II Kounis syndrome secondary to anaphylaxis following ceftriaxone treatment administered for cryptic tonsillitis, against a background of critical multivessel coronary artery disease.

## Case Presentation

A 70-year-old male patient presented to the emergency department with throat and right ear pain. He was in good general condition, alert, oriented, and cooperative, with a blood pressure of 120/70 mmHg and a pulse rate of 80/min. During the physical examination, findings consistent with cryptic tonsillitis were detected, including bilateral tonsil hypertrophy and pharyngeal erythema along with tonsil crypts. His medical history included hypertension, a previous myocardial infarction, lumbar disc herniation, and inguinal hernia surgeries. With no known drug allergies, the patient was started on 2 g of ceftriaxone in 100 mL of normal saline, as cryptic tonsillitis was suspected. After approximately 10 cc of intravenous administration of serum containing ceftriaxone, the patient developed sudden changes in consciousness and hypotension (blood pressure dropped to 70/40 mmHg). The patient was clinically diagnosed with anaphylaxis. According to the anaphylaxis treatment guidelines, 0.5 mg of epinephrine was immediately injected into the anterolateral thigh (vastus lateralis) muscle. At the same time, intravenous treatments containing 45.50 mg of pheniramine, 60 mg of prednisolone, and 1000 mL of saline solution for fluid resuscitation were initiated as a bolus. Due to inadequate clinical improvement, a second 0.5 mg dose of epinephrine was administered intramuscularly to the same site 5 minutes after the first dose (total epinephrine dose: 1 mg). An electrocardiogram obtained during this acute episode showed widespread ST depression in V2-6 leads (Figure I). Although hemodynamic stabilization was achieved, considering the patient's cardiac history and the developing picture, further evaluation was planned due to the possibility of myocardial ischemia secondary to an allergic reaction. A cardiology consultation was requested, and the patient was admitted to the percutaneous coronary intervention (PCI) laboratory on an emergency basis.

Laboratory tests performed after admission showed glucose 110 mg/dL, aspartate aminotransferase (AST) 23 U/L, alanine aminotransferase (ALT) 14 U/L, gamma-glutamyl transferase (GGT) 23 U/L, alkaline phosphatase (ALP) 58 U/L, C-reactive protein (CRP) 0.74 mg/L, total bilirubin 1.1 mg/dL, direct bilirubin 0.3 mg/dL, lactate dehydrogenase (LDH) 231 U/L, albumin 4.0 g/dL, urea 23 mg/dL, creatinine 0.95 mg/dL, sodium 143 mmol/L, potassium 4.4 mmol/L, uric acid 9.0 mg/dL, creatine kinase (CK)

174 U/L. Complete blood count showed white blood cell count (WBC) 5.33×10$^3$/µL, hemoglobin (HGB) 16.6 g/dL, hematocrit (HCT) 47.7%, platelet count (PLT) 328×10$^3$/µL; lymphocyte percentage was 57.8% and lymphocyte count was 3.08×10$^3$/µL. Blood gas analysis reported glucose 111 mg/dL, lactate 3.9 mmol/L, $pO_2$ 37.7 mmHg, $pCO_2$ 56.4 mmHg, $HCO_3$ 28 mmol/L, and pH 7.31. The most notable finding was a Troponin-I level of 1928.3 ng/L. Accordingly, the patient was admitted to the coronary care unit, and an emergency coronary angiography was planned.

The initial angiography revealed approximately 80% stenosis in the left main coronary artery, 90% stenosis at the left anterior descending artery (LAD) ostium, 80% stenosis in the post-stent segment, and 80% stenosis at the left circumflex artery ostium; the right coronary artery showed 99% proximal and 100% distal occlusion (Figure II). Due to the critical nature of the findings, interventional treatment was planned after a council evaluation. Subsequent advanced measurements demonstrated that the calcified stenosis in the left main coronary artery was hemodynamically significant. Consequently, revascularization was first achieved in the right coronary artery through interventional treatment, followed by successful treatment of the critical calcified lesion in the left main coronary artery. No complications developed during any of the procedures, and adequate coronary flow was achieved.

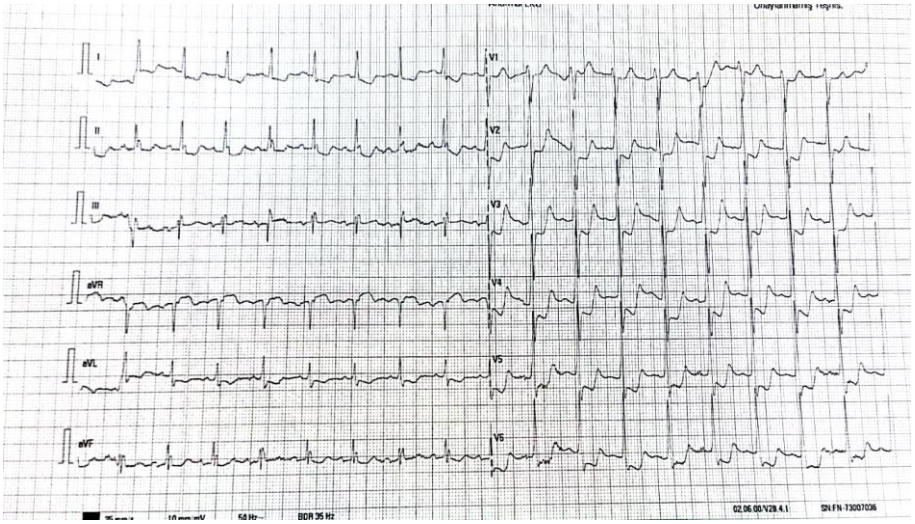


**Figure I.** Electrocardiogram Showing Widespread ST-segment Depression

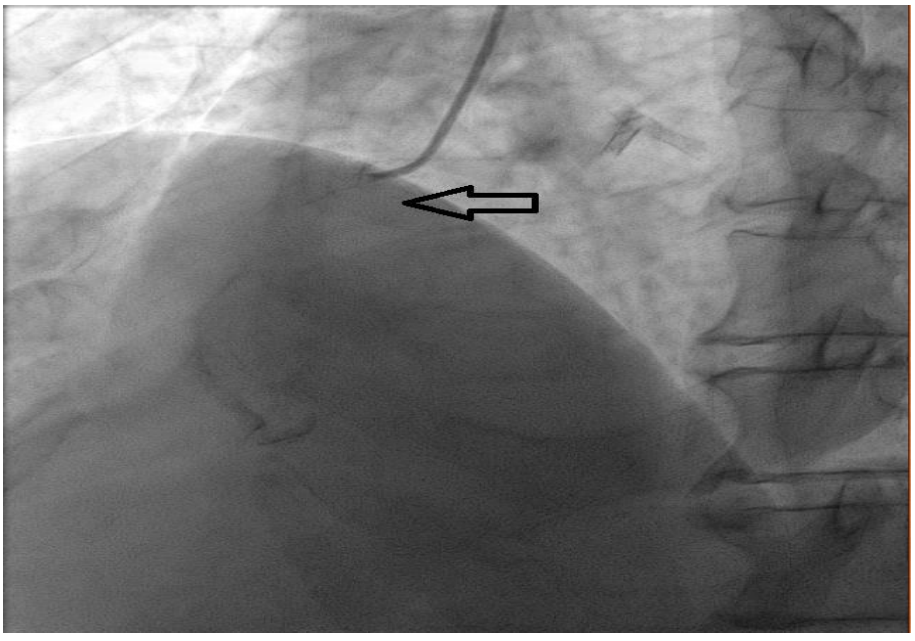

**Figure II.** Coronary Angiography Showing Critical Stenosis in the Proximal Right Coronary Artery

During follow-up, the patient did not experience recurrent chest pain, hemodynamic status remained stable, and no new signs of ischemia were detected on the ECG. Biochemical and cardiac enzyme tests showed improvement. It was deemed appropriate to continue Brilinta therapy. The patient, who had clinically stabilized, was discharged after being informed of the criteria for emergency presentation and scheduled for a follow-up visit one week later.

## Discussion

This case is important in that it demonstrates how an anaphylactic reaction to ceftriaxone, a commonly used antibiotic, triggered a life-threatening myocardial infarction in a 70-year-old patient with a history of coronary artery disease. The patient's development of altered consciousness and hypotension shortly after presenting to the emergency department are classic signs of anaphylaxis. Concurrently, the detection of widespread ST depression in V2-6 leads on the ECG and a marked elevation in Troponin-I levels (1928.3 ng/L) confirmed the presence of acute myocardial injury.

The diagnosis of Type II Kounis syndrome in our case was established based on several criteria. First, there was a clear temporal relationship between the allergic reaction (anaphylaxis) and the acute coronary event. Second, the patient had documented pre-existing coronary artery disease, as evidenced by his history of previous NSTEMI and confirmed by the critical multi-vessel stenoses found on coronary angiography. Third, the ECG changes (widespread ST depression) and elevated cardiac biomarkers occurred during the anaphylactic episode, suggesting plaque destabilization triggered by inflammatory mediators rather than simple coronary vasospasm. Fourth, the severity and distribution of coronary stenoses were consistent with pre-existing atherosclerotic disease rather than acute vasospasm alone. These findings collectively meet the diagnostic criteria for Type II Kounis syndrome, where allergic mediators cause rupture or erosion of pre-existing vulnerable atherosclerotic plaques, initiating an acute thrombotic event (3, 4, 5).Regarding the initial examination, since the patient did not present with chest pain or other cardiac symptoms, an ECG was not obtained for cardiac evaluation. The ECG recorded during the anaphylactic episode indicated acute myocardial injury.

Anaphylaxis management in this patient was performed in accordance with current international guidelines, with 0.5 mg of intramuscular epinephrine administered as first-line treatment and repeated once more at the same dose five minutes later due to an inadequate clinical response; this approach is the standard recommended practice for anaphylaxis management in adults (6,7). However, the clinical timing and findings strongly support that myocardial ischemia was primarily attributable to allergic myocardial ischemia, i.e., Kounis syndrome, rather than an isolated effect of epinephrine. The appearance of electrocardiographic changes shortly after the onset of the anaphylactic reaction is consistent with the typical features of Kounis syndrome, characterized by coronary vasospasm due to mast cell activation and inflammatory mediator release (5,8). Furthermore, the critical coronary artery stenoses detected in the patient constitute an important background that increases susceptibility to myocardial ischemia in response to allergic triggers; this clinical picture is consistent with the definition of Type II Kounis syndrome (5). The alpha and beta adrenergic effects of epinephrine could theoretically increase myocardial oxygen demand and exacerbate existing ischemia; however, the use of epinephrine is indispensable in life-threatening anaphylaxis and is considered safe when administered at appropriate doses and routes (6,7).

In Type II Kounis syndrome, inflammatory mediators released during anaphylaxis, such as histamine, tryptase, and arachidonic acid products, cause rupture of pre-existing vulnerable atherosclerotic plaques, initiating an acute thrombotic event (3,5). Triggers for Kounis syndrome include medications (particularly beta-lactam antibiotics and non-steroidal anti-

inflammatory drugs), insect bites, foods, and various environmental allergens (9). In our case, the trigger was ceftriaxone, a beta-lactam antibiotic. Multiple case reports in the literature have documented ceftriaxone triggering Kounis syndrome (10). This situation emphasizes the need for careful monitoring of cardiac symptoms and ECG changes in patients who develop allergic reactions during antibiotic administration, especially in emergency departments.

There are several limitations to our case that should be considered. First, serum tryptase levels were not measured during the allergic reaction. Serum tryptase measurement is not available in our emergency department. Serial tryptase measurements are recommended to provide objective evidence of mast cell degranulation, and these measurements could have further strengthened the diagnosis of Kounis syndrome (3). Second, we administered epinephrine according to standard anaphylaxis protocols (0.5 mg intramuscularly, repeated once after 5 minutes due to an inadequate response, for a total of 1 mg), but the hemodynamic stress caused by the cardiovascular effects of epinephrine may have contributed to myocardial stress. Finally, the absence of a baseline ECG obtained at the initial presentation (as the patient did not present with cardiac symptoms) precludes direct comparison, despite previous cardiology records confirming that the ST changes were new.

In conclusion, Kounis syndrome is a rare but potentially fatal complication of allergic reactions and should be kept in mind, especially in patients with known cardiovascular risk factors. As seen in this case, even commonly used antibiotics such as ceftriaxone can trigger myocardial infarction in the presence of critical coronary lesions. In patients who develop allergic reactions, ECG monitoring, measurement of cardiac biomarkers, and emergency coronary angiography when necessary can be life-saving. Increasing clinicians' awareness of this syndrome and adopting a multidisciplinary approach are critical for reducing mortality and morbidity.

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