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# WHEN ALLERGY STRIKES THE HEART: KOUNIS SYNDROME AND CARDIAC ARREST

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## ABSTRACT

*Introduction:* Kounis syndrome is an acute coronary syndrome precipitated by allergic or hypersensitivity reactions and mediated by the release of inflammatory substances that affect the coronary circulation. In spite of increasing awareness of this syndrome, it remains underdiagnosed, particularly in young patients without conventional cardiovascular risk factors.

*Case description:* We report the case of a patient with recurrent Kounis syndrome presenting with two distinct acute coronary syndromes within one month, initially classified as myocardial infarction with nonobstructive coronary arteries and subsequently recognised after angiographic documentation of transient coronary vasospasm. A 28-year-old man with a history of non-steroidal anti-inflammatory drug (NSAID) hypersensitivity presented with acute chest pain shortly after NSAID intake. Electrocardiography showed ischemic changes, and cardiac biomarkers showed a modest elevation. Coronary angiography revealed severe, reversible multivessel coronary artery spasm in the absence of structural coronary disease, consistent with type I Kounis syndrome. During the procedure, the patient developed ventricular fibrillation, successfully treated with electrical defibrillation and intracoronary nitrates. Left ventricular function fully recovered, and the patient was discharged with strict avoidance of NSAIDs. Subsequent allergological evaluation confirmed NSAID hypersensitivity.

*Conclusion:* This case highlights that type I Kounis syndrome may present as a severe acute coronary syndrome complicated by malignant ventricular arrhythmias. A careful allergological and pharmacological history is essential for accurate diagnosis, guide management, and prevent recurrent potentially fatal events.

## KEYWORDS

Kounis syndrome, coronary vasospasm, NSAID, hypersensitivity, ventricular fibrillation

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## LEARNING POINTS

- Kounis syndrome should be considered in young patients presenting with acute coronary syndromes and non-obstructive coronary arteries, especially when symptoms occur after exposure to drugs or allergens.
- Type I Kounis syndrome, despite the absence of structural coronary artery disease, may be complicated by life-threatening ventricular arrhythmias, underscoring that it is not always a benign condition.
- A detailed allergological and pharmacological history is crucial in patients with suspected myocardial infarction with nonobstructive coronary arteries to avoid misdiagnosis, prevent repeated exposure to triggering agents such as non-steroidal anti-inflammatory drugs, and guide appropriate multidisciplinary management.

## INTRODUCTION

Kounis syndrome is an acute coronary syndrome triggered by anaphylactic or anaphylactoid reactions, resulting from the release of inflammatory mediators that affect the coronary circulation. It represents the intersection between allergic disorders and cardiovascular disease and remains an underdiagnosed clinical entity, despite its potentially life-threatening nature[1].

Three variants of Kounis syndrome have been described. Type I occurs in patients with angiographically normal coronary arteries, in whom the acute event is caused by coronary artery spasm without underlying atherosclerosis. Type II affects patients with pre-existing coronary artery disease, in whom allergic mediators may induce plaque erosion or rupture. Type III involves stent thrombosis associated with hypersensitivity reactions to stent components or drugs. Among these, type I is considered the rarest presentation, particularly when complicated by malignant ventricular arrhythmias[2]. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently implicated triggers of Kounis syndrome, especially in individuals with a history of drug hypersensitivity or atopic conditions[3]. We report a rare and severe case of type I Kounis syndrome induced by NSAID exposure, complicated by ventricular fibrillation during coronary angiography, highlighting the importance of recognizing allergic triggers in young patients presenting with acute coronary syndromes in the absence of traditional cardiovascular risk factors.

## CASE DESCRIPTION

A 28-year-old man presented to the Emergency Department with acute retrosternal chest pain. He had no conventional cardiovascular risk factors, was normal weight, did not smoke, and reported a healthy and physically active lifestyle, with regular sports medical follow-up. His medical history was notable for glucose-6-phosphate dehydrogenase (G6PDH) deficiency (World Health Organization class III, moderate deficiency, with no history of haemolytic crises), chronic rhinosinusitis with nasal polyposis and mild asthma treated with salbutamol as needed. The patient had a documented history of severe hypersensitivity reactions to several NSAIDs, including diclofenac and ibuprofen, which occurred in the setting of repeated use at high doses, complicated by laryngeal oedema and bronchospasm. One month before the current admission, he had experienced a non–ST-segment elevation myocardial infarction while taking ketorolac and intranasal naphazoline; consequently, the nasal decongestant was discontinued and replaced with an intranasal and oral corticosteroid. Due to persistent rhinosinusitis-related headache unresponsive to this treatment associated with paracetamol, he had continued to use ketorolac intermittently over the preceding months.

At that time, the patient was admitted for a non–ST-segment elevation myocardial infarction, with a modest increase in cardiac troponin. Coronary angiography, performed approximately 24 hours after symptom onset, showed no significant obstructive coronary artery disease. In particular, the left anterior descending artery appeared angiographically normal, with no evidence of focal stenosis or spasm *(Fig. 1A)*. Based on these findings, the event was classified as myocardial infarction with non-obstructive coronary arteries (MINOCA), and the patient was treated with dual antiplatelet therapy.

During the current admission, one month later, the patient presented with ST-segment elevation myocardial infarction, with constrictive retrosternal chest pain that developed shortly after the intake of ketorolac. On admission, vital signs were within normal limits. The initial electrocardiogram showed sinus rhythm with hyperacute T waves in the anterior leads. A repeat electrocardiogram demonstrated sinus rhythm at 55 beats per minute, ST-segment elevation in lead aVR, and diffuse ST-segment depression in the remaining leads. Transthoracic echocardiography showed mid-apical akinesia with a left ventricular ejection fraction of 40%. Urgent coronary angiography revealed severe multivessel coronary artery spasm involving both the anterior and posterior interventricular arteries, with predominant involvement of the left anterior descending artery and not present during the previous angiographic evaluation *(Fig. 1B)*. During coronary angiography, the patient developed episodes of ventricular fibrillation, which were successfully treated with prompt electrical defibrillation. Intracoronary nitrates were administered, leading to complete resolution of the coronary spasm and restoration of coronary flow.

Laboratory monitoring revealed low-grade eosinophilia,

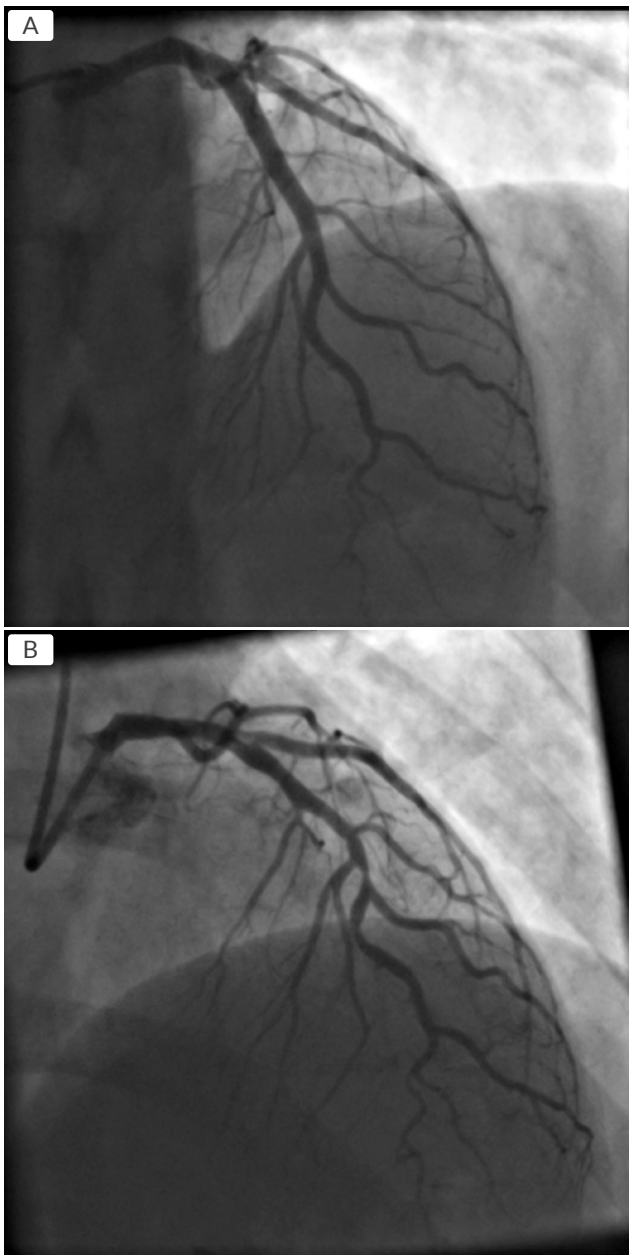



*Figure 1. Coronary angiography of the left anterior descending artery during two distinct acute coronary events. A) Angiographically normal left anterior descending artery during the first admission for non–ST-segment elevation myocardial infarction, with coronary angiography performed approximately 24 hours after symptom onset; B) Marked diffuse vasospasm of the left anterior descending artery observed during the subsequent admission for ST-segment elevation myocardial infarction.*

consistent with the allergic background and already documented during the previous non-ST-elevation myocardial infarction.

An extended etiological work-up was performed. Plasma homocysteine levels, antiphospholipid antibodies, protein C and protein S activity, and factor V Leiden mutation testing were all within normal limits.

Cardiac magnetic resonance imaging was negative for myocardial oedema, ischemic lesions or late gadolinium enhancement, thereby excluding irreversible myocardial injury related to coronary lesions and supporting a transient ischemia due to reversible coronary vasospasm *(Fig. 2)*.

The patient was discharged asymptomatic and hemodynamically stable, with recovery of left ventricular systolic function (ejection fraction 62%). He was advised to strictly avoid NSAIDs and topical intranasal vasoconstrictors and to undergo allergological and pneumological follow-up.

Allergological evaluation confirmed the intake of ketorolac 10 mg for sinus headache a few hours before the acute coronary event. According to the Naranjo Adverse Drug Reaction Probability Scale, the causal relationship between ketorolac intake and the acute coronary event was classified as definite (score=11). Specific IgE testing for ketorolac or other NSAIDs was not available. Low-dose aspirin was tested in a protected in-hospital setting only to preserve a potential therapeutic option should coronary artery disease develop later in life.

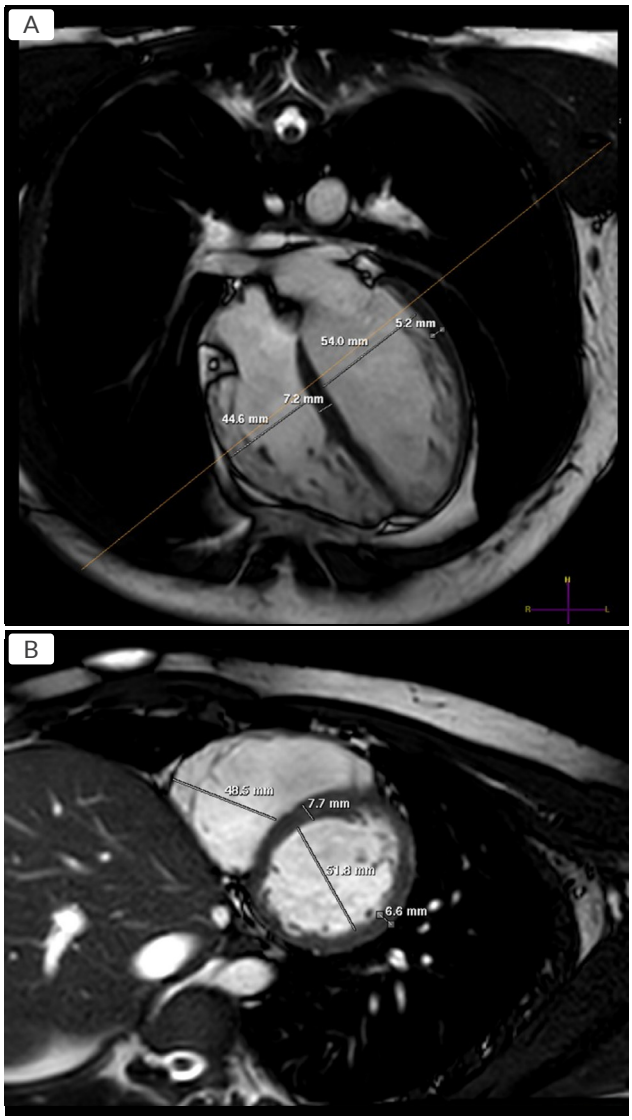



*Figure 2. Cardiac magnetic resonance cine imaging. A) Long-axis cine view showing a normal left ventricular size and geometry, preserved global systolic function, and no regional wall motion abnormalities; B) Short-axis cine view confirming normal left ventricular dimensions, symmetric wall thickness, and absence of macroscopic myocardial abnormalities.*

Skin prick tests were positive for *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. Eosinophils and IgE were found elevated in the subsequent evaluation (respectively 150 cells/µl and 174 IU/ml). Inhaled beclomethasone/formoterol was prescribed, followed by biological therapy with mepolizumab and subsequent allergen-specific immunotherapy. After approximately 18 months, due to reduced treatment efficacy, mepolizumab was replaced with dupilumab. Respiratory symptoms related to chronic rhinosinusitis with nasal polyposis, including nasal obstruction and sinus headache, together with asthma-related respiratory symptoms, remained well controlled during follow-up. The patient expressed awareness of the allergic trigger and reported adherence to medical recommendations, with no cardiac symptoms reported during this period.

## DISCUSSION

Kounis syndrome is a well-recognized yet underdiagnosed cause of acute coronary syndrome, resulting from the interaction between allergic or anaphylactoid reactions and coronary artery dysfunction[1,2]. It is driven by mast cell activation and the release of vasoactive and pro-inflammatory mediators, including histamine, leukotrienes, platelet-activating factor, prostaglandins, and cytokines, released through both IgE-mediated allergic reactions and non–IgE-mediated hypersensitivity mechanisms, such as direct mast cell activation or cyclooxygenase inhibition–related pathways[4]. These processes may result in intense coronary vasoconstriction, endothelial dysfunction, and myocardial ischemia. In addition, they may promote electrical instability through ischemia-related mechanisms, direct effects on cardiomyocyte ion channels, and autonomic imbalance, potentially predisposing to malignant ventricular arrhythmias[5]. In type I Kounis syndrome, these processes occur in the absence of structural coronary artery disease and are typically characterized by transient coronary artery spasm[1].

The clinical presentation of Kounis syndrome overlaps with other conditions within the spectrum of myocardial infarction with non-obstructive coronary arteries (MINOCA), including primary coronary vasospasm and other causes of acute myocardial injury without angiographic evidence of atherosclerosis[5,6]. However, the temporal relationship between symptom onset and exposure to a known allergenic trigger and the angiographic demonstration of reversible multivessel coronary spasm and negative findings on cardiac magnetic resonance imaging strongly support the diagnosis of type 1 Kounis syndrome in this case. Eosinophilia was documented during the MINOCA episode and at slightly higher values shortly after the subsequent ST-segment elevation myocardial infarction.

The present case is clinically significant for several reasons. It documents a type I Kounis syndrome complicated by ventricular fibrillation in a young patient with angiographically normal coronary arteries, highlighting that even in the absence of structural coronary disease, anaphylactic or anaphylactoid-induced coronary events may lead to life-threatening ventricular arrhythmias. Malignant ventricular arrhythmias have only sporadically been reported in type I Kounis syndrome, making this presentation particularly uncommon[7].

In addition, the clear temporal relationship with NSAID exposure and the extensive history of NSAID hypersensitivity, including previous anaphylactoid reactions, strengthen the causal link between the anaphylactoid trigger and the acute coronary events. This association is further supported by a Naranjo Adverse Drug Reaction Probability Scale score of 11, indicating a definite drug-related adverse reaction. The reactions were consistent with a non–IgE-mediated, dose-dependent intolerance mechanism with cross-reactivity among different NSAIDs, rather than a classic IgE-mediated allergy. Failure to recognize this allergic background may lead to misdiagnosis and inappropriate management, particularly in young patients presenting with acute coronary syndromes or MINOCA.

Biological therapy was prescribed exclusively for respiratory disease management and was independent of cardiac manifestations. The patient fulfilled established criteria for biological treatment, including asthma with recurrent exacerbations despite optimized inhaled therapy and severe, refractory chronic rhinosinusitis with nasal polyposis. Given the eosinophilic type 2 inflammatory profile, mepolizumab was initially selected as first-line biological therapy, with documented clinical benefit. After approximately two years of treatment, a progressive loss of efficacy was observed during follow-up, particularly in terms of sinonasal symptom control, leading to a switch to dupilumab. This stepwise biological approach resulted in improved and sustained respiratory disease control. Transient eosinophilia documented during acute cardiac events was reported as an observational finding and did not influence the choice or sequence of biological therapies.

From a clinical perspective, this report emphasizes that Kounis syndrome should be considered in young patients presenting with acute coronary syndromes in the absence of traditional cardiovascular risk factors, particularly when symptoms follow exposure to drugs or allergens. Even type I Kounis syndrome, often regarded as a benign entity, may be complicated by malignant ventricular arrhythmias. Early recognition, avoidance of triggering agents such as NSAIDs in sensitized individuals, and a multidisciplinary approach involving cardiologists, allergists, and pulmonologists are essential to ensure accurate diagnosis, appropriate management, and prevention of potentially fatal outcomes.

## REFERENCES


1. Rochel-Perez E, Santaularia-Tomas M, Martin-Dorantes M, Villareal-Jimenez E, Olivera-Mar A, Sanchez-Felix E, et al. Triggers, Types, and Treatments for Kounis Syndrome: A Systematic Review. *Clin Pract* 2025;**15**:59. doi: 10.3390/clinpract15030059
2. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol* 2006;**110**:7-14. doi: 10.1016/j.ijcard.2005.08.007
3. Ollo-Morales P, Gutierrez-Niso M, De-la-Viuda-Camino E, Ruiz-de-Galarreta-Beristain M, Osaba-Ruiz-de-Alegria I, Martel-Martin C. Drug-Induced Kounis Syndrome: Latest Novelties. *Curr Treat Options Allergy* 2023:1-18. doi: 10.1007/s40521-023-00342-9
4. Kounis NG, Mplani V, Koniari I. Kounis syndrome: A natural paradigm for preventing mast cell activation-degranulation. *Int J Cardiol* 2025;**419**:132704. doi: 10.1016/j.ijcard.2024.132704
5. Benchea LC, Anghel L, Scripcariu DV, Diaconu A, Zanfirescu RL, Lucaci LV, et al. Kounis Syndrome in Clinical Practice: Insights from Clinical Case Series and Mechanistic Pathways. *J Clin Med* 2025;**14**:768. doi: 10.3390/jcm14030768
6. Kounis NG. The "Neglected aVR Lead": Kounis Syndrome of MINOCA Type, Severe Left Main or 3-Vessel Disease and Type A Dissecting Ascending Aortic Aneurysm. *Kans J Med* 2024;**17**:90. doi: 10.17161/kjm.vol17.22352
7. Campo G, Pavasini R, Pollina A, Petrini L, Ferrari R. Kounis-Zavras syndrome presenting with ventricular arrhythmias and cardiogenic shock. *J Cardiol Cases* 2012;**7**:e74-e77. doi: 10.1016/j.jccase.2012.11.003