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Case report

AN UNUSUAL PRESENTATION OF TYPE I KOUNIS SYNDROME: HIGH TROPONIN WITHOUT CHEST PAIN AFTER ANAPHYLAXIS

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Abstract: **Introduction:** Kounis syndrome is defined as the simultaneous occurrence of acute coronary syndrome and an allergic or anaphylactic reaction. It primarily affects men between 40 and 70 years of age and is often associated with chest pain. Owing to limited awareness, this syndrome is frequently under-recognized and under-diagnosed in clinical practice.

Case presentation: We report a case of type I Kounis syndrome in a young woman without chest pain. The patient, who had allergic asthma since childhood, developed anaphylactic shock during the administration of bronchodilators, corticosteroids, and an antibiotic in an emergency outpatient setting, followed by cardiac arrest. Subsequent laboratory testing confirmed acute coronary syndrome.

Conclusion: Although Kounis syndrome is uncommon, particularly in young women, clinicians should consider the possibility of acute coronary syndrome in severe allergic reactions. In this case, myocardial injury was documented by electrocardiographic changes and later by cardiac biomarkers consistent with coronary syndrome.

Keywords: allergic reaction, acute coronary syndrome, resuscitation.

INTRODUCTION

Kounis syndrome is defined as acute coronary syndrome (ACS) occurring simultaneously with an allergic or anaphylactic reaction, mediated by mast-cell activation and the release of inflammatory mediators and cytokines (1, 2). Three mechanistic types are recognized: type I, vasospastic ACS in angiographically normal coronaries without atherosclerosis; type II, ACS triggered by erosion or rupture of pre-existing atheromatous plaques; and type III, ACS in the presence of intracoronary stents, subclassified into IIIa (stent thrombosis) and IIIb (in-stent restenosis) (2, 3). Triggers include drugs, foods, and insect stings, which induce mast-cell degranulation with histamine, leukotrienes, prostaglandins, chymase, and related mediators that promote coronary vasoconstriction, platelet activation, and thrombosis, resulting in ACS (1, 2, 4). Limited clinical awareness leads to under-recognition and under-diagnosis in routine practice (5).

Epidemiological data indicate an occurrence of approximately 1.1–3.4% among patients with allergic manifestations (6, 7). Men are more frequently affected (~74%), the peak age ranges from 40 to 70 years (~68%), and chest pain is reported in ~87% of cases (8). We report a type I presentation in a 25-year-old woman without chest pain, illustrating a painless phenotype that may delay recognition.

CASE PRESENTATION

A 25-year-old female patient with allergic asthma since childhood, treated with fenoterol hydrobromide plus ipratropium bromide aerosols and, more recently, theophylline capsules, presented to the intensive care unit with chest wheezing, a choking sensation, and cough. On admission, her temperature was 36.8 °C, blood pressure 110/80 mmHg, peripheral oxygen saturation (SpO_2) 91% on room air, and pulse 85/min. Lung auscultation revealed prolonged expiration with diffuse wheezes. She denied chest pain. Family history was notable for maternal allergic asthma. She denied drug allergies. She reported frequent asthma attacks; the current attack began during the night, and she sought care in the intensive care unit at 09:30.

Treatment was initiated with intravenous infusion solutions, a systemic corticosteroid, an antihistamine,

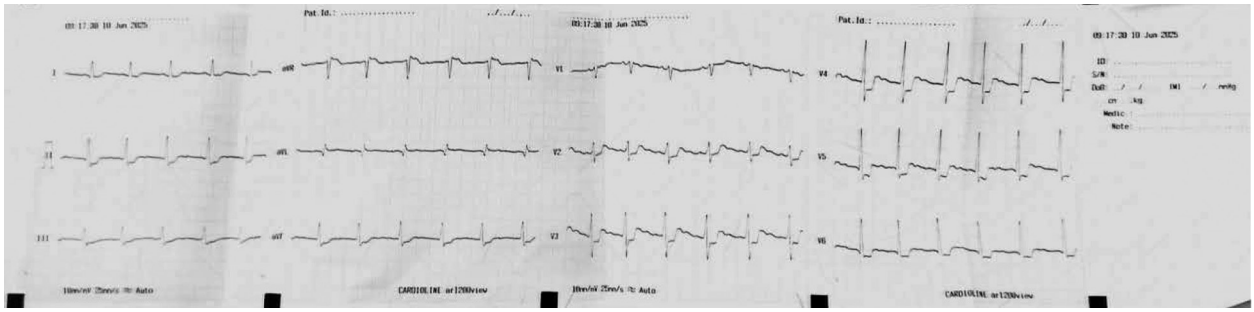

Figure 1. *ECG recording after resuscitation measure*

and bronchodilators. Initial subjective improvement was followed by rapid deterioration, with impaired consciousness and increasing respiratory difficulty, progressing to respiratory arrest with cardiac arrest and unmeasurable blood pressure. Cardiopulmonary resuscitation (CPR) was commenced, including administration of epinephrine, to which she responded. Return of spontaneous circulation was achieved, with restoration of spontaneous breathing and heart activity. She vomited several times and subsequently became communicicative, reporting headache as the predominant symptom. She continued to deny chest pain. A post-resuscitation electrocardiogram (ECG) demonstrated ST-segment depression in leads II, III, aVF, V2, V3, V4, V5, and V6, with ST-segment elevation in aVR (Figure 1).

The post-resuscitation ECG, in sinus rhythm at a rate of 120/min, shows marked ST-segment depression in leads II, III, aVF, and V2–V6, with ST-segment elevation in aVR. The patient reported no chest pain at the time of recording.

The patient was transported to a higher-level health facility hemodynamically stable, with normal vital parameters. Laboratory results on admission were as follows: troponin I 512 pg/mL (reference 29.62–74.64 pg/mL), D-dimer 2.86 mg/L FEU (reference 0–0.55 mg/L FEU), leukocytes 14.10 × 10^9/L (reference 3.9–10.0 × 10^9/L), and prothrombin time 13.5 s (reference 9.3–11.6 s) (Table 1 and 2).

The leukocyte count was elevated above the reference range, supporting an inflammatory component in the overall clinical picture. In anaphylactic reactions, generalized vasomotor disturbances and complex pathophysiological mechanisms can affect coagulation; accordingly, the findings included mildly prolonged prothrombin time and elevated D-dimer values.

The next day, troponin I was 1264.15 pg/mL (reference 29.62–74.64 pg/mL). On 09/09/2025, four days after the anaphylactic shock, the findings were as follows: leukocytes 14.00 × 10^9/L, D-dimer 0.87 mg/L FEU, troponin I 108.11 pg/mL, and BNP 31.80 pmol/L (reference 0–28.9 pmol/L).

During hospitalization, transthoracic echocardiography was performed, and no segmental wall-motion abnormalities were observed.

Table 1. *Troponin values*

Troponin values			
Day	Hour	Result	Reference value
05.09.2025	11.41	512.92 pg/ml	29.62-74.64 pg/ml
05.09.2025	14.29	1117.64 pg/ml	29.62-74.64 pg/ml
05.09.2025	19.35	1545.44 pg/ml	29.62-74.64 pg/ml
06.09.2025	06.26	1264.15 pg/ml	29.62-74.64 pg/ml
09.09.2025	06.28	108.11 pg/ml	29.62-74.64 pg/ml
11.09.2025	06.31	34.7 pg/ml	29.62-74.64 pg/ml

Table 2. *Additional Laboratory Findings*

Other laboratory analysis				
Date	Hour	Analysis	Result	Reference value
05.11.2025	14:35	Leukocites	19x10^9/L	3.9 - 10x10^9/L
05.11.2025	14:35	Prothrombin time	13.1 s	9,3-11,6 s
05.11.2025	14:35	D - dimer	2,21mg/L FEL	0-0,55 mg/LFEL

DISCUSSION

Symptoms of myocardial ischemia and infarction in Kounis syndrome exhibit sex-related differences, with women reporting chest pain less frequently than men (9-17). Although the mechanisms underlying sex differences in the presentation of coronary artery disease are incompletely defined, estrogen has been implicated in the modulation of pain sensitivity and nociceptive processing (18–21). The absence of chest pain at presentation in the current case may therefore be related, at least in part, to female sex. Kounis syndrome is most frequently reported in middle-aged men (8), a distribution that likely reflects the burden of atherosclerotic risk factors in that population, including hypertension, dyslipidemia, diabetes, and smoking (22).

Medications constitute the most common trigger for Kounis syndrome (23). In a 2019 series, 142 of 252 cases (56.3%) were drug-induced (24). In the present case, which involves a young woman with a low atherosclerotic risk profile, onset plausibly relates to exposure to drugs or other agents known to precipitate anaphylaxis and mast-cell degranulation (11). We document a type I Kounis presentation without chest pain in a young female patient. Because Kounis syndrome is typically described in men aged 40–70 years and commonly accompanied by chest pain (8), a painless presentation in a young woman is uncommon. Clinicians evaluating patients with severe allergic reactions, including anaphylaxis, should consider concurrent acute coronary syndrome irrespective of age, sex, or the presence of chest pain.

Among patients with allergic reactions, in-hospital mortality has been reported at 7.0% for those with concomitant acute coronary syndrome attributed to Kounis syndrome, compared with 0.4% in those without acute coronary involvement (6). Higher rates of stroke and venous thrombosis have also been observed in this population (6). These outcomes underscore the need for rapid recognition and timely management. In most cases, symptom onset occurs within one hour of exposure to the inciting trigger (8). When Kounis syndrome is suspected, prompt 12-lead electrocardiography and transthoracic echocardiography are recommended, with early consideration of vasodilator therapy or coronary angiography when clinically indicated.

In this case, the induced vasospasm led to an increase in cardiac injury biomarkers, which gradually decreased over time toward reference values, indicating ischemia. Prolonged vasospasm caused myocardial cell necrosis, resulting in an increase in the cardiac-specific biomarker troponin. The spasm persisted at a high level for hours and then gradually returned to reference values over the course of days.

Kounis syndrome is a less heavily studied topic compared to other cardiovascular diseases. Therefore, existing protocols have not adequately addressed this condition. In a cross-sectional study published in March 2025 (25) on 150 cases of Kounis syndrome, coronary angiography was performed in only 119 cases. This leaves space for the cardiologist to assess the necessity of coronary angiography or other diagnostic approaches on a case-by-case basis.

Management of Kounis syndrome differs from that of other acute coronary syndromes because it requires concurrent treatment of the underlying allergic reaction. Intravenous corticosteroids and H1 and H2 antihistamines are commonly used as part of the initial approach. For types II and III, standard reperfusion strategies are required in addition to antiallergic therapy (4). Early diagnosis and coordinated treatment targeting both coronary and allergic pathophysiology are essential to improve outcomes.

CONCLUSION

Kounis syndrome, although uncommon in young women and particularly rare without chest pain, should remain in the differential diagnosis for any severe systemic allergic reaction, including anaphylaxis. Clinical management should be protocol driven: after initial stabilization, obtain a 12-lead ECG, perform serial high-sensitivity troponin testing, conduct bedside transthoracic echocardiography, and involve cardiology early, with coronary angiography considered when clinically indicated. Treatment must address both the allergic cascade and myocardial ischemia, with careful selection of agents that do not exacerbate coronary vasospasm.

This case underscores two practice-critical points. First, absence of chest pain does not exclude acute coronary involvement in anaphylaxis; ECG changes and elevations in hs-troponin require immediate interpretation and action. Second, the differential diagnosis should explicitly consider epinephrine-induced vasospasm, Takotsubo cardiomyopathy, and myocarditis, because therapeutic decisions depend on their distinction.

Given the documented risk of adverse outcomes and the persistent under-recognition of this entity, institutions should implement standardized operating procedures in emergency and critical care settings, provide targeted staff education, and integrate allergy and cardiology input early in the care pathway. Timely diagnosis coupled with coordinated therapy is essential to reduce morbidity and mortality in Kounis syndrome.

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Note: Artificial intelligence was not utilized as a tool in this study.

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Sažetak

NEOBIČNA PREZENTACIJA KOUNISOVOG SINDROMA TIPA I: VISOK TROPONIN BEZ BOLA U GRUDIMA NAKON ANAFILAKSE

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Uvod: Kounisov sindrom se definiše kao istovremenost akutnog koronarnog sindroma i alergijskih ili anafilaktičkih reakcija. Prvenstveno pogađa muškarce u dobi od 40 do 70 godina i često je povezan s bolovima u grudima. Ovaj sindrom često ostaje neprepoznat i nedijagnostikovan u kliničkoj praksi zbog niskog nivoa informisanosti.

Prikaz slučaja: Ovde predstavljamo slučaj Kounisovog sindroma tipa I kod mlade žene bez bolova u grudima. Radi se o mladoj ženi sa dijagnozom alergijske astme od detinjstva, kod koje se tokom aplikacije bronhodilatatora, kortikosteroida i antibiotika u ambulanti HMP, desio anafilaktički šok, zastoj rada srca i kasnije po laboratorijskim nalazima dokazan akutni koronarni sindrom.

Zaključak: Iako je Kounisov sindrom dosta redak, naročito kod mladih žena, ipak treba usmeriti pažnju kod alergijskih rekacija teže kliničke prezentacije, na mogučnost razvoja akutnog koronarnog sindroma. Ovde smo kroz snimak EKG i kasnije laboratorijskim testovima potvrdili oštećenje na srčanom mišiću preko markera koronoranog sindroma.

Ključne reči: alergijska reakcija, akutni koronarni sindrom, reanimacija.

REFERENCES

1. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. Clin Chem Lab Med. 2016; 54(10): 1545-59. doi: 10.1515/cclm-2016-0010.

2. Kounis NG. Coronary hypersensitivity disorder: the Kounis syndrome. Clin Ther. 2013; 35(5): 563–71. doi: 10.1016/j.clinthera.2013.02.022.

3. Biteker M, Biteker FS, Özlek B, Özlek E, Başaran N. Classification of Kounis syndrome. Int J Cardiol. 2017; 247:13. doi: 10.1016/j.ijcard.2017.06.002.

4. Kounis NG, Koniari I, Velissaris D, Tzanis G, Hahalis G. Kounis syndrome-not a single-organ arterial disorder but a multisystem and multidisciplinary disease. Balkan Med J. 2019; 36: 212–21. doi: 10.4274/balkanmedj.galenos.2019.2019.5.62.

5. Akoz A, Tanboga HI, Emet M, Bayramoglu A, Kizrak Y, Kantarci M, et al. A prospective study of Kounis syndrome: clinical experience and cardiac magnetic resonance imaging findings for 21 patients. Acta Med Mediterr. 2013; 29(4): 811–6.

6. Desai R, Parekh T, Patel U, Fong HK, Samani S, Patel C, et al. Epidemiologyof acute coronary syndrome co-existent with allergic/hypersensitivity/anaphylactic reactions (Kounis syndrome) in the United States: a nationwide inpatient analysis. Int J Cardiol. 2019;292:35–8. doi: 10.1016/j.ijcard.2019.06.002.

7. Kounis NG, Cervellin G, Koniari I, Bonfanti L, Dousdampanis P, Charokopos N,et al. Anaphylactic cardiovascular collapse and Kounis syndrome: systemic vasodilation or coronary vasoconstriction? Ann Transl Med. 2018; 6(17): 332. doi: 10.21037/atm.2018.09.05.

8. Abdelghany M, Subedi R, Shah S, Kozman H. Kounis syndrome: a review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. Int J Cardiol. 2017; 232:1–4. doi: 10.1016/j.ijcard.2017.01.124.

9. Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005; 352(5): 539–48. doi: 10.1056/NEJMoa043046.

10. Soufras GD, Kounis NG. Adrenaline administration for anaphylaxis and the risk of takotsubo and Kounis syndrome. Int J Cardiol. 2013; 166(2): 281–2 doi: 10.1016/j.ijcard.2012.12.075.

11. Kounis NG, Koniari I, Tsigkas G, Soufras GD, Plotas P, Davlouros P, et al. Angina following anaphylaxis: Kounis syn-

drome or adrenaline effect? Malays Fam Physician. 2020; 15(3): 97–8.

12. Rubio Caballero JA, Oteo Domínguez JF, Maicas Bellido C, Cantón T, BarcielaR, García Moreno LM et al. Vasoespasmo inducido por adrenalina como formade presentación de una angina variante [An adrenaline-induced vasospasmas the form of presentation of variant angina]. Rev Esp Cardiol. 1999; 52(4): 273-6. [Article in Spanish]. doi: 10.1016/S0300-8932(99)74911-0.

13. Saff R, Nahhas A, Fink JN. Myocardial infarction induced by coronary vasospasm after self-administration of epinephrine. Ann Allergy. 1993; 70(5): 396–8.

14. Shaver KJ, Adams C, Weiss SJ. Acute myocardial infarction after administrationof low-dose intravenous epinephrine for anaphylaxis. CJEM. 2006; 8(4): 289–94. doi: 10.1017/s1481803500013890

15. Kawakami T, Ando T, Kimura M, Wilson BS, Kawakami Y. Mast cells in atopicdermatitis. Curr Opin Immunol. 2009; 21(6): 666–78. doi: 10.1016/j.coi.2009.09.006

16. Liu FT, Goodarzi H, Chen HY. IgE, mast cells, and eosinophils in atopic dermatitis. Clin Rev Allergy Immunol. 2011; 41(3): 298–310. doi: 10.1007/s12016-011-8252-4.

17. Sederholm Lawesson S, Isaksson RM, Thylén I, Ericsson M, Ängerud K, Swahn E, et al. Gender differences in symptom presentation of ST-elevation myocardial infarction – an observational multicenter survey study. Int J Cardiol. 2018; 264: 7–11. doi: 10.1016/j.ijcard.2018.03.084.

18. Mehta PK, Wei J, Shufelt C, Quesada O, Shaw L, Bairey Merz CN. Gender related differences in chest pain syndromes in the frontiers in CV medicine special issue: sex & gender in CV medicine. Front Cardiovasc Med. 2021; 8: 744788. doi: 10.3389/fcvm.2021.744788.

19. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. Br J Anaesth. 2013; 111(1): 52–8. doi: 10.1093/bja/aet127.

20. Craft RM. Modulation of pain by estrogens. Pain. 2007;132(Suppl 1): S3–S12. doi: 10.1016/j.pain.2007.09.028.

21. Smith YR, Stohler CS, Nichols TE, Bueller JA, Koeppe RA, Zubieta JK. Pronociceptive and antinociceptive effects of estradiol through endogenous opioid neurotransmission in women. J Neurosci. 2006; 26(21): 5777–85. doi: 10.1523/JNEUROSCI.5223-05.2006.

22. Giovannini M, Koniari I, Mori F, Ricci S, De Simone L, Favilli S, et al. Kounis syndrome: a clinical entity penetrating from pediatrics to geriatrics. J Geriatr Cardiol. 2020; 17(5):294–9. doi: 10.11909/j.issn.1671-5411.2020.05.011.

23. Ollo-Morales P, Gutierrez-Niso M, De-la-Viuda-Camino E, Ruiz-de-GalarretaBeristain 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.

24. Raschi E, Fertonani Affini L, Antonazzo IC, Diemberger I, Poluzzi E, De Ponti F. Drug-induced Kounis syndrome: a matter of pharmacovigilance. Int J Cardiol. 2019; 274: 381. doi: 10.1016/j.ijcard.2018.07.119.

25. 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(3): 59. doi: 10.3390/clinpract15030059.

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