



The allergic myocardial infarction dilemma: is it the anaphylaxis or the epinephrine?

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Abstract

We highlight two distinct cases of myocardial infarction occurring concurrently with anaphylaxis at our centre in Singapore. The first case had cardiac symptoms and electrocardiogram changes concomitant with his anaphylaxis presentation, suggestive of Kounis syndrome, while the second case presented with anaphylaxis and only developed cardiac symptoms and electrocardiogram changes after treatment with intramuscular epinephrine, suggestive of epinephrine-induced myocardial infarction. Both these conditions are uncommon and under-recognised, and we review the current literature to compare the similarities and differences in their clinical manifestations, pathophysiology, and management. Kounis syndrome occurs secondary to mast cell degranulation ultimately resulting in coronary vasospasm, platelet activation and inflammatory response, whereas epinephrine causes platelet aggregation. Therefore, treatment priorities of Kounis syndrome are treatment of allergy, treatment of vasospasm, and treatment with anti-platelet therapy and revascularization if coronary plaques are present. For epinephrine-induced myocardial infarction, after epinephrine treatment is discontinued, considerations in management are re-vascularisation or pharmacotherapy. Further research will help with better understanding of both conditions and formulation of clinical management guidelines.

Keywords Anaphylaxis · ST-segment elevation myocardial infarction · Epinephrine · Kounis syndrome

Highlights

- Kounis syndrome and epinephrine-induced myocardial infarction while present similarly, can be distinguished clinically by the onset of symptoms and signs as well as ECG and cardiac enzyme changes.
- Kounis syndrome occurs secondary to degranulation of mast cells, whereas epinephrine-induced myocardial

infarction results from platelet aggregation caused by epinephrine.

- Due to different pathophysiology, management of each is distinct.
- Further research is needed for establishment of practice guidelines to aid clinicians in management

Introduction

Myocardial infarction in the setting of anaphylaxis can occur either as a result of allergic acute coronary syndrome, also known as Kounis Syndrome, or from anaphylaxis treatment with epinephrine. Differentiating the aetiology is important in successful treatment. While there have been case reports of both conditions, to our knowledge there has not been any literature comparing their presentation, pathophysiology, and management. In this article, we present a case of Kounis syndrome and a case of epinephrine-induced myocardial infarction, and review the literature on both to provide a head-to-head comparison.

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Case 1: Kounis syndrome

A 42-year-old man with medical history significant for inferior ST-segment elevation myocardial infarction 1 year prior, poorly controlled type 2 diabetes mellitus, hypertension, hyperlipidemia, asthma, allergic rhinitis, has a 3-year history of recurrent chronic urticaria precipitated by exercise every 3 months. Coronary angiogram a year ago showed triple vessel coronary artery disease with 100% occlusion in the middle segment of left anterior descending artery, 100% occlusion in the middle segment of circumflex artery, 90% stenosis in the second obtuse margin branch, and 90% stenosis in the right coronary artery. Percutaneous coronary intervention with drug-eluting stents was performed for the circumflex and obtuse marginal lesions. Residual disease were treated medically. Left ventricular ejection fraction was assessed to be 40% on trans-thoracic echocardiogram.

He presented to the emergency department with acute onset of generalized urticarial rash, angioedema, wheezing and breathlessness without chest discomfort. Prior to his symptom onset, he had eaten pizza with garlic bread and exerted himself by walking home. Electrocardiogram (ECG) obtained prior to arrival to hospital revealed ST-segment elevation in the inferior and lateral leads (Fig. 1). He was loaded with Ticagrelor 180 mg and arranged for emergency coronary angiogram with no epinephrine given.

Coronary angiogram revealed a culprit lesion of 90% stenosis in the left circumflex artery and 90% stenosis in

the right coronary artery (Fig. 2a, c). Drug-eluting balloon was performed to the middle segment of left circumflex artery (Fig. 2b) and balloon angioplasty performed to the proximal segment of right coronary artery (Fig. 2d). Serial troponin trended up to 9121 ng/L (range 0.0–17.4) after 12 h. He was continued on dual antiplatelet therapy and referred for coronary artery bypass grafting. Repeat ECG showed resolution of dynamic changes. A review by the allergist diagnosed him to have wheat-dependent exercise induced anaphylaxis with a positive omega-5 gliadin IgE result, and recommended for treatment with oral anti-histamines with standby epinephrine auto-injector.

Case 2: epinephrine-induced myocardial infarction

A 58-year-old man with chronic smoking history, minor coronary artery disease, hypertension, transient ischemic attack, and has yearly urticaria triggered by jogging since 20 years of age. Six months ago, he was admitted for chest pain for which a trans-thoracic echocardiogram showed preserved ejection fraction and no regional wall motion abnormality and a computed tomography coronary angiography showed minor irregularities in the proximal segment of right coronary artery (Fig. 3a) with normal left anterior descending and left circumflex arteries.

He presented to the emergency department with acute onset of breathlessness, generalised urticarial rash, and giddiness with no chest pain. The symptoms started 30 min after eating fried flat noodles and Malay glutinous rice cakes followed by directing traffic under the sun. Initial ECG

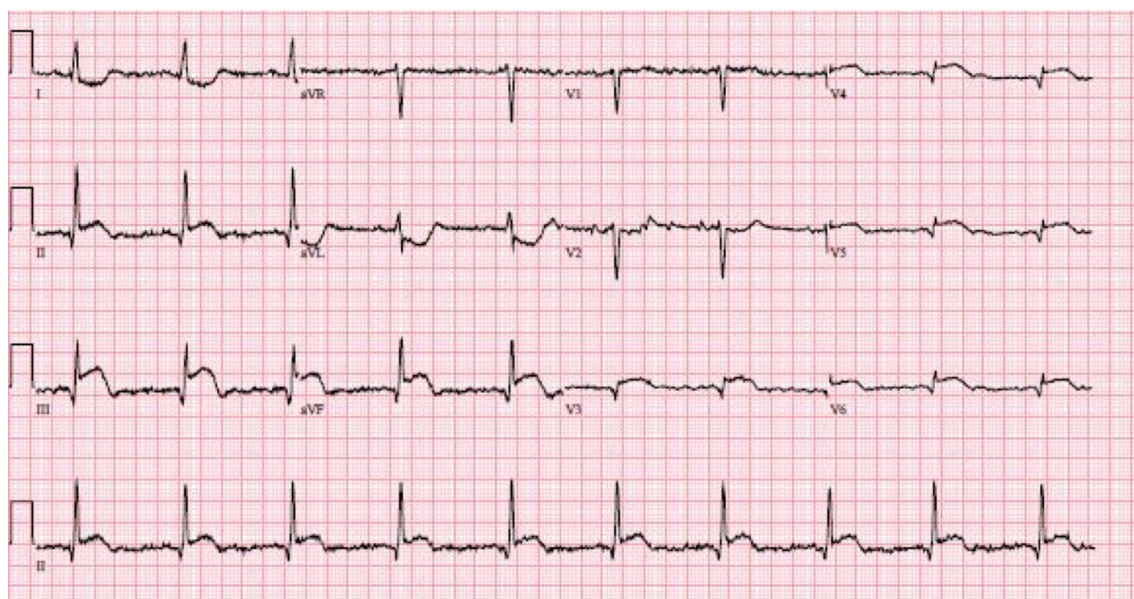


Fig. 1 Electrocardiogram showing ST-segment elevations over II, III, aVF and V3–6 with reciprocal ST depression and T wave inversion in aVL and I, consistent with inferolateral ST-elevation myocardial infarction

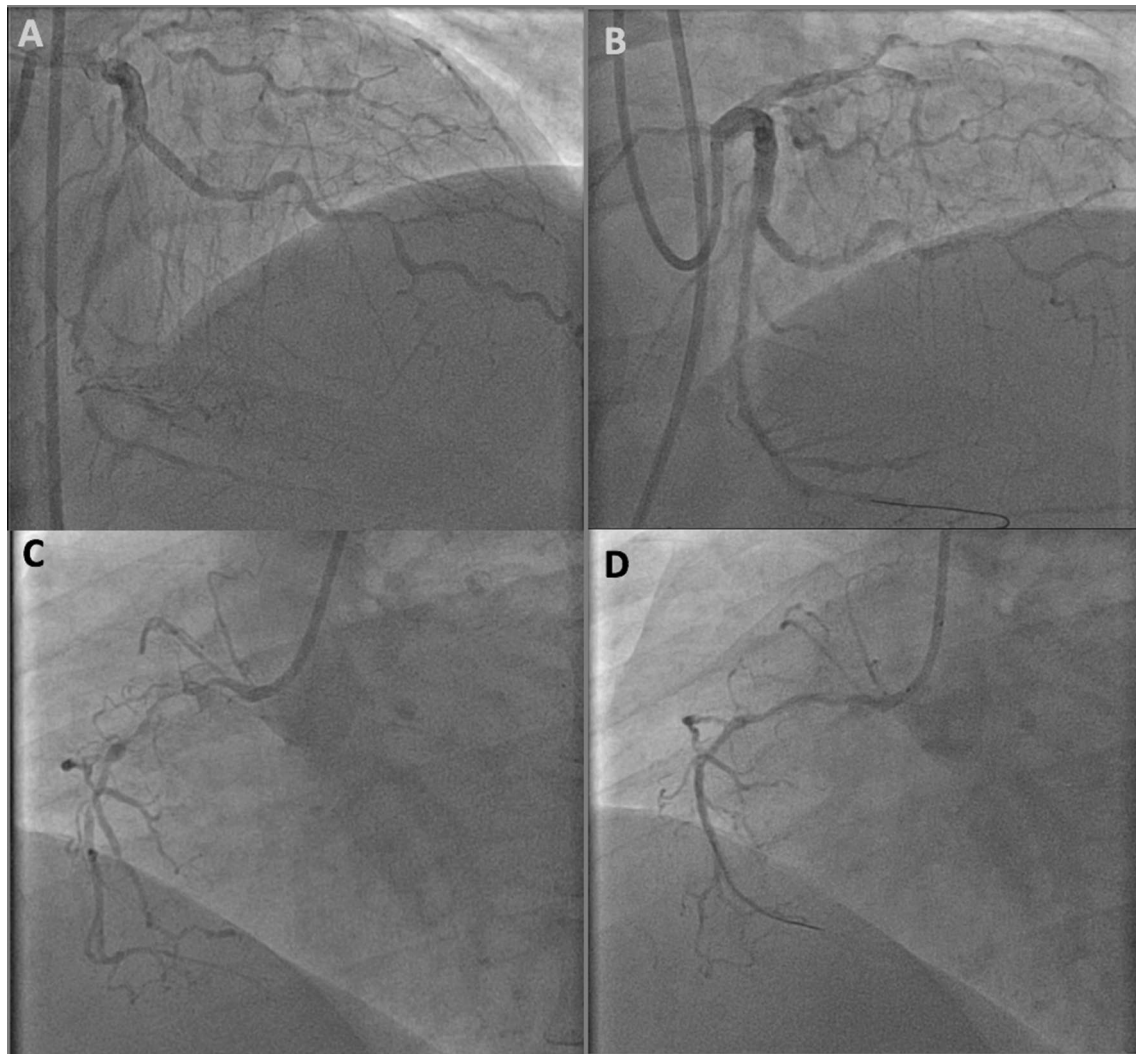


Fig. 2 Coronary angiogram showing **a** 90% stenosis in the mid left circumflex artery pre-intervention; **b** status/post drug eluting balloon to the mid left circumflex artery; **c** 90% diffuse right coronary artery

disease pre-intervention; **d** status/post plain old balloon angioplasty to proximal right coronary artery

showed normal sinus rhythm without any ischemic ST-T changes (Fig. 3b). A diagnosis of anaphylaxis was made and he was given intramuscular epinephrine 0.5 mg. Ten minutes later, he developed severe chest pain and ECG showed new ST-segment elevations in the inferior leads (Fig. 3c).

After loading with Ticagrelor, he underwent emergency coronary angiogram which revealed a 50% stenosis from a developing thrombus in the proximal segment of right coronary artery (Fig. 4a). There were minor irregularities in the left anterior descending and left circumflex arteries. A drug eluting stent was used for the lesion in the right coronary artery (Fig. 4b). Serial troponin-I rose to 4288.0 ng/L (range 0.0–17.4) 9 h later. Trans-thoracic echocardiogram demonstrated left ventricular ejection fraction of 60% with no regional wall motion abnormalities. He was continued on dual anti-platelet therapy. A review by the allergist

diagnosed him to have possible food-dependent exercise induced anaphylaxis from wheat allergy but he defaulted outpatient confirmatory tests.

Discussion

Anaphylaxis refers to an acute, life threatening systemic allergic reaction occurring minutes to hours after exposure to a known or highly probable allergen [1, 2]. It involves the skin and/or mucosal tissue with respiratory, cardiovascular or gastrointestinal systems. Food-dependent exercise-induced anaphylaxis is a rare type of anaphylaxis, where food triggers anaphylaxis only if eating is followed by exercise, which acts as a cofactor [3]. Separately, either the culprit food or exercise is well-tolerated. Leading theories have



Fig. 3 **a** Computed tomography coronary angiogram showing mild stenosis in the proximal right coronary artery. **b** Invasive coronary angiogram showing 50% stenosis in the proximal right coronary

artery with haziness from a developing thrombus. **c** Coronary angiogram post-percutaneous coronary intervention with a drug-eluting stent across the proximal right coronary artery

postulated that exercise triggers food-induced anaphylaxis in sensitised patients by increasing gastric permeability and food allergen absorption [4], and that exercise lowers the activating threshold for interactions between antigens and IgE on mast cells [5]. Onset of anaphylactic symptoms occur within 4 h preceding exercise (usually within 30 min) [6], with exercise intensity ranging from low levels of exertion (e.g. walking, brisk walking, raking leaves) to vigorous exertion (e.g. jogging, aerobics). Most common food culprits are wheat, grains, and nuts in Western populations and wheat and shellfish in Asian populations [7].

Myocardial infarction in the setting of anaphylaxis can arise from Kounis syndrome or be induced by epinephrine. In the first case described, the patient presented with anaphylaxis and ST-segment elevation on the pre-hospital ECG. As no epinephrine was administered, Kounis syndrome is suggested. In contrast, the second case presented with a normal presenting ECG, but with the onset of ischemic symptoms and ST-segment elevation on ECG only after epinephrine was administered. This suggested epinephrine-induced myocardial infarction [8].

Kounis syndrome

First described by Kounis in 1991, Kounis syndrome refers to the concurrence of acute coronary syndromes (which includes coronary spasm, acute myocardial infarction, and stent thrombosis) with mast cell and platelet activation in the setting of hypersensitivity, allergy, or anaphylaxis. During anaphylaxis, degranulation of mast cells occurs and releases compounds such as histamine, neutral proteases (tryptase, chymase), platelet activating factors, cytokines, chemokines, and others by metabolism of arachidonic acid [9]. Histamine causes coronary vasoconstriction, activation

of platelets, induction of tissue factor expression and activity, intimal thickening, inflammatory cell activity modulation, pro-inflammatory cytokine production, P-selective upregulation, and sensitisation of nerve endings in atherosclerotic coronary arteries [10]. Tryptase and chymase activate matrix-degrading metalloproteinases, which ultimately cause destabilisation of atherosclerotic plaque [11].

Food-dependent exercise-induced anaphylaxis is a rare allergy. To our knowledge, only three cases associated with Kounis syndrome have been reported [12]. Interestingly, aspirin, which is the mainstay of treatment for coronary artery disease, appears to provoke the symptoms of food-dependent exercise-induced anaphylaxis [13]. It is speculated that aspirin lowers the threshold of mast cell histamine release.

Kounis syndrome can be sub-divided into three types—type I, type II, or type III [10]. Type I variant involves coronary vasospasm in patients with normal or near normal coronary arteries, and without predisposing factors for coronary artery disease. Type II variant involves patients with pre-existing but quiescent coronary plaques. An allergic reaction triggers coronary vasospasm, plaque erosion, or rupture and results in acute myocardial infarction. Type III variant occurs in patients with coronary stent thrombosis, including patients who died suddenly following stent implantation. Our case exemplifies type II Kounis syndrome.

The incidence of Kounis syndrome varies worldwide, ranging from 7.9 to 9.6 per 100,000 inhabitants annually in Canton Bern, Switzerland [14] to 4.33 per 100,000 inhabitants annually in Achaia, Greece [15]. In the emergency department in Erzurum, Turkey, the incidence amongst all admissions was 19.4 per 100,000 or 3.4% among all allergy patients [16] while in Shizoka, Japan, it is 2.0–2.2% [17] in patients with anaphylaxis.

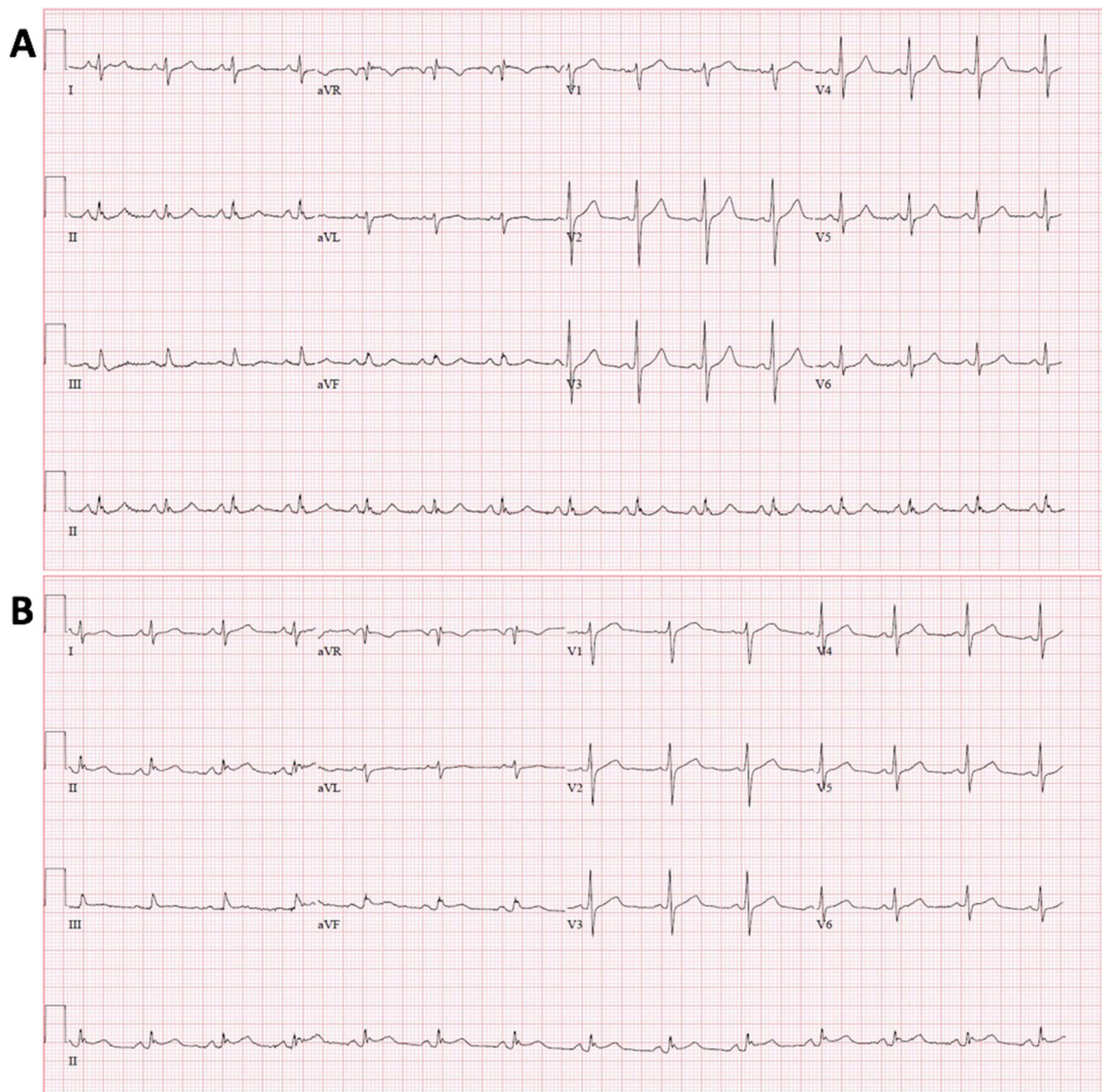


Fig. 4 Electrocardiogram shows **a** Normal sinus rhythm with no ST-T changes before administration of epinephrine; **b** ST-segment elevations in leads II, III, and aVF suggestive of inferior ST-elevation myocardial infarction

Kounis syndrome is a clinical diagnosis based on presenting symptoms, laboratory findings, ECG, echocardiography and coronary angiogram [10]. Risk factors include a past history of allergy, hypertension, smoking, diabetes, and hyperlipidemia [18]. Majority of the symptoms occur within 1 h of exposure to the trigger (80%), although some cases have been reported to have onset of more than 6 h (9.2%) [18]. Chest pain (86.8%) was the most common symptom, followed by anaphylaxis (53%), rash (26.8%), wheezing (14%), and pulmonary oedema (5.1%) [18].

Treatment of Kounis syndrome requires simultaneously addressing and balancing the management of coronary vasospasm and/or thrombosis with allergy. There have not been any consensus clinical guidelines for the management

of Kounis syndrome although authors, based on case reports or series, have followed the principles of treatment guidelines of acute coronary syndrome and anaphylaxis [19]. In type I Kounis syndrome, patients may benefit from treatment of the allergic reaction to prevent further complications [19]. The inciting allergen should be removed and fluid resuscitation given in shock. Pharmacological agents such as H1 and H2 anti-histamines for relief of allergic symptoms and glucocorticoids to prevent biphasic anaphylactic reactions can be administered. Intramuscular epinephrine however, can worsen ischemia by inducing vasospasm and triggering arrhythmias. Those who are elderly, and especially with concurrent hypertension and coronary artery disease, are more prone to these effects [20]. To relieve vasospasm,

vasodilators such as calcium channel blockers and nitrates can be given, with cautious use if blood pressure is low as nitroglycerin can cause hypotension and tachycardia and further complicate anaphylactic shock [10, 19]. In type II and III Kounis syndrome, management is as per type I variant with acute coronary syndrome management by established guidelines, which includes loading of dual anti-platelets with aspirin and P2Y₁₂ receptor inhibitor followed by revascularisation [21]. In type III variant, aspiration of intra-stent thrombus for histological examination and staining for eosinophils and mast cells is helpful [22]. β -blockers should be avoided in Kounis syndrome because it can worsen coronary vasospasm by unopposed α -adrenergic receptor activity [22]. Opioids (e.g. morphine, codeine, meperidine), typically given for relief of acute chest pain, should also be used with caution as it can induce mast cell degranulation and aggravate the allergy [22].

Epinephrine-induced myocardial infarction

In the treatment of anaphylaxis in adults, intramuscular epinephrine 0.01 mg/kg 1:1000 1 mg/ml solution to a maximum of 0.5 mg is first-line [1]. Epinephrine is an endogenous catecholamine which at low dose, has more pronounced β -adrenergic effects whereas at higher doses, has more pronounced α 1-adrenergic effects [23].

Epinephrine-induced myocardial infarction is an understudied and lesser known condition compared to Kounis syndrome. The mechanism proposed is that epinephrine promotes platelet aggregation by increasing the production of thromboxane B₂ by platelets, lowering the threshold for adenosine diphosphate (ADP)-induced platelet aggregation [24], as well as increasing thrombin-induced platelet fibrinogen binding [25].

A literature search of epinephrine-induced myocardial infarction revealed 12 case reports (in English), without reported incidence. Their age ranged from 21 [26] to 78 years old [27], 3 occurred in females [27–30] while majority occurred in males [8, 26, 27, 30–36]. 2 of the cases involved a past history of coronary artery disease with percutaneous coronary interventions [27, 33], while many did not have any pre-existing heart conditions. In terms of presentation, the onset of symptoms post-epinephrine administration ranged from immediate to within 15 min. Amongst the articles which reported on symptoms present (10), majority of the cases had chest pain (9/10), while other symptoms included tachycardia (5/10), palpitations (3/10), nausea (2/10), and diaphoresis (2/10). There was a wide range of inciting allergens, from drugs to foods to bee sting. Many of the cases described normal coronary arteries on angiogram [29, 34, 36] or computed tomography coronary angiogram [26, 30], suggestive of type 2 myocardial infarction from coronary artery spasm. Three case reports revealed type 1

myocardial infarction with acute thrombosis on coronary angiogram post epinephrine administration [27, 32, 33]. Two of these cases had known significant coronary artery disease with multiple percutaneous coronary interventions [27, 33]. Our case was an example of an acute thrombosis induced by exogenous epinephrine in a setting where coronary anatomy was assessed as minor artery disease 6 months prior.

There are currently no consensus guidelines on the management of epinephrine-induced myocardial infarction. Authors have opted to manage conservatively when there is low suspicion of coronary thrombosis and the suspected mechanism is coronary vasospasm rather than plaque rupture. This included patients with few or no cardiovascular risk factors, young age, no ECG changes or changes which resolve after a short period. Pharmacotherapy included sublingual or intravenous nitroglycerin, anti-platelets, and statin. Some patients were followed up with cardiac imaging such as echocardiography, CT or invasive coronary angiogram. On the other hand, acute management with emergency coronary angiogram with a view of percutaneous coronary interventions [27, 32, 33] was usually chosen if patients have significant cardiovascular risk factors.

Comparing Kounis syndrome and epinephrine-induced myocardial infarction

Clinicians should consider the possibility of Kounis syndrome or epinephrine-induced myocardial infarction in patients with concurrence of anaphylaxis and cardiac symptoms and signs. Presentations for both may be similar but they have different pathophysiology and need to be distinguished to be managed differently (Table 1).

The first clue would be the onset of cardiac symptoms. Although these symptoms are common to anaphylaxis, if it occurs during or after administration of epinephrine, an epinephrine-induced aetiology is more likely. In Kounis syndrome, the onset of cardiac symptoms and ECG changes precedes any epinephrine administration. Similarly, ECG or cardiac enzyme changes occur only after epinephrine is given in an epinephrine-induced aetiology. In both conditions, the provoking agent should be stopped. In epinephrine-induced myocardial infarction, this would be epinephrine while in Kounis syndrome, this would be the inciting allergen. In Kounis syndrome, epinephrine should also be avoided to prevent worsening of coronary vasospasm and ischemia.

Management of epinephrine-induced myocardial infarction is based on the cardiac risk stratification and suspicion of coronary thrombosis. The treatment can be pharmacotherapy or with percutaneous coronary intervention. In comparison for Kounis syndrome, the allergic reaction should be treated with anti-histamines and corticosteroids

Table 1 Comparison between Kounis syndrome and epinephrine-induced myocardial infarction

	Kounis syndrome	Epinephrine-induced myocardial infarction
Presentation	Concurrent symptoms and signs of anaphylaxis and acute coronary syndrome	
Onset	Symptoms and signs of acute coronary syndrome, ECG or cardiac enzyme changes precede epinephrine	Symptoms and signs of acute coronary syndrome, ECG or cardiac enzyme changes occur during or after epinephrine given
Pathophysiology	Degranulation of mast cells releasing histamine, neutral proteases and other compounds resulting in coronary vasospasm, platelet activation and inflammatory response	Platelet aggregation caused by epinephrine
Management	Stop inciting allergen Avoid use of epinephrine Treat allergy with anti-histamines and corticosteroids Treat vasospasm with vasodilators, but avoid use of β -blockers In type II or III variant, treat with dual anti-platelets and re-vascularisation	Stop epinephrine Percutaneous coronary intervention vs conservative pharmacotherapy

and coronary vasospasm with vasodilators, with avoidance of vasospasm-aggravating β -blockers. If this is a type II or III Kounis syndrome, patients should be given dual anti-platelets and re-vascularised.

Conclusion

We outlined 2 cases who had both anaphylaxis and myocardial infarction, but with distinct pathophysiology. Acute signs and symptoms can be similar for both conditions but warrant distinctly different managements. Physicians should be vigilant for acute coronary syndrome and anaphylaxis occurring concomitantly. Epinephrine remains the first line therapy for anaphylactic shock, whereas prompt discontinuation is warranted if epinephrine induced myocardial infarction is suspected and avoided in Kounis syndrome.

Overall, both epinephrine-induced myocardial infarction and Kounis syndrome are uncommon causes of myocardial infarction. Further studies will be needed to understand both condition's epidemiology, presentation, pathophysiology, and to formulate investigation and treatment guidelines for clinicians.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Informed consent Informed consent was signed by the above 2 patients for publication of their case and cardiac investigations.

References

- Shaker MS, Wallace DV, Golden DBK et al (2020) Anaphylaxis—a 2020 practice parameter update, systematic review, and grading of recommendations, assessment, development and evaluation (GRADE) analysis. *J Allergy Clin Immunol* 145(4):1082–1123. <https://doi.org/10.1016/j.jaci.2020.01.017>
- Simons FER, Ebisawa M, Sanchez-Borges M et al (2015) 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J* 8:1–16. <https://doi.org/10.1186/s40413-015-0080-1>
- Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G et al (2014) EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy* 69(8):1008–1025. <https://doi.org/10.1111/all.12429>
- Matsuo H, Morimoto K, Akaki T et al (2005) Exercise and aspirin increase levels of circulating gliadin peptides in patients with wheat-dependent exercise-induced anaphylaxis. *Clin Exp Allergy* 35(4):461–466. <https://doi.org/10.1111/j.1365-2222.2005.02213.x>
- Kivity S, Sneh E, Greif J et al (1988) The effect of food and exercise on the skin response to compound 48/80 in patients with food-associated exercise-induced urticaria-angioedema. *J Allergy Clin Immunol* 81(6):1155–1158. [https://doi.org/10.1016/0091-6749\(88\)90884-6](https://doi.org/10.1016/0091-6749(88)90884-6)
- Tam C-J, John RM (2017) Food-dependent exercise-induced anaphylaxis: a review. *J Nurse Pract* 13(5):313–321
- Feldweg AM (2017) Food-dependent, exercise-induced anaphylaxis: diagnosis and management in the outpatient setting. *J Allergy Clin Immunol Pract* 5(2):283–288. <https://doi.org/10.1016/j.jaip.2016.11.022>
- Li J, Zheng J, Zhou Y et al (2018) Acute coronary syndrome secondary to allergic coronary vasospasm (Kounis Syndrome): a case series, follow-up and literature review. *BMC Cardiovasc Disord* 18(1):42. <https://doi.org/10.1186/s12872-018-0781-9>
- Kounis NG (2006) Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol* 110(1):7–14. <https://doi.org/10.1016/j.ijcard.2005.08.007>
- Kounis NG (2016) Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med* 54(10):1545–1559. <https://doi.org/10.1515/ccm-2016-0010>

11. Johnson JL, Jackson CL, Angelini GD et al (1998) Activation of matrix-degrading metalloproteinases by mast cell proteases in atherosclerotic plaques. *Arterioscler Thromb Vasc Biol* 18(11):1707–1715. <https://doi.org/10.1161/01.atv.18.11.1707>
12. Toya T, Kagami K, Adachi T (2019) Friend or foe: food-dependent exercise-induced anaphylaxis associated with acute coronary syndrome aggravated by adrenaline and aspirin: a case report. *Eur Heart J Case Rep* 3(3):ytz143. <https://doi.org/10.1093/ehjcr/ytz143>
13. Aihara M, Miyazawa M, Osuna H et al (2002) Food-dependent exercise-induced anaphylaxis: influence of concurrent aspirin administration on skin testing and provocation. *Br J Dermatol* 146(3):466–472. <https://doi.org/10.1046/j.1365-2133.2002.04601.x>
14. Helbling A, Hurni T, Mueller UR et al (2004) Incidence of anaphylaxis with circulatory symptoms: a study over a 3-year period comprising 940,000 inhabitants of the Swiss Canton Bern. *Clin Exp Allergy* 34(2):285–290. <https://doi.org/10.1111/j.1365-2222.2004.01882.x>
15. Kounis NG, Soufras GD, Davlouros P et al (2015) Combined etiology of anaphylactic cardiogenic shock: amiodarone, epinephrine, cardioverter defibrillator, left ventricular assist devices and the Kounis syndrome. *Ann Card Anaesth* 18(2):261–264. <https://doi.org/10.4103/0971-9784.154498>
16. Akoz A, Tanboga HI, Emet M et al (2013) A prospective study of Kounis syndrome: clinical experience and cardiac magnetic resonance imaging findings for 21 patients. *Acta Med Mediterr* 9:811–816
17. Yanagawa Y, Kondo A, Ishikawa K et al. (2017) Kounis syndrome should be excluded when physicians treat patients with anaphylaxis. *Ann Allergy Asthma Immunol* 119(4):392. <https://doi.org/10.1016/j.anai.2017.08.003>
18. Abdelghany M, Subedi R, Shah S et al (2017) Kounis syndrome: a review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. *Int J Cardiol* 232:1–4. <https://doi.org/10.1016/j.ijcard.2017.01.124>
19. Fassio F, Losappio L, Antolin-Amerigo D et al (2016) Kounis syndrome: a concise review with focus on management. *Eur J Intern Med* 30:7–10. <https://doi.org/10.1016/j.ejim.2015.12.004>
20. Ridella M, Bagdure S, Nugent K et al (2009) Kounis syndrome following beta-lactam antibiotic use: review of literature. *Inflamm Allergy Drug Targets* 8(1):11–16. <https://doi.org/10.2174/187152809787582462>
21. O’Gara PT, Kushner FG, Ascheim DD et al (2013) American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 127(4):e362–e425. <https://doi.org/10.1161/CIR.0b013e3182742cf6>
22. Kounis NG (2013) Coronary hypersensitivity disorder: the Kounis syndrome. *Clin Ther* 35(5):563–571. <https://doi.org/10.1016/j.clinthera.2013.02.022>
23. Overgaard CB, Dzavík V (2008) Inotropes and vasopressors: review of physiology and clinical use in cardiovascular disease. *Circulation* 118(10):1047–1056. <https://doi.org/10.1161/CIRCULATIONAHA.107.728840>
24. Laustiola K, Kaukinen S, Seppälä E et al (1986) Adrenaline infusion evokes increased thromboxane B2 production by platelets in healthy men: the effect of beta-adrenoceptor blockade. *Eur J Clin Invest* 16(6):473–479. <https://doi.org/10.1111/j.1365-2362.1986.tb02164.x>
25. Wallén NH, Goodall AH, Li N et al (1999) Activation of haemostasis by exercise, mental stress and adrenaline: effects on platelet sensitivity to thrombin and thrombin generation. *Clin Sci (Lond)* 97(1):27–35
26. Jayamali WD, Herath HMMTB, Kulathunga A (2017) Myocardial infarction during anaphylaxis in a young healthy male with normal coronary arteries—is epinephrine the culprit? *BMC Cardiovasc Disord* 17(1):237. <https://doi.org/10.1186/s12872-017-0670-7>
27. Jackson CE, Dalzell JR, Hogg KJ (2009) Epinephrine treatment of anaphylaxis: an extraordinary case of very late acute stent thrombosis. *Circ Cardiovasc Interv* 2(1):79–81. <https://doi.org/10.1161/CIRCINTERVENTIONS.108.820266>
28. Zakka K, Gadi S, Koshlelashvili N et al (2020) Acute myocardial injury after administration of intravenous epinephrine for allergic reaction. *SAGE Open Med Case Rep*. <https://doi.org/10.1177/2050313X20933104>
29. Cunnington C, McDonald JE, Singh RK (2013) Epinephrine-induced myocardial infarction in severe anaphylaxis: is non-selective β -blockade a contributory factor? *Am J Emerg Med* 31(4):759.e1–2. <https://doi.org/10.1016/j.ajem.2012.11.022>
30. Shaver KJ, Adams C, Weiss SJ (2006) Acute myocardial infarction after administration of low-dose intravenous epinephrine for anaphylaxis. *CJEM* 8(4):289–294. <https://doi.org/10.1017/s1481803500013890>
31. Shrestha B, Kafle P, Thapa S, Dahal S, Gayam V, Dufresne A (2018) Intramuscular epinephrine-induced transient ST-elevation myocardial infarction. *J Investig Med High Impact Case Rep* 6:2324709618785651. <https://doi.org/10.1177/2324709618785651>
32. Tummala K, Maniyal VK, Chandrashekar R et al (2013) Cardiac anaphylaxis: a case of acute ST-segment elevation myocardial infarction after IM epinephrine for anaphylactic shock. *Am J Emerg Med* 31(7):1157.e1–3. <https://doi.org/10.1016/j.ajem.2013.03.025>
33. Park JS, Min JH, Kang JH, In YN (2015) Acute myocardial infarction due to stent thrombosis after administration of intravenous epinephrine for anaphylaxis. *Chin Med J (Engl)* 128(19):2692–2693. <https://doi.org/10.4103/0366-6999.166020>
34. O-uchi J, Komukai K, Tohyama J et al (2003) Coronary artery spasm discovered in thorough examination of perioperative VT in a 26-year-old Japanese male. *Jpn Heart J* 44(6):1021–1026
35. Karch SB (1989) Coronary artery spasm induced by intravenous epinephrine overdose. *Am J Emerg Med* 7(5):485–488. [https://doi.org/10.1016/0735-6757\(89\)90250-7](https://doi.org/10.1016/0735-6757(89)90250-7)
36. Ferry DR, Henry RL, Kern MJ (1986) Epinephrine-induced myocardial infarction in a patient with angiographically normal coronary arteries. *Am Heart J* 111(6):1193–1195. [https://doi.org/10.1016/0002-8703\(86\)90023-2](https://doi.org/10.1016/0002-8703(86)90023-2)

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