

Acute myocardial injury after administration of intravenous epinephrine for allergic reaction

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Abstract

Myocardial injury or infarction in the setting of anaphylaxis can be due to anaphylaxis itself, known as Kounis syndrome, or as a result of treatment with epinephrine. Myocardial ischemia caused by therapeutic doses of epinephrine in the setting of anaphylaxis is a rare event attributed to coronary artery vasospasm. A 41-year-old female with past medical history of recurrent costochondritis, chronic thrombocytopenia, and nonspecific palindromic rheumatism presented to the emergency department with perioral numbness, flushing and throat tightness after a meal containing fish and almonds. Intramuscular epinephrine was ordered but inadvertently administered intravenously, after which she developed sharp, substernal chest pain and palpitations. Electrocardiogram showed normal sinus rhythm with QT interval prolongation. Troponin peaked at 1.41 ng/mL. She was given 324 mg of aspirin in the emergency department. Transthoracic echocardiogram showed normal ejection fraction with lateral wall motion abnormality. We present a case of a patient with no significant risk factors for coronary artery disease who developed myocardial injury following inadvertent IV administration of a therapeutic dose of epinephrine for an anaphylactic-like reaction. The development of myocardial injury after epinephrine is rare, with only six reported cases in literature and just one after intravenous administration. This is the first described case of known myocardial injury without ST-T wave changes on electrocardiogram. The proposed mechanism is an alpha-1 receptor-mediated coronary vascular spasm resulting in myocardial ischemia. The aim of this case is to raise awareness of the potential for acute myocardial injury after inadvertent intravenous administration of epinephrine for anaphylaxis, even in patients with no known risk factors for coronary artery disease, as well as to demonstrate that this clinical scenario can present regardless of troponin elevation and without ST-T wave ECG changes.

Keywords

Myocardial injury, epinephrine, anaphylaxis, allergic reaction

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Background

Myocardial injury in the setting of anaphylaxis can be due to the anaphylaxis itself in an entity known as Kounis syndrome or epinephrine treatment.¹ Kounis syndrome is an acute coronary syndrome occurring in association with conditions that involve mast cell activation and in turn chemical mediators that induce coronary vasospasm resulting in myocardial ischemia and infarction.¹ Myocardial ischemia caused by therapeutic doses of epinephrine in the setting of anaphylaxis is a rare event and is thought to be due to coronary artery vasospasm.² In addition to coronary artery vasospasm, mast cell-derived mediators and epinephrine can cause platelet aggregation leading to thrombotic occlusion of coronary arteries.³

Epinephrine is lifesaving in the treatment of anaphylaxis. It is recommended to give an intramuscular injection of epinephrine 1:1000 up to a maximum dose of 0.5 mg over 5 minutes and to repeat doses after 15 minutes if there is no clinical improvement.⁴ Epinephrine is considered safe for the management of anaphylaxis when given at the correct

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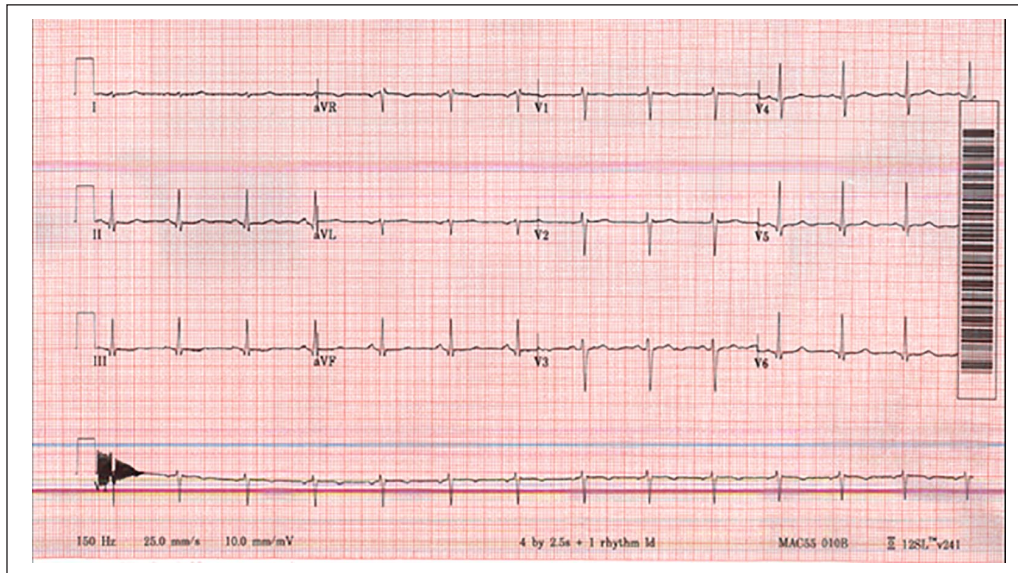


Figure 1. Electrocardiogram (ECG) at presentation (17:55 pm). Normal sinus rhythm. Normal ECG. Vent. Rate 80 bpm, PR interval 134 ms, QRS duration 88 ms, QT/QTc 404/465 ms, P-R-T axes 74 88 45.

dose by the intramuscular (IM) route. The intravenous (IV) route of administration is less often used in anaphylaxis. The majority of cardiovascular adverse events occur when epinephrine is given intravenously or incorrectly dosed.⁵ We report a case in which a therapeutic dose of intravenous epinephrine was used to treat anaphylaxis-like symptoms resulting in an increase in cardiac biomarkers and regional wall motion abnormalities on resting transthoracic echocardiogram but without changes in the electrocardiogram, likely as a result of epinephrine-induced coronary vasospasm.

Case description

A 41-year-old female presented to the emergency department (ED) with anaphylaxis-like symptoms shortly after eating fish and almonds. This was the second ED visit within two days for the same complaint. During her previous visit, she was treated with prednisone 60 mg, famotidine 20 mg, and diphenhydramine 25 mg in the ED with clinical improvement, and was discharged on cetirizine 10 mg daily, prednisone 20 mg daily, and famotidine 20 mg daily. Complete blood count was pertinent for mild thrombocytopenia (platelet count = 125,000/microliter). Basic metabolic panel was unremarkable. Electrocardiogram (ECG) (Figure 1) showed normal sinus rhythm, and chest X-ray was unremarkable for an acute cardiopulmonary process. During her second visit to the ED for the same complaint, the patient had facial flushing but no rash or shortness of breath. She reported nausea, perioral numbness, flushing, tingling, and throat tightness. She denied any chest pain, cough, swelling, or loss of consciousness.

Her past medical history is pertinent to costochondritis, chronic thrombocytopenia, and a nonspecific palindromic

rheumatism. She has a history of mild allergic reaction to trimethoprim-sulfamethoxazole and H1N1 vaccine, but never to food. She has no history of asthma, seasonal allergies or eczema. Family history was pertinent to early cardiac death in a cousin, but no atopy. She has no history of tobacco or drug use and drinks alcohol on social occasions.

Her vital signs upon presentation were the following: blood pressure 137/92 mm Hg, heart rate 90 beats per minute (bpm), temperature 36.2°C, respiratory rate 17 breaths/minute, oxygen saturation of 100% on room air, and a body mass index of 19.2 kg/m². Physical examination revealed a well-appearing woman of stated age in no respiratory distress. She had no swelling in the eyelids/lips/cheeks/tongue, no drooling, no stridor, and no voice changes. Cardiovascular and pulmonary examination was normal. There was no rash on examination of her skin. The rest of the examination was otherwise normal. She was given prednisone 60 mg and diphenhydramine 25 mg, and IM epinephrine was ordered as initial therapy but she was inadvertently administered IV epinephrine (0.3 mg). Shortly after this dose, she developed sharp central chest pain and palpitations, with a maximum heart rate of 99 bpm. Results of an ECG revealed normal sinus rhythm, QTc prolongation, and no ST-T wave changes (Figure 2). She received one dose of aspirin (324 mg). Increased severity of her chest pain improved over the course of two hours, after which she described her chest pain as similar to that of her previous episodes of costochondritis. She denied any previous chest pain with exertion. In addition to the previous lab tests performed, a serum TSH, d-dimer, lipid panel, and urinalysis were performed and were normal. Her labs were significant for mild thrombocytopenia (platelets = 131,000), glucose 149 mg/dL, and troponin 0.05 ng/mL (normal: < 0.03 ng/mL). Serial troponins were performed

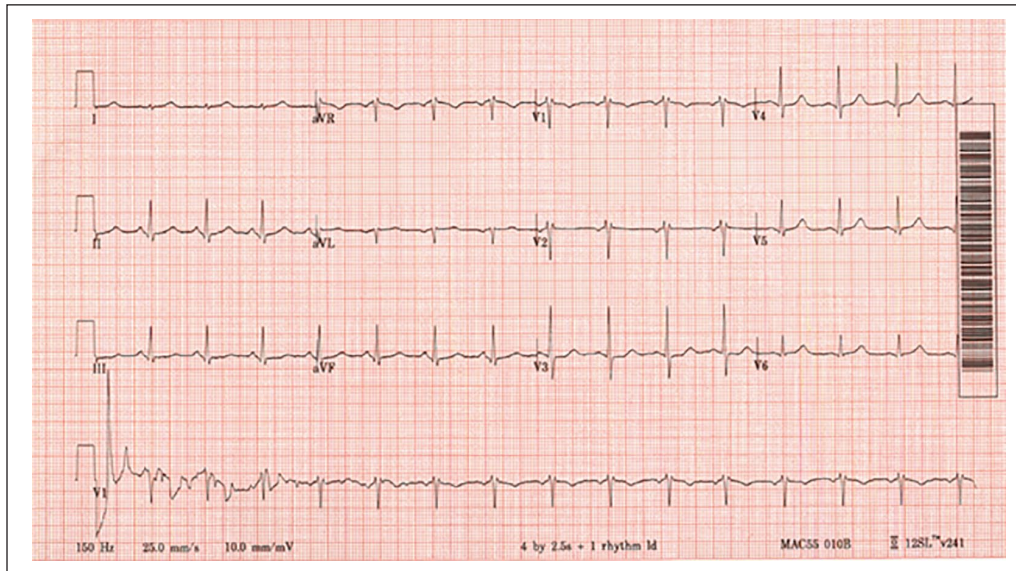


Figure 2. ECG after IV administration of epinephrine (18:26pm). Normal sinus rhythm. Prolonged QT. Abnormal ECG. Vent. Rate 91 bpm, PR interval 122ms, QRS duration 98ms, QT/QTc 392/482ms, P-R-T axes 83 87 50.

Table 1. Troponin trend.

Time	Troponin I (ng/mL) (normal value < 0.03)
18:40 pm	0.05
22:09 pm	0.98
00:09 am	1.04
04:32 am	1.30
06:32 am	1.41 (peak)
08:04 am	1.34

with peak troponin of 1.41 ng/mL (Table 1). A third ECG was performed, which demonstrated normal sinus rhythm with sinus arrhythmia, rightward axis, and no ST-T wave changes (Figure 3).

The patient was admitted to hospital for observation. Due to the patient's age, lack of cardiac risk factors, close correlation between her symptoms and the administration of epinephrine, and ECG with no ST-T wave changes, the consulting cardiology team concluded that plaque rupture was unlikely to be the etiology of the patient's symptoms. She was started on aspirin 81 mg daily. A transthoracic echocardiogram (TTE) was done twenty hours after symptoms started to evaluate for structural heart disease that may have predisposed the patient. Her cardiac echocardiogram showed a normal left ventricular size measuring 4.9 cm, low-normal left ventricular ejection fraction (50%), elevated right atrial pressure (dilated inferior vena cava, with respiratory size variation less than 50%), and left ventricle lateral wall abnormality (Figure 4; <https://www.youtube.com/watch?v=soLXgVVLXppU>).

The left ventricle's mid-inferolateral segment and mid-anterolateral segment were akinetic, and the mid-inferior segment was hypokinetic. Given these findings, a coronary

computed tomography angiography (CCTA) or nuclear perfusion stress test was recommended; however, the patient declined testing and was discharged home with plans to do further workup in the outpatient setting.

Discussion

Epinephrine-induced myocardial ischemia in the setting of treatment of anaphylaxis has been reported on rare occasions. To date, six cases were reported where therapeutic doses of epinephrine had caused myocardial infarction.¹ Out of these reports one was after IV injection, two after IM injection, and three after subcutaneous injection. It has been suggested that patients with multiple risk factors for coronary artery disease (CAD) may be more susceptible to complications of epinephrine injection.⁶ However, the six case reports were of relatively young individuals without risk factors for CAD, as was the case in this report. The patients of the six case reports all developed myocardial infarction after the use of epinephrine with ST wave changes detected on ECG, which was not seen in our patient.

Experimentally, epinephrine is known to induce spasm in susceptible patients, and has been used to diagnose Prinzmetal's angina.⁷ Epinephrine has a high affinity for beta-1/beta-2 receptors at low doses and alpha-1/alpha-2 receptors at higher doses in cardiac and smooth muscles of the vascular walls.⁸ Stimulation of beta-1/beta-2 receptors leads to increased cardiac contractility, rate, and dilates coronary arteries, whereas alpha-1/alpha-2 receptors mediate vasoconstriction including that of the coronary vasculature.⁸

This patient is a 41-year-old relatively healthy female who did not have any modifiable or non-modifiable risk factors for CAD. She developed chest pain few minutes after

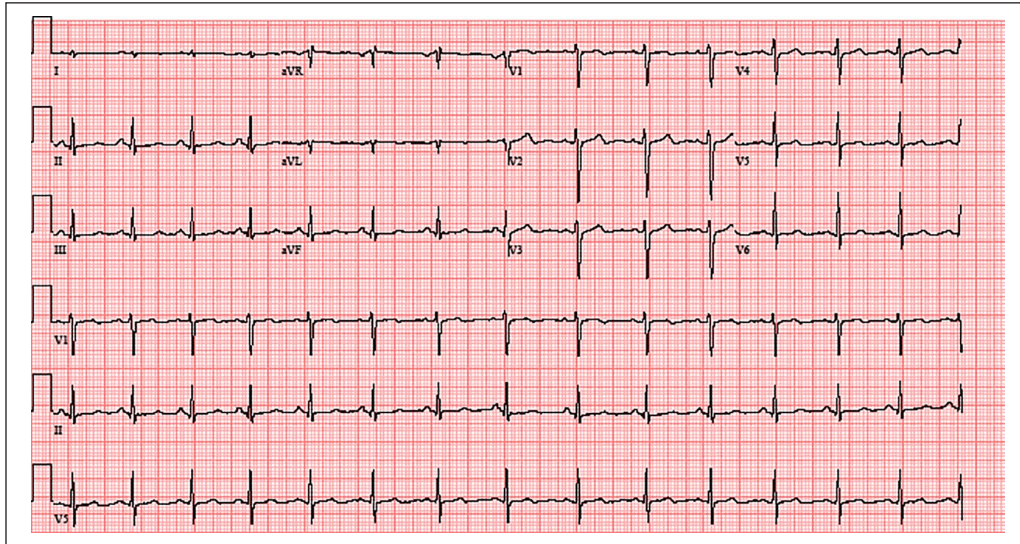


Figure 3. ECG after IV administration of epinephrine (08:23 am). Normal sinus rhythm with sinus arrhythmias. Rightward axis. Borderline ECG. Vent. Rate 86 bpm, PR interval 134 ms, QRS duration 88 ms, QT/QTc 362/433 ms, P-R-T axes 75 91 72.

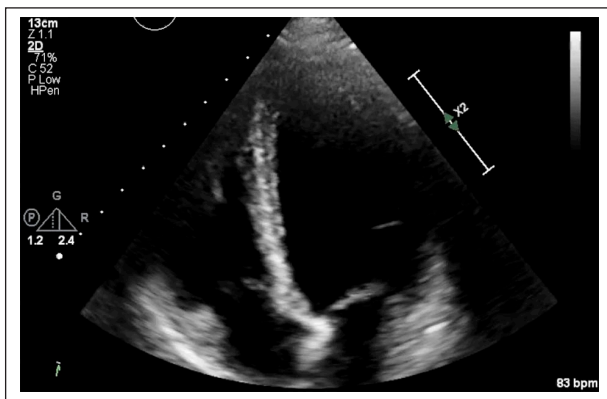


Figure 4. Transthoracic echocardiogram (TTE) video clip demonstrating left ventricle lateral wall abnormality.

administration of epinephrine. There were no ECG changes; however, cardiac biomarkers increased and left ventricle lateral wall abnormalities were seen on echocardiogram. Mechanisms of microvascular myocardial infarction with non-obstructive coronary arteries involve microvascular coronary spasm, Takotsubo syndrome, myocarditis, and coronary thromboembolism.⁹ We believe this temporal relationship is more in favor of epinephrine as the cause of chest pain and myocardial injury rather than Kounis syndrome since the patient was treated for anaphylaxis in a previous admission with antihistamines, and her chest pain did not begin until after administration of epinephrine. The patient denied chest pain with her allergic symptoms, and the nature of the chest pain changed dramatically after the administration of epinephrine into a “sharp, pressing” pain. The postulated mechanism is an alpha-1 receptor-mediated coronary vascular spasm. In addition, it is unlikely that the

patient experienced coronary vasospasm secondary to Takotsubo since the characteristic apical left ventricle ballooning¹⁰ was not seen on initial TTE. Furthermore, Takotsubo is associated with electrocardiogram changes mimicking a myocardial infarction of the anterior wall,¹⁰ which also was not seen in our patient.”

The most likely cause of the anaphylaxis-like reaction was the fish and/or almonds due to the temporal relationship of the symptoms beginning shortly after ingestion. The use of epinephrine in this case is debatable as there were no respiratory symptoms at presentation. However, some authors have suggested that emergency physicians should be treating more patients with anaphylaxis with the use of epinephrine.¹¹ Although most documented adverse events have been associated with IV administration,¹² opinions differ on the use of IV epinephrine for anaphylaxis. Brown *et al.* used it successfully in anaphylaxis secondary to insect stings.¹³ It is also considered to be a preferred route in some instances where an IV line is in place (e.g. during surgery), but potential lethal arrhythmias have been seen with IV epinephrine, thus careful monitoring is encouraged.¹⁴ Overall, the recommendation is to use IM epinephrine as the preferred route of administration. Although IM epinephrine was ordered in our case, IV epinephrine was inadvertently given. Ultimately, this patient did well clinically and will likely not have any permanent sequelae. Patient had repeat echocardiogram one month post discharge with the resolution of wall motion abnormality, and a nuclear stress test showed no coronary ischemia six months post discharge.

Patients at the risk of developing coronary artery spasms following the administration of epinephrine is an area that is understudied. Old age, preexisting CAD, and the use of beta blocker were some of the risk factors for epinephrine-induced myocardial ischemia reported in the literature.^{11,15,16}

Even though myocardial injury could occur on rare occasions with therapeutic doses of epinephrine, this should not discourage the early use of epinephrine as a lifesaving medication in anaphylaxis. The physician should be made aware of this potential adverse effect of epinephrine in this clinical setting and take the remediable steps if necessary.

Conclusion

This case report describes the first reported case of cardiac complications with IV epinephrine without ischemic findings on electrocardiogram. Epinephrine is still the mainstay of the treatment of anaphylaxis but we hope physicians will be aware of this potential adverse effect, which can occur in patients with no risk factors for CAD in the acute setting.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Written informed consent for patient information and images to be published was provided by the patient on 8 September 2018. Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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