Case report

Kounis syndrome: ST elevations in the setting of anaphylaxis

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Acute coronary syndrome in the presence of an allergic reaction is known as Kounis syndrome, which is an underdiagnosed disorder and has nuances regarding management. We present a patient brought to the hospital as an ST segment elevation myocardial infarction (STEMI) alert in the setting of an allergic reaction triggered by food. (J Allergy Clin Immunol Global 2023;2:100152.)

Key words: *Anaphylactic shock, STEMI, Kounis syndrome, angioedema*

Kounis syndrome is described as acute coronary syndrome in the presence of an allergic reaction. The association between allergic reactions and acute coronary syndrome was first noted in 1950 in a case involving a penicillin-induced allergic reaction complicated by myocardial infarction.[1] In 1991, Kounis and Zavras demonstrated that allergic mediators could induce coronary vasospasm, leading to an allergic acute coronary syndrome.[2] Kounis syndrome is thought to be underdiagnosed rather than a rare disorder.[3] One study demonstrated a prevalence of Kounis syndrome of 1.1% in patients hospitalized for allergic reaction.[3,4] Understanding both the pathophysiology and presentation of Kounis syndrome is important for emergency medicine providers to aid in diagnosis and recognize nuances in management of these patients. In this case report, we describe a case of ST segment elevations on an electrocardiogram (ECG) in the setting of anaphylactic shock.

Abbreviations used
ECG: Electrocardiogram
EMS: Emergency medical services

CASE PRESENTATION

Patient information

A 41-year-old male with a medical history significant for hypertension necessitating that the patient was brought in by emergency medical services (EMS) personnel as an ST segment elevation myocardial infarction alert. The EMS personnel report included an ECG with ST segment elevations in leads V1 through V4. The patient was given aspirin and nitroglycerin by the EMS personnel. On arrival at the hospital, the patient denied chest pain and shortness of breath. He stated that he called EMS because he had been at a barbecue at which he ate 2 grapes. Shortly after this, he started to feel mucus in his throat and noted facial swelling. While in the ambulance, he vomited multiple times. He stated that he felt as if he was having abdominal cramping and was about to have diarrhea. He reported taking loratadine at home. The patient stated that he had experienced multiple similar reactions after eating bananas and chocolate and peanut butter candy.

The patient's medical history was significant for hypertension and gastroesophageal reflux disease. He reported taking 0.1 mg of clonidine 3 times per day, 20/12.5 mg lisinopril/hydrochlorothiazide daily, and 10 mg of amlodipine daily. He had been taking lisinopril since 2016.

Clinical findings

The patient's initial vital signs showed a blood pressure of 91/60 mm Hg, heart rate of 94 beats per minute, respiratory rate of 14, oxygen saturation of 100% in room air, and temperature of 36.6°C. His physical examination findings included upper and lower lip edema and periorbital edema. No intraoral swelling was present. All respiratory, abdominal, and skin examination findings were normal.

Diagnostic assessment and therapeutic intervention

When the patient was transported to his room, his blood pressure dropped, with a systolic blood pressure in the 70s. His point-of-care glucose level was 182 mg/dL. A dose of 0.3 mg of intramuscular epinephrine was given, leading to an improvement in blood pressure to 133/82 mm Hg. Subsequently, 125 mL of intravenous methylprednisolone and 40 mg of intravenous famotidine were given as adjunctive therapy. The patient also received 2 L of normal saline.

The patient's initial EMS ECG results were as follows: sinus rhythm with normal intervals and axis, ST segment elevated present in leads V1 to V4, and no reciprocal ST depressions.

A repeat ECG at the time of the patient's arrival at the hospital (Fig 1) showed sinus rhythm with rate 94 beats per minute, normal intervals, and normal axis. ST elevations were present

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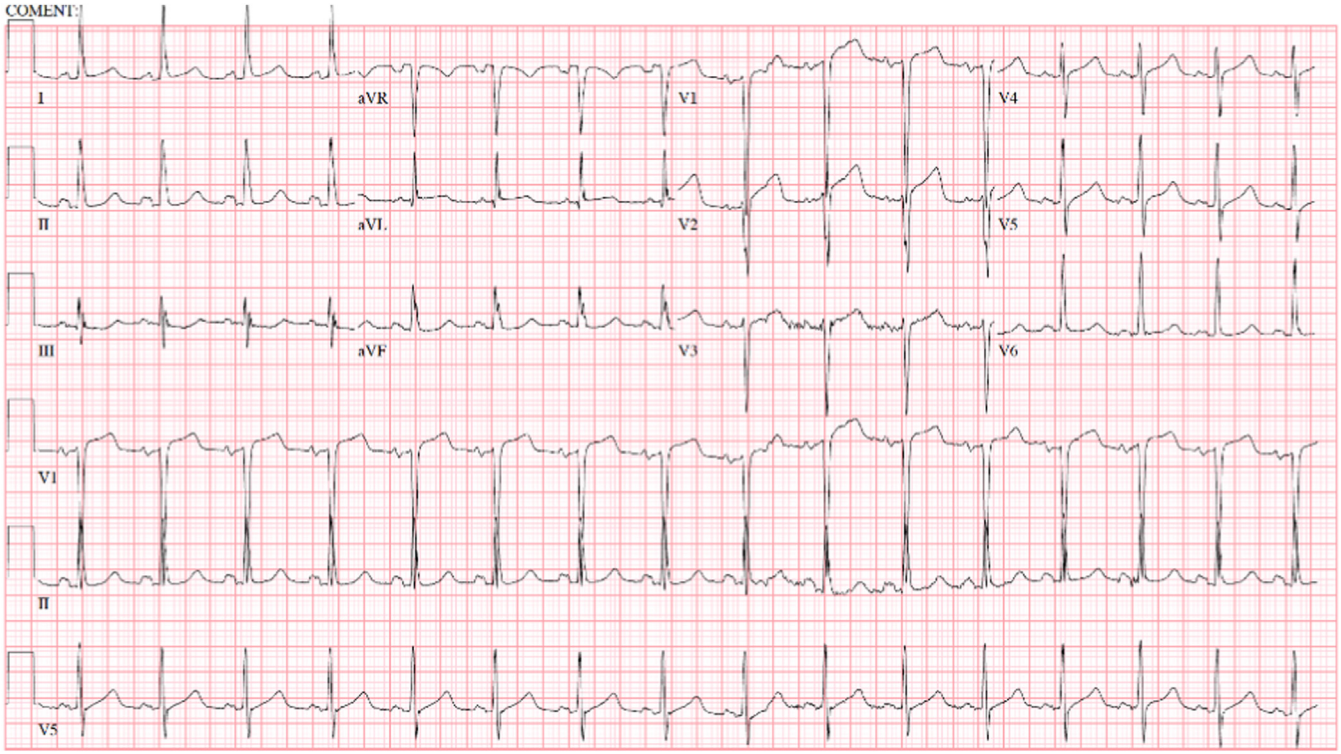

FIG 1. ECG taken on the patient's arrival at the hospital. ST elevations seen in leads V1 to V3.

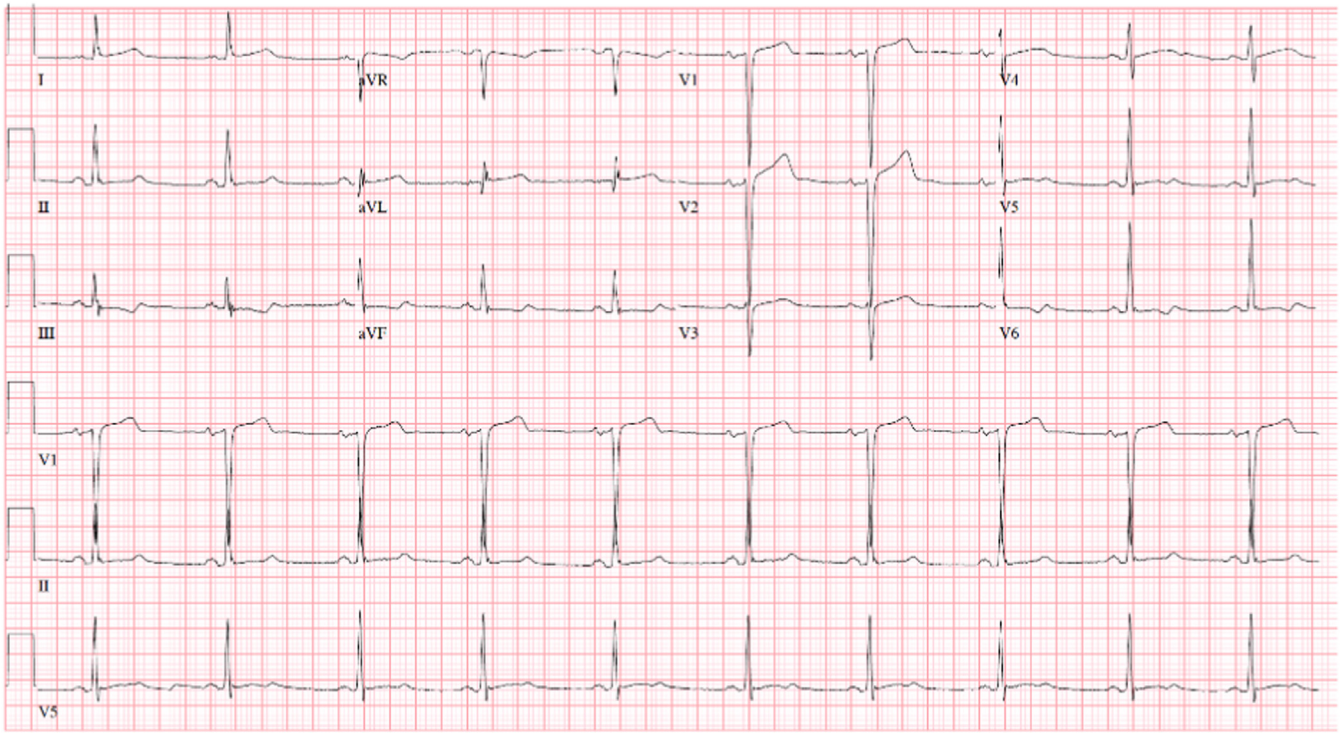

FIG 2. Improvement noted in ST elevations. Almost complete resolution of ST elevations in leads V1 and V3, with minimal elevation present in lead V2. The patient no longer meets the ST segment elevation myocardial infarction (STEMI) criteria.

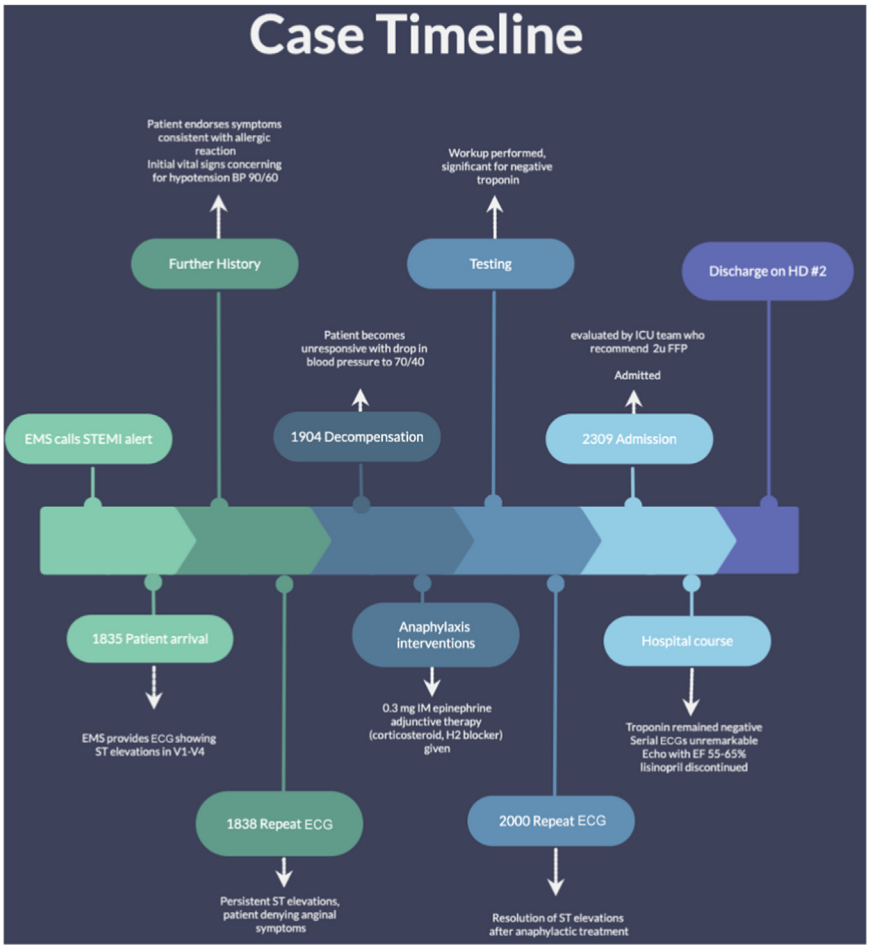

FIG 3. Case time line.

in leads V1 through V3. No reciprocal ST depressions were found.

A repeat ECG at 2000 (after medication interventions) (Fig 2) showed sinus rhythm with a rate of 60 beats per minute, normal intervals, and normal axis. Marked improvement was seen in the ST elevations previously seen in leads V1 to V3. Leads V1 and V2 showed minimal ST elevation, and the V3 ST elevation had completely resolved.

In addition to ECGs, the patient had a workup significant for normal chest radiograph findings. The patient was found to have leukocytosis (14.4×10^3 cells/μL). Mild hyponatremia of 134 mEq/L was present. His creatinine level was 1.69 mg/dL with a blood urea nitrogen level of 12 mg/dL. All of his liver function test results were normal. His troponin level was less than 0.02 ng/mL. His brain natriuretic peptide level was 654 pg/mL, which was mildly elevated. The patient had a normal partial thromboplastin time and normal prothrombin time and international normalized ratio.

On reevaluation at 2132, the patient was feeling improved, with resolution of his gastrointestinal symptoms. His vital signs remained within normal limits. The intensive care unit was consulted; its staff deemed the patient to be stable for an intermediate level of care. They recommended 2 units of fresh frozen plasma. At this time, the patient was admitted to an intermediate level of care.

Time line

For the time line, see Fig 3.

Follow-up and outcomes

The patient was admitted, and a cardiology consultation was obtained because of his abnormal ECG findings in the emergency department. His troponin values continued to trend negative. His repeat ECGs after admission showed signs of left ventricular hypertrophy but no acute coronary syndrome.

A repeat ECG on hospital day 1 (Fig 4) showed further improvement

The patient's lisinopril/hydrochlorothiazide was discontinued. An echocardiogram was done; it showed normal left ventricular systolic function with an ejection fraction of 55% to 60%. Mildly increased wall thickness and concentric hypertrophy were found, but there were no wall motion abnormalities. The patient was discharged with instructions to follow up with primary care. The patient was discharged with an epinephrine autoinjector for any future reactions.

DISCUSSION

The precise definition of anaphylaxis is debated. In general, however, anaphylaxis is typically defined as a multisystem

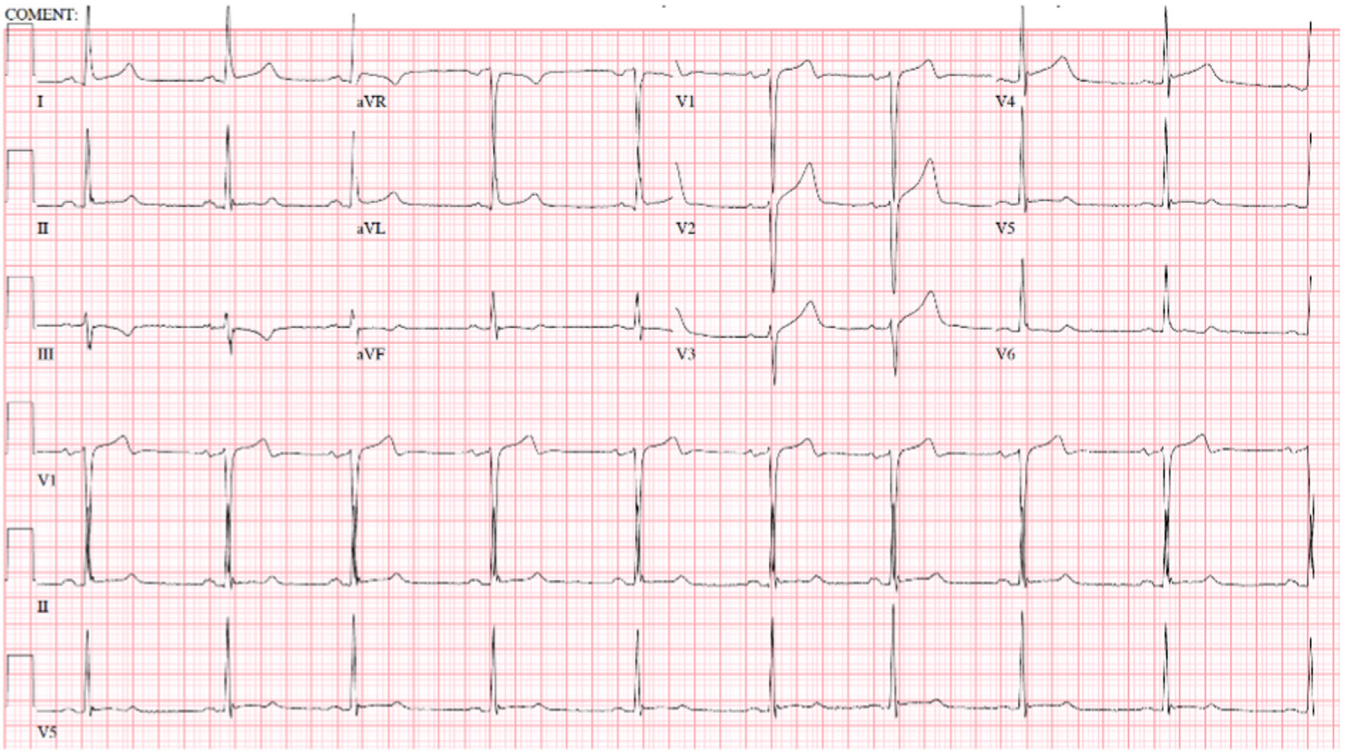

FIG. 4. Further improvement in ST elevations on hospital day 1.

TABLE I. Defining anaphylaxis

Rapid onset of the following symptoms within seconds to minutes, possibly in the setting of an allergic trigger:
Presence of skin or mucosal involvement (erythema, urticaria, pruritus, and/or edema)
AND any of the following:
● Respiratory system involvement manifested by dyspnea, stridor, wheezing, and/or hypoxia
● Gastrointestinal system involvement manifested by abdominal cramping, nausea, vomiting, and/or diarrhea
● Signs of end organ dysfunction manifested by syncope, hypotension, and/or tachycardia

Data from Turner et al,[5] Tupper et al,[6] and Manivannan et al.[7]

reaction to an allergic trigger occurring within seconds to minutes, with common symptoms including skin findings (including urticarial rash, erythema, and edema) and involvement of other organ systems.[5,6] Common organ systems include respiratory (dyspnea, wheezing, stridor, and mucosal edema), gastrointestinal (abdominal cramping, nausea, vomiting, and diarrhea), and cardiovascular (syncope and reduced blood pressure).[5,6] Table I[5-7] shows the definition of anaphylaxis in more detail.

Anaphylaxis results from the development of antigen-specific IgE antibodies.[8] When a person is reexposed to the antigen, IgE antibodies bind these antigens, resulting in formation of complexes otherwise known as a type I hypersensitivity reaction.[8] Both mast cells and basophils contain high-affinity receptors for the IgE antigen antibody complexes.[8] These IgE antigen-antibody complexes can bind mast cells and basophils via cross-linking, causing subsequent activation of these cells.[8,9] This results in a process known as degranulation.[2,6] Degranulation leads to a release of several inflammatory mediators, including histamine, TNF-α, tryptase, phospholipase A2, and leukotrienes.[8,10] These mediators bind receptors and lead to several of the clinical signs and symptoms of anaphylaxis, including bronchoconstriction, vascular permeability, and peripheral vasodilation.[8] Histamine causes vasodilation, increased vascular permeability, elevated heart rate, and increases in cardiac contractility.[6,8-10]

The mechanism of anaphylaxis plays an important role in understanding Kounis syndrome. Acute coronary syndrome is a rare presentation of anaphylaxis. This phenomenon is known as Kounis syndrome or allergic acute coronary syndrome.[11] As in anaphylaxis, in Kounis syndrome an allergic insult results in release of inflammatory mediators, notably histamine.[11-13] In addition to causing peripheral vasodilation, histamine can act on coronary histamine receptors that lead to vasospasm and constriction of coronary vessels.[2,10,13,14] This vasospasm leads to the clinical manifestations of Kounis syndrome, which includes various ECG changes (including but not limited to ST segment elevations, ST segment depressions, heart block, and other cardiac arrhythmias).[13,14] ST segment elevations are considered the most common ECG change associated with Kounis syndrome.[15] The clinical manifestations of Kounis syndrome are broad and include classic anginal symptoms, including chest pain, dyspnea,

palpitations, and sudden cardiac death[13-15]; 25% of patients will have a medical history of allergic reaction, and 53% of patients will present with anaphylaxis.[15]

Kounis syndrome has been described as having 3 major variants. Type I occurs in patients without known preexisting coronary artery disease, who after release of inflammatory mediators from mast cell degranulation develop coronary artery vasospasm without elevated cardiac biomarkers or progression to an acute coronary syndrome.[11] In contrast, the type II Kounis variant occurs in patients with preexisting coronary artery disease.[11,13] In this variant, inflammatory mediators cause vasospasm that results in plaque rupture and subsequent myocardial infarction.[11] Lastly, the type III Kounis variant results from inflammatory mediators leading to stent thrombosis.[11]

Diagnosing Kounis syndrome can be difficult. One way to help screen for this condition includes performing an ECG and measuring troponin levels in patients presenting with anaphylaxis.[16] In addition to the clinical features, the ECG findings, and troponin values, there are other diagnostic tests to consider. Histamine levels can be helpful, but they need to be collected within 10 minutes after onset of symptoms, given its short half-life.[16] Tryptase levels are another known marker of anaphylaxis; they can be measured 30 minutes after the event and trended.[16] IgE levels are another marker that have been shown to be elevated in Kounis syndrome.[16,17] In addition, newer imaging techniques, including thallium-201 single-photon emission computer tomography (SPECT) and dynamic cardiac magnetic resonance imaging have been used to show myocardial ischemia and diagnose Kounis syndrome.[18] This is of particular importance in diagnosing the type I variant of Kounis syndrome, as these patients may not have elevation in cardiac biomarkers or evidence of ischemia on coronary angiography.[18]

It is important to keep Kounis syndrome on the differential for patients presenting with symptoms concerning for acute coronary syndrome or with symptoms consistent with an allergic reaction because it has implications regarding management. Important general considerations include avoidance of morphine for treatment of anginal symptoms, as it could worsen mast cell degranulation, thereby worsening vasospasm.[11,14] Fentanyl is a better option for pain control if needed.[14] Epinephrine is the cornerstone of treatment of anaphylactic shock.[6] However, in the setting of Kounis syndrome, it can worsen vasospasm.[6] Furthermore, it can have a negative impact by prolonging the QT interval and inducing arrhythmias.[15] If epinephrine is used, providers should choose sulfite-free intramuscular epinephrine.[14] When hemodynamic stability is present, antihistamines, steroids, and removal of the allergic insult are indicated in the management of Kounis syndrome.[9,14] The emergency care provider should also provide standard of care acute coronary syndrome treatments. Despite the unknown effects of aspirin on allergic reaction pathways, it should be administered to patients with suspected Kounis syndrome, given its clear benefits in treatment of acute coronary syndrome.[9] Vasospasm is reduced by use of vasodilating medications such as nitroglycerin or calcium channel blockers, which can be given if the patient is hemodynamically stable.[14] β-Blockers are frequently used in the management of acute coronary syndrome; however, in the setting of Kounis syndrome, they could worsen vasospasm through an unopposed α-effect and should be avoided.[11,14] Use of β-blockers leads to less effective treatment of allergic symptoms.[9,14] In these patients, reversal of the β-blocker with glucagon may be useful by bypassing the β-adrenergic pathway, and stimulating myocardial contractility and heart rate through glucagon is recommended.[9]

CONCLUSION

It is important for emergency physicians to consider Kounis syndrome in the differential diagnosis of patients presenting to the emergency department with allergic reactions. ECG changes, troponin elevations, or anginal symptoms in these patients indicate possible Kounis syndrome. Knowledge of Kounis syndrome in the acute care setting can help tailor the management of both acute coronary syndrome and allergic reactions/anaphylaxis.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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