

Challenges in Clinical Electrocardiography

Electrocardiographic Changes After Overdose of Epinephrine in a Patient With Anaphylaxis

Kounis Syndrome or Epinephrine?

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An adult man underwent coronary computed tomography angiography (CTA) to evaluate intermittent chest tightness with normal electrocardiogram (ECG). One minute after undergoing CTA, he developed shortness of breath, wheezing, flushing, and then loss of consciousness, with heart rate and blood pressure dropping to 50 bpm and 60/45 mm Hg, respectively, within 5 minutes. He was treated with 1 mg of epinephrine (1:1000) by intravenous (IV) bolus. A few minutes later, he regained consciousness but developed chest discomfort, with new-onset ST elevation in leads II, III, and aVF and ST depression in leads I, aVL, and V1 through V3 (Figure).

He was transferred to cardiac care unit. On physical examination, no abnormality was found except for blood pressure of 85/34 mm Hg. The results of electrolyte and myocardial enzyme assays were normal.

Questions: What is the most likely cause of his ECG changes? What would you do next?

Interpretation and Clinical Course

The patient was injected with 5 mg of dexamethasone intravenously. His symptoms improved, and ST elevation returned within

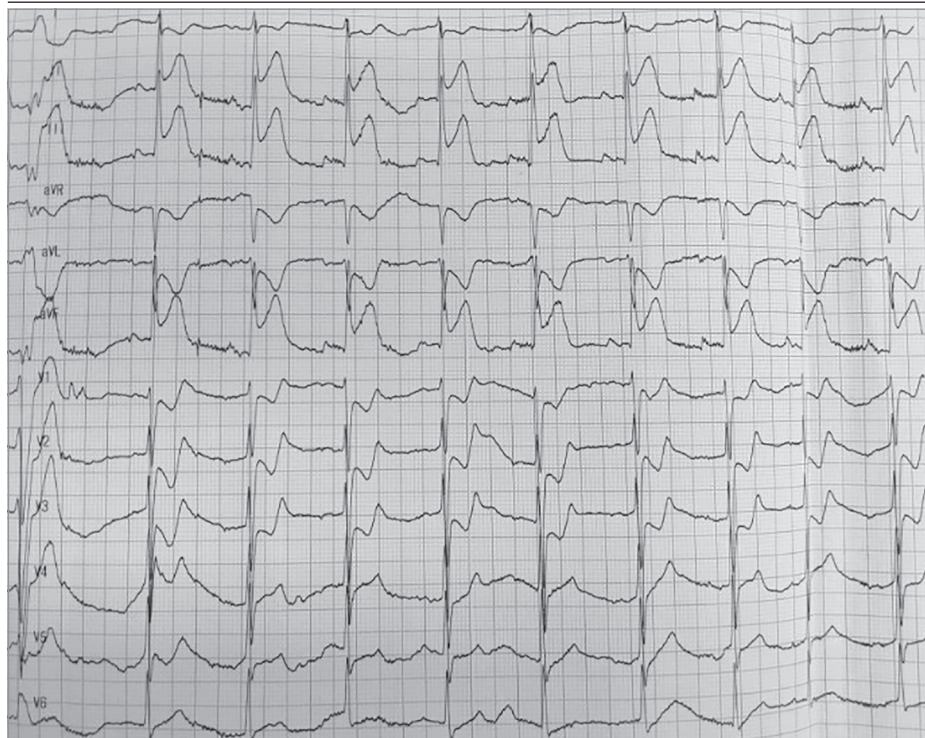
16 minutes, suggestive of coronary spasm. A bedside echocardiogram showed no wall motion abnormality, with ejection fraction of 67%. Coronary CTA revealed no significant coronary artery disease. His troponin I level was 0.091 ng/mL at 24 hours after presentation and had reduced to normal levels by 48 hours.

Discussion

Anaphylaxis is an acute, life-threatening clinical emergency that may be triggered by foods, insect stings, or medications. Contrast agents are one of the most common triggers of iatrogenic anaphylaxis. In the present case, the diagnosis of anaphylactic shock is clear, based on the rapid onset of multiple symptoms and signs after exposure to the iodinated contrast. For the transient ECG changes after the onset of anaphylaxis and treatment with epinephrine, there are several possible causes.

The most likely cause is Kounis syndrome (KS), a hypersensitivity coronary disorder induced by exposure to drugs, foods, and other triggers. It was first described in 1991 by Kounis and Zavras¹ as "the syndrome of allergic angina" due to coronary artery spasm provoked by the release of histamine. It is now defined as the

Figure. Electrocardiogram After Intravenous Overdose of Epinephrine for Anaphylactic Shock



concurrence of acute coronary syndromes (ACS, including vaso-spasm, plaque rupture, and stent thrombosis) associated with mast cell activation in the setting of allergic or anaphylactic insults.² The acute release of inflammatory mediators, such as histamine, platelet-activating factor, and a variety of cytokines and chemokines, may induce coronary artery spasm (type I variant) with or without increased myocardial enzymes.

The second possible cause is adverse effect of epinephrine. According to international guidelines, epinephrine (adrenaline) is the first-line drug of choice for anaphylaxis, but it should be injected intramuscularly at a dose of 0.01 mg/kg of a 1:1000 (1 mg/mL) solution, to a maximum dose of 0.5 mg in adults.³⁻⁵ Epinephrine exerts effects on (1) α 1 receptors causing peripheral vasoconstriction; (2) β 1 receptors increasing both the rate and force of cardiac contractions; and (3) β 2 receptors reversing bronchoconstriction and reducing the release of inflammatory mediators. Both α (1- and 2-) and β 1-adrenergic receptors are present in the coronary arteries but with different distributions.⁶ The large coronary arteries are equipped mainly with α receptors, which mediate contraction. Overdoses of epinephrine, for example, IV bolus administration, overly rapid IV infusion, and dosing error because of IV injection or IV infusion of the 1:1000 (1 mg/mL) solution appropriate for intramuscular injection, instead of the dilute solutions appropriate for IV administration (1:10 000 [0.1 mg/mL] or 1:100 000 [0.01 mg/mL]), may contribute to coronary spasm.⁷

For the differential diagnosis, takotsubo syndrome (TTS) should be considered. Characterized by a sudden-onset, temporary wall motion abnormality of the left ventricle (LV), TTS shares common features with ACS including similar symptoms, ECG changes, and elevated cardiac biomarkers. It was first reported by Sato et al⁸ described 5 cases in 1990.⁸ Takotsubo syndrome is also referred to as "stress cardiomyopathy," "broken-heart syndrome," and "apical ballooning syndrome" in the literature.⁹ Although the pathophysiologic mechanisms of TTS remain incompletely understood, sympathetic stimulation is considered central to its pathogenesis. Moreover, TTS is associated with catecholamine excess that is either administered exogenously or secreted by neuroendocrine tumors.⁹ However, in the present case, a transthoracic echocardiogram

performed 3 hours after the onset of anaphylaxis showed no LV wall motion abnormality or LV dysfunction, which is essential for the diagnosis of TTS. So, it was unlikely that the cause is TTS.

Another hypersensitivity-associated coronary syndrome, ATAK (adrenaline, Takotsubo, anaphylaxis, and KS), should also be considered. It has been emphasized that ATAK constitutes a challenging contemporary complex.¹⁰ Anaphylactic reaction can induce KS by activation of inflammatory cells such as mast cells. These cells release inflammatory mediators such as histamine, which stimulate the release of catecholamine. Moreover, compensatory catecholamine released by the renin-angiotensin-aldosterone system during the anaphylactic process, as well as administration of epinephrine for hemodynamic support of anaphylactic shock, would also increase the level of plasma catecholamine, which can induce TTS and perpetuate this vicious cycle.

In the present case, the patient's ECG changes could be most likely explained by KS with sudden coronary spasm and therapeutic response to glucocorticoids. Meanwhile, he received an overdose of epinephrine for anaphylaxis, which may also induce coronary spasm. But epinephrine seems less likely to be the cause with the absence of other symptoms or signs typically induced by epinephrine overdose such as tachycardia. However, without evidence of LV dysfunction, it is not possible for TTS, or even ATAK, to explain the ECG changes.

Take-Home Points

- Both KS and TTS could occur in anaphylaxis and induce ACS including coronary artery spasm, but TTS is characterized by a temporary LV wall motion abnormality.
- In anaphylaxis, epinephrine should be injected intramuscularly at a dose of 0.01 mg/kg of a 1:1000 (1 mg/mL) solution, to a maximum of 0.5 mg in adults. Overdose of epinephrine may increase the risk of contribution to coronary spasm and TTS.
- ATAK constitutes a challenging contemporary complex in anaphylaxis. It is vital to use epinephrine correctly and monitor vital signs and ECGs for patients with acute anaphylaxis.

ARTICLE INFORMATION

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