

Acute Myocardial Injury Following Penicillin-Associated Anaphylactic Reaction in a Patient With Normal Coronary Arteries

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ABSTRACT: Cardiac involvement is uncommon and important clinical finding during an anaphylactic reaction, and it occurs primarily in subjects with underlying ischemic heart disease. The main mechanism proposed is the vasospasm of coronary arteries. We report a rare case of acute ST-elevation myocardial injury after penicillin-induced anaphylaxis in a patient with normal coronary arteries. Physicians should be alert for such a

serious complication in order to diagnose it early and treat properly. We suggest that cardiac monitoring and appropriate therapy should be available for patients with severe allergic reactions especially during parenteral administration of epinephrine. **KEY INDEXING TERMS:** Anaphylaxis; Myocardial injury; Epinephrine; Penicillin; Mast cells. [*Am J Med Sci* 2007;334(4):305–307.]

Cardiac involvement in allergic reactions to drugs or other chemicals is uncommon, and only sporadic cases have been reported. Antibiotics have been rarely reported in allergy-induced acute coronary syndromes. Cardiac involvement represents an important clinical finding during an anaphylactic reaction and it occurs primarily in subjects with underlying ischemic heart disease. The main mechanism proposed is the vasospasm of coronary arteries. We report a rare case of acute ST-elevation myocardial injury after penicillin-induced anaphylaxis in a patient with normal coronary arteries. The case provides insight into the pathophysiology of anaphylaxis-induced myocardial injury.

Case Report

A healthy, 55-year-old Caucasian woman presented to the emergency department (ED) because of anaphylaxis. The patient was seen on the day of admission by her family physician because of sinusitis and was given an intramuscular (IM) injection of penicillin. 3 minutes later, she became dizzy, hypotensive, tachycardic, and had generalized urticaria. The patient was given oxygen; epinephrine (0.2 mg), or 0.2 mL of a dilution 1:1000 was injected subcutaneously, 50 mg diphenhydramine, dopamine, and bolus 500 mL of normal saline were administered intravenously. Due to unsatisfac-

tory clinical response (persistence of hypotension and tachycardia), two more doses of epinephrine SQ (0.2 mg and 0.3 mg) were given 20 and 40 minutes later, respectively, and she was sent to the ED. She had no history of having taken other medications, herbal remedies, or any illicit drugs. Furthermore, she had no history of drug or food allergies and had no recent travel.

On arrival, the patient was lethargic, with blood pressure (BP) of 85/60 mm Hg, pulse of 98 beats per minute, and regular respiratory rate of 24 breaths per minute, temperature of 98.3°F, and oxygen saturation (SpO₂) of 95%. Physical examination was remarkable for generalized skin urticaria. The lungs, heart, abdomen, and neurologic examinations were normal. The patient was in sinus rhythm on the monitor. Patient was treated with oxygen, intravenous corticosteroid (125 mg methylprednisolone), H₂ blocker (30 mg cimetidine), normal saline, and H₁ blocker (25 mg diphenhydramine). Twenty minutes into the resuscitation, the patient's BP was 101/65 mm Hg, her mental status was dramatically improved, and the skin urticaria had started to resolve. ST-segment elevation developed on the lead II monitor. A 12-lead electrocardiogram (ECG) showed marked ST-segment elevation in leads II, III, AVF, and V₄ to V₆, and ST-T segment depression in leads V₁ to V₃, compatible with acute inferolateral myocardial infarction. The patient did not have any chest pain at that time. In the next 3 minutes, ST-segment elevations resolved followed by high T waves in leads II, III, and AVF, and deep T waves inversion in leads AVL and V₁ to V₃. Significant laboratory findings included serum potassium 2.8 mmol/L (normal = 3.5 to 5.0 mmol/L), and WBC 17.0 × 10³/mm³. The initial serum levels of creatine kinase (CK) and troponin I were within normal limits: 70 U/L and 0.00 ng/mL, respectively. She was admitted to the intensive care unit (ICU) and underwent coronary angiogram that showed no evidence of obstructive coronary artery disease. Subsequent ECG showed only slight T-wave inversion in leads III and V₁, and serial cardiac enzymes levels remained normal. The patient recovered completely and was discharged home within 48 hours.

Discussion

Cardiovascular complications in the setting of anaphylaxis have been described primarily in patients with underlying ischemic heart disease^{1,2} and rarely in

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individuals with normal coronary arteries.³⁻⁷ Acute coronary syndrome after antibiotic-induced anaphylaxis is uncommon and only few cases have been reported.^{1,3,5,8-10} Penicillins were the most common antibiotics leading to anaphylaxis in these cases. A number of mechanisms have been proposed to explain the phenomenon of myocardial injury induced by anaphylaxis. There is constantly growing evidence that the human heart is the target as well as the site of anaphylaxis. In 1984, Kalsner and Richards¹¹ found substantially increased concentration of histamine in coronary tissues of cardiac patients, suggesting a role of allergic reactions in coronary artery disease. Ginsburg et al¹² found that histamine provoked coronary artery spasm in 4 out of 12 patients with non-exertional chest pain. A number of studies by Marone et al^{13,14} and others^{15,16} have demonstrated cardiac mast cells located perivascularly, in close proximity to myocytes, in the arterial intima and the shoulder region of atheromas. The mast cells are the major primary effector cell in immediate hypersensitivity reactions including urticaria and angioedema. Cardiac mast cells express on their surface high affinity receptors for IgE and C5a receptors.¹⁶ Activation of mast cells through immunological (cross-linking of Fc receptors for IgE) and less-specific stimuli (histamine-releasing factors, physical stimuli, and opiate drugs) leads to the release of a number of mediators (histamine, prostaglandins, leukotrienes, enzymes, cytokines) that cause both an immediate phase response and a more persistent state of inflammation referred to as a late phase response.^{13,17} The direct vasoactive and smooth muscle spasmogenic effect of these mediators is capable of causing coronary spasm. In addition, endothelial cell swelling and interstitial edema may cause further narrowing and a state of severe occlusion of the blood vessels.² Mast cells also are likely to affect coagulation and fibrinolysis at different levels through enzymes and mediators they secrete.¹⁸ Therefore, mediators from perivascular and interstitial cardiac mast cells—as well as those reaching the heart from the pulmonary circulation—might affect coagulation, leading to platelet aggregation and thrombus formation.^{15,18}

Coronary arterial spasm has been postulated to be a cause of myocardial ischemia for more than 100 years. It was not until the work of Prinzmetal et al¹⁹ in 1959, however, that major clinical attention and research began to be addressed to the role of vasospasm in the manifestations of ischemic heart disease. It is now known that spasm may be clinically important in patients with significant underlying atherosclerotic coronary artery disease as well as in patients with anatomically normal or subcritically stenosed coronary vessels. The incidence of angiographically normal coronary arteries in patients post myocardial infarction (MI) is approximately 1%. The most commonly postulated mechanism of

myocardial infarction in patients with normal coronary arteries is coronary spasm with superimposed thrombosis.^{21,22}

In the present case, the temporal sequence of events suggests that cardiac anaphylaxis was the triggering factor of myocardial injury. We propose that prolonged coronary vasospasm induced by vasoactive and inflammatory mediators, released during anaphylaxis, was the main causative mechanism. Systemic hypotension associated with anaphylaxis, as it has been emphasized in previously reported cases,²⁰ probably caused further reduction of the myocardial perfusion.

The administration of epinephrine has been implicated as a cause of acute MI in a limited number of reports.^{23,24} In these cases, however, epinephrine-induced MI developed 5 to 15 minutes after injection. However, one might argue that the exogenous epinephrine could have aggravated a preexisting coronary spasm, induced by mast cell-derived mediators.

Acute ST-elevation is a rare but potential complication of anaphylactic reactions, even in subjects with normal coronary arteries. Physicians should be alert for such a serious complication in order to diagnose it early and treat properly. We suggest that cardiac monitoring and appropriate therapy should be available for patients with severe allergic reactions especially during parenteral administration of epinephrine.

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