Acute myocardial infarction after amoxycillin-induced anaphylactic shock in a young adult with normal coronary arteries

Aristofanis Gikas, MD (1)
George Lazaros, MD (2)
Kalliopi Kontou-Fili, MD, PhD (3)

Health Centre of Salamis, Salamis (1), Cardiology Department, ‘Elpis’ General Hospital of Athens, Athens (2), Department of Allergology and Clinical Immunology, ‘Laiko’ General Hospital of Athens, Athens (3), Greece.

Address correspondence to:
Aristofanis Gikas M.D.
6, Gavriilidou Street, 11141, Ano Patisia, Athens, Greece
Tel: (+30)-2102286830, Fax: (+30)-2104650150
e-mail: argikas@internet.gr
Abstract

Background
Myocardial infarction following anaphylaxis is extremely uncommon, especially in subjects with normal coronary arteries. The underlying pathogenetic mechanisms of infarction complicating anaphylaxis remain unclear.

Case presentation
We report the case of a 32-year-old atopic man who presented with anaphylactic shock, complicated by myocardial infarction with ST segment elevation, following oral administration of amoxycillin. The patient had an uncomplicated in-hospital course and coronary arteriography performed before discharge disclosed normal coronary arteries. Subsequently, in vivo allergological evaluation was strongly positive to amoxycillin.

Conclusions
Acute ST segment myocardial infarction, even in young adults with normal coronary arteries, is a rare but potential complication of anaphylactic reactions. Coronary artery spasm does not appear to be the exclusive causative mechanism. Thrombotic occlusion, induced by inflammatory mediators and facilitated by hemodynamic collapse, is suggested as a contributing (or even primary) mechanism.
Background

Acute myocardial infarction (MI) complicating anaphylaxis induced by drugs [1-5] or other agents [6-9] is uncommon and only sporadic cases have been reported. The underlying pathogenetic mechanisms of such a complication remain unclear. We report the case of a 32-year-old man, who developed acute MI following amoxycillin-induced anaphylactic shock. The possible pathogenetic mechanisms are also discussed.

Case presentation

A 32-year-old man was admitted to the emergency room of the local Health Centre because of anaphylactic shock, which developed 2 hours and 15 minutes after the ingestion of amoxycillin (500 mg), which was prescribed by his dentist. The prodromal signs of anaphylaxis (flushing, pruritus, warmth, urticaria) reportedly occurred about 15 minutes before collapse. Ten days earlier the patient, who was asthmatic since childhood, had received amoxycillin 500mg TID for 4 days without any adverse effects.

On admission the patient was in acute distress. He complained of dizziness, blurred vision, dyspnea and abdominal pain. Initial examination revealed an obese man (Body Mass Index =38kg/m²) with generalized erythema, angioedema, cyanosis and diffuse wheezing. The systolic blood pressure was 70 mmHg. The patient was immediately connected to a cardiac monitor. An electrocardiogram (ECG) showed sinus tachycardia (approximately 120bpm) without ST segment and T wave abnormalities. The pulse oxymeter showed an oxygen saturation (SpO₂) of 90%. Epinephrine (0,3 mg) was injected subcutaneously (SC), whereas dimethindene (4 mg), and hydrocortizone (500 mg) were administered intravenously. Nebulized salbutamol and
supplemental oxygen were administered as well. In addition, normal saline with 50 mg ranitidine hydrochloride and Ringer’s solution were infused through separate intravenous lines.

Due to an unsatisfactory clinical response a second dose of epinephrine was given SC at 20 minutes. Immediately after the second dose of epinephrine, ST-segment elevation appeared on the monitor and the patient complained of substernal chest pain. A 12-lead electrocardiogram (ECG) showed ST segment elevation in leads II, III, aVF, and V₃ to V₆ suggesting an infero-lateral MI (Figure 1). Acetylsalicylic acid at a dose of 325mg was subsequently given per os whereas heparin (5000 UI) and pethidine hydrochloride (25mg) were intravenously administered. Within an hour the patient was stabilized hemodynamically. The arterial blood pressure rose to 125/90 mmHg and the SpO₂ to 96%. Due to persistence of chest pain, nitroglycerin was also infused intravenously and the patient was transferred to the Coronary Care Unit (CCU) of the nearest general hospital. Treatment in the CCU included thrombolysis with reteplase, which was given approximately at 2 hours after the onset of chest discomfort. After thrombolysis the patient remained asymptomatic. The peak troponin I serum level was 45.5 ng/ml (normal = 0-2 ng/ml), and the peak creatine phosphokinase level was 575 U/L (normal = 25-195 U/L) with an MB fraction of 77 U/L (normal = 0-24 U/L). The rest of the laboratory findings were unremarkable. An ECG performed before discharge showed complete loss of potentials in leads III and aVF and partial loss of potentials, with a small q wave in lead II (Figure 2). An echocardiographic study performed on the 5th hospital day revealed preserved systolic function (ejection fraction 60%) without wall motion abnormalities. A coronary angiography disclosed normal coronary arteries (Figure 3,4), while left
ventriculography was normal as well. The patient recovered without further complications and was discharged exactly one week from admission.

Six months after the acute episode the patient was subjected to allergological evaluation. Skin tests (prick) were performed using penicilloyl polylysine (PPL), minor determinant mixute (MDM) [supplied as Allergopen by Allergopharma (Reinbeck, Germany)], and also amoxycillin, ampicillin, and cefamandole solutions for injection. Prick skin tests were strongly positive (on a scale of 1-4, 4+ reactions, i.e. wheal > 5mm in diameter with pseudopodes, with no reaction at all to the negative control) to amoxycillin and ampicillin (concentration 20mg/mL each). Intradermal tests were performed to PPL, MDM and cefamandole and resulted strongly positive only to MDM (dilution 1/10). Circulating specific IgE to penicillin V, penicillin G, amoxycillin, ampicillin, and cefaclor was not demonstrable by CAP (Pharmacia, Sweden).

Discussion

It is well known that anaphylactic reactions may trigger cardiovascular events, including MI [1-9]. The occurrence of such events, however, concerns mainly subjects with underlying ischemic heart disease [1,2,4,7,9] and rarely those with normal coronary arteries [3,5,6,8]. As a rule, cardiovascular complications in the setting of anaphylaxis are extremely uncommon in subjects less than 35 years old [10].

Myocardial infarction following antibiotic administration is uncommon and only few cases have been reported so far [1,11]. To our knowledge, only a single case of amoxycillin-induced anaphylaxis complicated with MI has been documented in 62-year-old man with a history CAD [4].
In the present case, acute infero-lateral MI developed in a 32 year-old-man with normal coronary arteries. The temporal relationship of the events suggests that anaphylaxis was the triggering factor of the MI. Coronary artery spasm, leading to thrombus formation, appears as the most probable underlying mechanism [12,13]. It is well established that coronary vasospasm can be induced by many inflammatory mediators released from mast cells. In addition to histamine [14], prostaglandins, thromboxane, leukotrienes and other powerful vasoactive mediators, such as endogenous epinephrine and serotonin [6,15], can provoke coronary artery spasm. Moreover, mast cells are located in ‘strategic’ positions of the entire vascular bed and contain a variety of enzymes and mediators, which regulate coagulation and fibrinolysis at different levels [15]. Therefore, the release of many mediators from perivascular and interstitial cardiac mast cells might affect coagulation, favoring platelet aggregation and thrombus formation [15,16]. In the present case, the fact that chest pain persisted after nitroglycerin infusion and disappeared with intravenous thrombolysis, suggests a thrombotic vascular occlusion.

Another contributing factor to be considered in our patient, as it has been previously reported cases [17], is the hemodynamic collapse, which compromised even more myocardial perfusion, thus, favoring in situ thrombus formation and coronary artery occlusion.

The administration of epinephrine - a life saving agent in cases of anaphylaxis – had been implicated as a cause of acute MI [18]. In the present case, however, it appears unlikely that exogenous epinephrine was the precipitating cause for the following reasons: First, the dose administered was rather low (0.3mg) to induce significant vasoconstriction in a subject with a body weight of 130 kg; second, the mode of administration (i.e. SC) is considered the safest in this regard; and, third, at 20
minutes no additive effect resulting from the second dose of epinephrine appears probable, given the short half-life of the drug (2 minutes). Moreover, the administration of the additional dose of epinephrine (0.2mg), coincided with the onset of chest pain, before any anticipated drug absorption; the possibility of inadvertent intravenous administration of epinephrine appears unlikely, since no blood was withdrawn in the syringe before drug injection. Furthermore, the allergological evaluation showed that our patient was highly sensitive to amoxycillin and the minor determinants, which are the allergenic epitopes associated with systemic anaphylaxis. The negative CAP results do not negate the in vivo findings since it is well established that the in vitro techniques are not as sensitive as skin tests; moreover, they are available only for the major determinants of penicillins.

Conclusions

In conclusion, acute MI, even in young adults with normal coronary arteries, is a rare but potential complication of anaphylactic reactions. Coronary artery spasm does not appear to be the exclusive causative mechanism. Thrombotic occlusion, induced by inflammatory mediators and facilitated by hemodynamic collapse, is suggested as a contributing (or even primary) mechanism.

Abbreviations

CAD = coronary artery disease; ECG = electrocardiogram; MDM = minor determinant mixute; MI = myocardial infarction; NV = normal values; PPL = penicilloyl polylysine; SC = subcutaneously.
Acknowledgement

We thank the physician K. Lidatakis and the nurses A. Koulouri and I. Lountzi for heir contribution in the first-hour management of the patient and the documentation of the case.

Note

Written consent for publication of the case was obtained from the patient.

Competing interests

None declared

References

Coronary artery spasm and acute myocardial infarction in naproxen-

6. Wagdi P, Mehan VK, Burgi H, Salzmann C: Acute myocardial infarction after 
wasp stings in a patient with normal coronary arteries. *Am Heart J* 1994, 
**128**:820-3.

7. Lopez-Minguez JR, Fernandez RG, Nunez VM, Herrera AM, Gomez JCA, 
Garcia-Andoain JM: Acute myocardial infarction secondary to anaphylactic 
reaction following shellfish ingestion. The need for rescue coronary 

8. Salam AM, Albinali HA, Gehani AA, Suwaidi JA: Acute myocardial infarction 

9. Vaswani SK, Plack RH, Norman PS: Acute severe urticaria and angioedema 


11. Rich MW: Myocardial injury caused by an anaphylactic reaction to 
ampicillin/sulbactam in a patient with normal coronary arteries. *Tex Heart 

Eguchi A, Ueyama T, Imaizumi T: Vasospastic angina induced by non-


Figure legends

**Figure 1:** ECG recorded at the chest pain onset.

**Figure 2.** ECG recorded at hospital day 4\textsuperscript{th}.

**Figure 3.** Left coronary angiogram.

**Figure 4.** Right coronary angiogram.