Author's response to reviews

Title: Acute myocardial infarction after amoxycillin - induced anaphylactic shock in a young adult with normal coronary arteries: a case report and review of literature

Authors:

Aristofanis Gikas (argikas@internet.gr)
George Lazaros (glaz35@hotmail.com)
Kalliopi Kontou-Fili (kontoufk@otenet.gr)

Version: 2 Date: 29 August 2004

Author's response to reviews: see over
Dear Editor,

Please receive the revised version of our manuscript prepared according to the reviewer's remarks, including changes aiming at improving the English quality of the text. The changes performed are highlighted in red font. Our point-by-point responses are stated below.

**Reviewer # 1:**
The authors wish to thank the Reviewer for his remarks and suggestions.

1. The Reviewer disagrees with the pathophysiologic mechanism suggested by the authors and proposes a prolonged coronary artery spasm, due to epinephrine administration, as the unique underlying mechanism. However, certain aspects should be taken into account. If vasoconstriction was the exclusive underlying mechanism, how could one interpret the persistence of chest pain and ST segment elevation in spite of IV niroglycerin administration? In addition, how could one explain the symptoms’ relief as well as the ST segment return to the baseline promptly after intravenous thrombolysis? Moreover, the dose of epinephrine administered was rather low, given the patient’s BMI, to induce a significant alpha stimulatory effect. Indeed, the first dose of 0.3mg did not cause chest discomfort and ECG changes in our patient. An additional effect of the second dose (0.2mg) is highly unlikely taking into account first, the very short half-life of epinephrine and second, the fact that chest pain appeared exactly upon needle removal (since IV injection has been ruled out as described in our text). In conclusion, we feel that the Reviewer’s point of view is not substantiated by the sequence of actual events. We believe that thrombotic occlusion, induced by vasoactive and inflammatory mediators (released during anaphylaxis) and facilitated by hemodynamic collapse, possibly on top of a vasospastic reaction, was the causative mechanism as suggested by the authors in the "Discussion" section. Nevertheless, we have added in the "Discussion" section, that an aggravation of a pre-existing coronary artery spasm, induced by inflammatory mediators, after epinephrine administration cannot be excluded (page 7, lines 21-23).

2. Regarding the localization of the infarction, the post discharge ECG showed q waves in the inferior leads, which indicate a (dominant) right coronary artery occlusion rather than a diffuse coronary artery spasm. The first ECG, recorded immediately after chest pain onset, showed ST segment elevation in leads II III aVF and V3 to V6. Except for lead V3 that reflects anteroseptal ischemia the rest of the above leads reflect inferolateral ischemia.

3. Concerning the arteriogram, the authors cannot exclude a vasospastic component. We also wish to stress that coronary arteriography has been performed and interpreted by interventional cardiologists experts in their field.

4. We agree that an emergent coronary angiography instead of thrombolysis should be the treatment of choice. However, this is not always feasible. In fact, the patient was admitted to the hospital at 11pm, when - for technical reasons - most catheterization laboratories are closed in our hospital settings. On the other hand, we would not feel very comfortable administering radio-contrast media in the setting of anaphylaxis. Moreover, there are similar cases (i.e. ref. 6, 27) where thrombolysis has been applied successfully.

5. The reviewer considers our case report unworthy of publication. However, this case is very unusual in reference to both, young age and the demonstration of normal coronary arteries. As we have emphasized in the manuscript, this is the first case in
the international literature of amoxycillin-induced anaphylactic shock in a young adult with normal coronary arteries, and we consider this very rare but a potential complication, important for physicians to be aware about.

Reviewer # 2:

We would like to thank the Reviewer for his useful comments and remarks.

1. The initial ECG was a lead II recording from the monitor rather than a 12 lead ECG. Due to the patient’s critical condition, we delayed the 12 lead ECG recording, and we made every effort to stabilize him before the occurrence of full collapse. As a result, the lead II tracing, as shown in the new Fig. 1, A, represents the baseline electrocardiographic recording. We emphasize that the above recording has been obtained before epinephrine administration.

2. The dose of the second administration of epinephrine is indicated in page 4, line 8.

3. Aspirin was administered according to the current guidelines for the management of acute MI due to coronary thrombotic occlusion (which, as explained in the "Discussion" section; we believe that the sequence of events supports our view that, along with coronary spasm, it contributed to coronary artery occlusion.

4. The delay in the allergological evaluation was due to an initial non-compliance (claiming work related problems and distance) of the patient to our advice and secondly the patient load of the Allergology dept.

5. The explanation for the negative *in vitro* test results is expanded in "Discussion" section (page 8, paragraph 1).

6, 7 and 8. The Discussion was revised according to the Reviewer’s suggestions (page 6, paragraph 2); additional references (number 12,13, 15-18, 21,23) are also quoted.

9. We believe that it is not the level of blood pressure reduction but its prolonged drop (for about 30 minutes, even after the first epinephrine injection) that compromised myocardial perfusion (page 7, paragraph 2).

10. Apart from obesity, there were no additional risk factors for coronary artery disease (namely dyslipidemia, family history of premature coronary disease, smoking, etc), as are stated in page 3, lines 15,16 and page 4, line 25.

11. The conclusions were expanded.

12. Finally, the manuscript is edited according to the Reviewer’s suggestion.

We are looking forward to your final decision.

Thank you for your kind cooperation.

Yours sincerely,

On behalf of the authors,

Aristofanis Gikas, MD