Author’s response to reviews

Title: Acute ST-segment elevation myocardial infarction after amoxycillin - induced anaphylactic shock in a young adult with normal coronary arteries: a case report

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Version: 3 Date: 7 November 2004

Dear Editor,

Please receive the 2nd revision of our manuscript entitled "Acute ST-segment elevation myocardial infarction after amoxycillin - induced anaphylactic shock in a young adult with normal coronary arteries: a case report". The authors wish to thank both of the reviewers for their suggestions, remarks, and contribution to improve our manuscript.

The following modifications (highlighted in red) have been performed in the text following the reviewers' suggestions.

Reviewer # 1:

1) We have removed from the text the term "infero-lateral MI" and we have used instead the term "ST-segment elevation myocardial infarction".

2) The reviewer suggested a prolonged coronary vasospasm as the exclusive causative mechanism of MI. The authors agree with the above mechanism but they consider that a thrombotic occlusion, on top of the vasospastic reaction, cannot be definitely excluded. As a result, according to the reviewer's remarks we have performed the following modifications:

A) In the "Abstract" the conclusions have been changed as follows:
<< Coronary artery spasm appears to be the main causative mechanism of MI in the setting of "cardiac anaphylaxis". However, on top of the vasoactive reaction, a thrombotic occlusion, induced by mast cell-derived mediators and facilitated by prolonged hypotension, cannot be excluded as a possible contributory factor >>.

B) In the section of "Discussion" we have modified our view concerning the pathogenetic mechanism as follows:
<< We propose that prolonged coronary vasospasm induced by vasoactive and inflammatory mediators, released during anaphylaxis, was the main causative mechanism. However, in view of the persistence of chest pain following IV nitroglycerin infusion, and its complete resolution promptly after IV thrombolysis, a thrombotic vascular occlusion, on top of the vasospastic reaction, cannot be excluded. The latter is also supported by the prolonged systemic hypotension, which, as it has been emphasized in previously reported cases [26], probably caused further reduction of the myocardial perfusion, thus, favoring in situ thrombus formation and subsequent coronary artery occlusion >>.

C) In the section of "Case presentation" we have added the following statement concerning the thrombolysis results: << Treatment in the CCU included thrombolysis with reteplase - administered according to the standard protocol - 2 hours after the onset of chest discomfort, which according to the established clinical and electrocardiographic criteria was considered successful [new reference #10].

D) We have modified our final conclusions as follows:
<< In the above case, mediator-induced coronary artery spasm was the main, but probably not the exclusive causative mechanism of anaphylaxis-related MI. The thrombotic vascular occlusion, induced by inflammatory mediators and facilitated by prolonged hypotension, cannot be excluded as a possible contributory factor >>.

3) Lastly, we have stated that urgent cardiac catheterisation is the strategy of choice for the diagnostic evaluation of MIs occurring as primary events. In the setting of acute anaphylaxis, however, particularly in cases in which the offending allergen has been administered orally, the main clinical task is to treat the patient and make sure that he remains stable for many hours, as explained below. The elucidation of the potential pathogenetic mechanism could be postponed.
<< In acute MI cases, presenting to centers with cardiac catheterization facilities, urgent coronary
arteriography appears as the management strategy of choice for the final diagnosis. However, in the setting of acute anaphylaxis this might not be the wisest choice, particularly in cases, like the present one, in which the offending allergen had been administered orally. Continuous or delayed allergen absorption could further aggravate anaphylaxis; in addition, a late phase reaction represents a potential risk in all anaphylactic reactions; lastly, no bibliographical data are available concerning the tolerability of IV administered contrast agents in patients who have suffered a recent episode of severe systemic anaphylaxis.

Reviewer # 2:

1. We have removed from the title the phrase "and review of the literature".
2, 3 and 4. Page 6, paragraph 2. We have performed the corrections as suggested.
5. On page 9th, 1st paragraph, references 16-18 have been added.
6. In reference #18 "Austeen" has been changed into "Austen".

Thank you very much for your kind cooperation.
Yours sincerely,
On behalf of the authors,

Aristofanis Gikas, MD.