Author’s response to reviews

Title: Myocardial Infarction during anaphylaxis in a young healthy male with normal coronary arteries- Is epinephrine the culprit?

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Author’s response to reviews:

Manan Pareek, M.D., Ph.D. (Reviewer 1): The authors present a case of epinephrine-induced myocardial infarction. The case itself is interesting and worthy of attention. However, I do have some concerns as stated below:

1. Linguistic errors make this paper a somewhat difficult read. For example, present tense, past tense, and present perfect are used inconsistently and incorrectly, commas and words are missing, etc. The authors should certainly have someone who is a native English speaker edit it thoroughly before resubmission.

I have corrected the linguistic errors.

2. Abstract: The diagnosis is given in the first sentence of the case presentation. I would suggest a more chronological description so that there is a natural lead-up. In addition, since the entire acute presentation took place at another hospital, the "referral" should not be mentioned prior to describing the work-up for underlying cardiac conditions.

I changed the order and made it more chronological as you suggested. I also changed the “referral” mentioned in the beginning.

3. Abstract: Concluding remarks include "immediate steps in the management", but the acute management is not described in the case presentation.

I briefly described the management in the abstract.
4. Introduction: The area covered is acceptable, but I do not understand the sentence "contrary to the belief..". If only few cases of myocardial infarction have been reported, why "contrary"?

I deleted that phrase.

5. Case presentation: Please include drug doses for hydrocortisone, chlorpheniramine, and nitroglycerine, if the information is available.

I entered the doses of all the drugs that were used

6. Case presentation: Although I understand that the authors want to present the case classically, with history, clinical examination, and laboratory tests in a specific order, it is a little difficult to make out exactly which parts of the case description take place at the first hospital and which ones take place at the second hospital. This has been done to some extent, but could be better.

I changed the order and tried to make a clearer description of what happened.

7. Case presentation: The quality of the ECG is poor. Do the authors have an alternative version or do they perhaps have access to a better scanner if using a paper copy? In addition, leads I and II seem suspicious for transmural ischemia, although the conventional criteria for ST-segment elevation are not fulfilled.

I included an ECG which I think has a better quality. But unfortunately I don’t have another one.

8. Case presentation: Part of the treatment is revealed early, whereas more details are mentioned at the end of this section. I suggest all treatment be described when relevant.

I changed that and mentioned all the treatment given in place.

9. Case presentation + Discussion: The authors need to clarify why the patient fulfills the criteria for myocardial infarction, use correct terminology (i.e., probable type 2 myocardial infarction), and how to distinguish between infarction and injury.

I included that in the first part of the discussion.
10. Discussion: "Epi pen" can be included within i.m. or s.c. 

It was subcutaneous

11. Discussion: I do not see the need for merely reciting all available case reports. The authors should summarize similarities and dissimilarities, including their own case, in a single paragraph. As you suggested I changed it and only summarized the available case reports.

12. Discussion: It is stated that epinephrine has high affinity for certain receptors, but the effect on beta 2 receptors is not described. Also, alpha 2 receptors are more complex than alpha 1 receptors, and "alpha receptors" should not be used as a general term.

I mentioned it as Alpha 1 receptors and described the effect of adrenaline on beta receptors as well.

13. Discussion: Areas covered are generally acceptable, but the section seems a little unfocused and fragmented and could benefit from some structuring. Besides elaborating on the term "myocardial infarction", the authors should propose a more specific management strategy for these patients instead of merely stating the two drugs previously used.

I tried to improve structure of the discussion to make it more clear. However I could not find much literature on management options for this situation other than the use of nitrates and calcium channel blockers.

Phillip L. Lieberman (Reviewer 2): This is an interesting report but the case described does not warrant the conclusion reached. There are two possibilities to explain the patient's infarction. Anaphylaxis itself can result in coronary vasoconstriction in the absence of epinephrine treatment. And, as you mentioned, epinephrine could be the culprit. But the former possibility is not discussed adequately. In other words you have documented an infarction but have not demonstrated the cause was epinephrine. The title itself is thus misleading and you should change it to indicate you are reporting a case of a myocardial infarct occurring during anaphylaxis in a healthy young male with normal coronary arteries. You need a much more thorough discussion of the effects of anaphylaxis on the heart with special mention of the fact that mast cell mediators can cause coronary vasospastic events. I suggest you read:
Anaphylaxis and cardiovascular disease: therapeutic dilemmas.

Lieberman P, Simons FE.


I made changes in the case report and included and discussed about kounis syndrome. I also changed the title. However as there is no way to exactly exclude kounis syndrome other than the temporal relationship it had with epinephrine injection I mentioned that kounis syndrome was still a possibility and it could not be excluded.

In addition you need to elaborate in more detail on where the epinephrine was given. It is not enough to say intramuscular because the pharmacodynamics differ according to whether the muscle was the deltoid or vastus lateralis. If in the deltoid it would be very unlikely that the epi was the culprit. See

Epinephrine for First-aid Management of Anaphylaxis.

Sicherer SH, Simons FE; SECTION ON ALLERGY AND IMMUNOLOGY..