

Adrenalin use in Kounis syndrome: a well-unknown entity

Running title: Kounis syndrome

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Dear Editor,

I have read the article titled '*Kounis syndrome: an underestimated emergency*' by Zisa et al. with great interest (1). Nevertheless, there are a couple of concerns raised in my mind about their study. And clarification of these concerns of this study will help understand better of the study.

Kounis syndrome (KS) is known as an acute coronary syndrome associated with hypersensitivity reactions to an allergen such as a drug or bee venom and is a life-threatening medical emergency that is under-diagnosed and under-treated (2).

First; in this retrospective study including 9 KS cases, only two patients received intramuscular epinephrine (patient 1 and patient 2) and the authors claim that this minimized the risk of cardiac side effects (1). We do not think this is entirely correct and caution is needed in the use of adrenaline during anaphylaxis, especially if KS is considered or at risk (3-7).

The management of the acute phase of KS is a real challenge for the clinician. Because it requires a complex balance between peripheral vasodilation due to anaphylactic shock, which requires the use of vasopressors, and coronary vasospasm, which requires the use of vasodilator drugs. Furthermore, some drugs used to treat cardiac symptoms may worsen the allergic reaction and conversely, those used to treat the allergic reaction may worsen cardiac symptoms (3-8).

Therefore, according to some authors, the administration of adrenaline should be reserved for cases with anaphylactic shock and laryngospasm, because of the worsening of vasospasm that adrenaline administration in KS can cause (9).

Second; it is said in the article that Patient 1 is reported to have had KS type 1 and type 2 reactions (1). Although this has never been discussed, it must be a rare case. Does one predispose to the other? What is the frequency of this kind of situation? It would be useful for the reader if this was discussed a little.

Third; there are some typographical and misrepresentations in Table I and Table II. In Table I, it is mentioned that the patient (patient 1,3,4) did not have atopy, whereas in the following lines, it is shown that they were allergic to bees and even received venom immunotherapy for this (1). This created a contradiction.

Also, as shown in Table II, the tryptase of the 7th patient increased to 92.4 mcg/l during the acute setting. Moreover, the diagnosis of this patient was confirmed by neither skin tests nor specific IgE for ceftriaxone (1). This very high tryptase value and the lack of confirmation of the diagnosis are puzzling. Could there be an underlying predisposing cause e.g. mast cell activation syndrome that could trigger these very high levels?

Minor points: table I also shows that the first patient had a KS type II reaction. However, when patient 1 is described in the text, it is mentioned that this person had type I and type II KS reactions. Again in Table II, the abbreviation CT for ceftriaxone was misspelled instead of CFT when intravenous CT was mentioned (1).

In conclusion; I would like to thank the authors for this nice and high-quality study and its results. This study of 9 cases with KS contributed to a better understanding of a rare life-threatening condition. This is a work that later paved the way for future work as well.

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