Letters to the Editor

Kounis Syndrome Induced by Lidocaine

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To the Editor:

We read the case report entitled “Kounis Syndrome After Lidocaine Use” written by Garcia-Nunez et al [1] with great interest. We believe that a few of the issues related to the clinical and laboratory findings of the case should be clarified in order to help the reader understand the case better.

First, the patient underwent a provocation test with local anesthetics, although the method by which the drug provocation was performed was not specified [1]. Drug provocation tests can be performed orally, intravenously, and subcutaneously. A provocation test with local anesthetics is performed subcutaneously [2]. Additionally, there may be a spelling error where the test is described as “simple-blind” (“single-blind”)? [1]. It would also be necessary to confirm the dosing range. The article says 5, 2.5, and 5 mg of each drug [1]. Should this not be 0.5, 2.5, and 5 mg of each drug? Did the local anesthetics used in provocation or skin tests contain adrenaline? This is also a condition that affects the results of the tests. Therefore, it is difficult to understand how the drug provocation test was performed.

Second, the authors state that the results of the tests performed with tetracaine and bupivacaine were negative; however, we do not know which tests were applied (drug provocation test, basophil activation test [BAT], or skin prick tests). The authors then state that a positive reaction was observed with 1 mg/mL and 10 mg/mL in the intradermal test [1]. It would be interesting to know with which preparation the intradermal test yielded a positive result and whether all skin tests and provocations were negative for lidocaine or only those with a positive stimulation index. The positivity/cut-off values in the BAT are also controversial and vary from drug to drug [3]. The text first states that testing with tetracaine and bupivacaine was negative whereas the intradermal test results were positive, then mentions cross-sensitization, and goes on to explain how these drugs were well tolerated when taken. The explanation is confusing and casts doubt on the real clinical picture of the patient.

Third, we do not know, from the text, which segment of the electrocardiogram (ECG) was depressed (ST segment?), as no depressed segment is visible on the ECG readout [1].

Fourth, the case is reported as the first case of Kounis syndrome after lidocaine injection. However, as mentioned [1], a case of Kounis syndrome with a lidocaine intradermal test has been reported [4]. Considering that the intradermal test is also performed by injection into the skin, the case in the article is not technically the first case induced by lidocaine injection.

Fifth, while the authors present details on diagnosis, no information on management is provided. Such information could be instructive; for example, the reader could learn whether adrenaline was administered owing to a suspicion of anaphylaxis. It is known that adrenaline, which is the first choice in the treatment of anaphylaxis, can exacerbate ischemia and worsen coronary vasospasm in Kounis syndrome [5]. We would like to know if the medical treatment mentioned in the article included the use of antihistamines and corticosteroids.

Sixth, the article stated that systemic mastocytosis was ruled out based on hematological parameters, although this information was not provided. It would be interesting to know if there was eosinophilia [5], which is among the laboratory findings of Kounis syndrome, and whether bone marrow aspiration was performed for the differential diagnosis of systemic mastocytosis. The differential diagnosis receives little attention. It would be good to have more information on how to distinguish Kounis syndrome from disorders such as anaphylaxis and Takotsubo-like syndrome [6,7].

Finally, we would like to thank the authors for helping us to update our knowledge and improve our understanding of Kounis syndrome.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

Letters to the Editor


To the Editor:

We are grateful to Dikici and Özdemir for their letter and are pleased to have this opportunity to answer all their questions and clarify doubts.

First point:

We performed skin tests (skin prick test [SPT] and intradermal test [IDT]) with the culprit and alternative drugs at the dilutions presented in the clinical report and a single-blind, placebo-controlled drug provocation test (DPT) using subcutaneous administration, as stated in the letter. You refer to the different doses used in the patient we discuss. The patient was challenged once with 5, 2.5, and 5 mg of each drug. That means that the patient received only 5 mg of tetracaine, 2.5 mg of bupivacaine, and 5 mg of lidocaine if needed; the clinical report shows that the lidocaine provocation test was not performed because the result of the skin test was positive.

To avoid false-negative results, we never use local anesthetics containing adrenaline, since adrenaline is a vasoconstrictor that can reduce erythema and hive diameter.

Second point:

The results of the in vivo study (skin test and DPT) were negative to tetracaine and bupivacaine, and the skin test results were positive to lidocaine (this was not addressed in detail in the clinical report). With a positive skin test result, we did not perform a DPT to lidocaine (see above). As for the basophil activation test, I agree that cut-off levels can change between drugs and there is not enough information about this test. This is the reason we tested lidocaine-induced basophil activation in 5 healthy controls, observing no changes (in contrast to the patient).

I hope this explanation prevents misinterpretation of the results and clarifies any remaining doubts about this interesting clinical report.

Third point:

We agree with your comment about the ECG reading: the correct interpretation is a minimum low rise (ie, minimal change) in II, III, and AvF. These mild alterations in the ECG reading with compatible symptoms and moderate-severe changes in laboratory values (blood test results returned to normal after a few days) point to a diagnosis of type I Kounis syndrome.

Fourth point:

You refer to Kounis syndrome after a skin test with lidocaine and articaine. In that clinical...