

Kounis syndrome after lidocaine use

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Local anaesthetics are critical medications for a wide range of procedures. They mainly act by stopping the depolarizing nerve fibres and can be divided into two categories: amide-type and ester-type. Systemic toxicity is their most feared adverse reaction, and anaphylaxis is the one of the greatest concern. We present a case of Kounis syndrome (KS) provoked by lidocaine injection. Our study confirms this diagnosis and the possible alternatives we proposed.

A 52 years-old male came to our Allergy Department referring an immediate episode of profuse sweating, severe pressure, fullness, squeezing and pain that spreads to the shoulders and in the center of the chest that lasts for more than a few minutes with an irregular pulse and a generalized urticaria with a great discomfort after lidocaine reception before local surgery 6 months ago, evolving to a severe cardiac arrest well-resolved in ICU with medical treatment and resuscitation maneuvers. The diagnosis was a lower myocardial infarction (EKG with depressed segment in II, III and aVF (Figure)). Coronariography and ergometry findings were normal. Troponin levels were 9 ng/ml at 4 hours after receiving the lidocaine injection, and declined over the following 5 days.

The patient reported nor previous complications with local anaesthetic or allergic reactions to food or medication.

Blood test revealed a serum tryptase level of 4.5ug/ml (normal levels 1-11,4); not recorded in acute phase, histamine of 50ug/ml (normal 25-65) and haematological parameters ruled out systemic mastocytosis.

After obtaining informed consent, skin prick tests were performed with tetracaine Braun™ (10 mg/ml), bupivacaine (5, 0.5 and 0.05 mg/ml) and lidocaine (10, 1, 0.1 mg/ml) and a simple blind, placebo-controlled drug provocation test (DPT) with 5, 2.5 and 5 mg of each one, respectively (when required). A basophil activation test (BAT) was also carried out.

Skin Prick Tests (SPT) are considered as positive with a mean wheal diameter ≥ 3 mm larger than the negative control, a positive result in the Intradermal Test (IDT) corresponded to an increase of ≥ 3 mm compared to the initial wheal, a positive BAT as activation $> 5\%$ and $SI > 2$ in at least one concentration.

Our patient's results were negative for tetracaine and bupivacaine, but positive in the IDT for 1mg/ml and 10mg/ml, with a mild rash on the forearm, which as well controlled with dexchlorpheniramine. The stimulation index was positive (2.6) to lidocaine.

The same study schedule was conducted in 5 healthy patients with negative results.

Our diagnosis was clinical. Symptoms and signs suggestive of an acute allergic reaction with features of angina and autonomic nervous system symptoms after the administration of medication should lead to a suspected diagnosis of Kounis Syndrome (KS). Although medications are the first cause of this condition, (with antibiotics as the main aetiology [1]), other possible causes must not be ignored [2,3], including excipients of lidocaine

such as sodium carboxymethylcellulose, methylparaben and propylparaben, especially in cases of no previous allergic reactions to food or medication. Here we are describing the first reported case of KS after lidocaine reception, and the alternatives drugs we proposed. An episode has been reported previously in the literature after IDT with lidocaine and articaine [4].

It was essential to study possible cross reactivity between lidocaine and other amide- (bupivacaine) and/or ester-anaesthetics (tetracaine). In fact, cross reactivity has been demonstrated previously between amides (mepivacaine and lidocaine) [5]. Here we observed a good tolerance to bupivacaine, despite cross reactivity between lidocaine and bupivacaine having been described in a previous study [6]. Yet another study has reported cross reactivity between mepivacaine, lidocaine and ropivacaine [7]. We, therefore, recommend the need for a broad allergologic study in these cases to rule out possible cross reactivities.

Cross reactivity between lidocaine and tetracaine was described as cosensitization [8]. In our patient, tetracaine was also well tolerated..

Moreover, it is important to take into account the KS subtypes. Several authors [9,10] have described three types of KS with very similar symptoms, but with different coronary angiographies. As our patient presented a normal coronary angiography, he was diagnosed as type I KS. In all patients with a severe reaction, the possibility of systemic mastocytosis must be considered. In our patient, clinical report and in vitro studies ruled out this possibility.

To conclude, we report a case of KS after lidocaine reception. Cross reactivity between these drugs is still unclear, and all patients with these reactions must be studied and tested to be able to offer our patients as wide a therapeutic choice as possible.

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Conflict of interests

All authors refer no conflict of interests for this publication.

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Figure.

