LETTER TO EDITOR

Angina following anaphylaxis: Kounis syndrome or adrenaline effect?


We have read with interest a report published in Malaysian Family Physician1 on a 23-year-old Malay atopic patient with a known allergy (angioedema) to metoclopramide, tramadol, aspirin, and CT contrast media who was stung by an insect and developed throat tightness, vomiting, and a swollen uvula. As he was being treated with intramuscular tetanus toxoid, intravenous hydrocortisone, intravenous chlorpheniramine, and 0.5mg (1:1000) of intramuscular adrenaline for anaphylactic shock, he presented, within minutes, with a sudden escalation of drowsiness, worsening throat tightness and chest pain so excruciating on his left side that he fainted. The patient’s electrocardiograms and cardiac enzymes were normal, however, and he regained consciousness with a high oxygen flow of 15 liters per minute. The following day, the patient was discharged in good condition. This report raises the issue of whether the excruciating chest pain was the result of the intramuscular adrenaline administration or of a Kounis Type 1 syndrome manifestation.

Paradoxically adrenaline, the drug that is life-saving in anaphylaxis, can by itself induce anaphylaxis. Indeed, every commercially available preparation of adrenaline contains sodium metabisulfite as a preservative, according to Drug Facts and Comparisons (a standard pharmacy reference published by Wolters Kluwer and updated monthly). Sodium metabisulfite is commonly used as an antioxidant in the food and pharmaceutical industries. Anaphylactic shock has been reported during the administration of epidural anesthesia for caesarian sections, in which the culprit was metabisulfite, an additive agent of local anesthetics containing adrenaline.8 This situation poses a therapeutic dilemma: Exogenous adrenaline administration is a life-saving procedure and, according to international guidelines, it should be injected intramuscularly at a dose of 0.01 mg/kg of a 1:1000 (1 mg/mL) solution,11 to a maximum dose of 0.5mg in adults.12 For IV administration, appropriately diluted solutions (1:10 000 [0.1mg/mL] or 1:100 000 [0.01mg/mL]), may contribute to coronary spasm.

Adrenaline actions include the following:
1. Peripheral vasoconstriction via α1 receptors13
2. Increasing both the rate and force of cardiac contractions via β1 receptors14
3. Reversing bronchoconstriction and reducing the release of inflammatory mediators via β2 receptors15
4. Promoting platelet activation via specific receptors found on the platelet surface16
5. Inducing platelet aggregation by increasing platelet production of thromboxane B217
6. Heightening platelet sensitivity to adenosine diphosphate18
7. Promoting thrombin-induced binding of platelets to fibrinogen.19

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References:
Actions 4–7, therefore, aggravate myocardial ischemia, prolong QTc intervals, and induce coronary vasospasm and arrhythmias. Elderly patients, especially those with histories of hypertension and coronary artery disease, are prone to these side effects. Both α1- and α2-receptors and β1-adrenergic receptors are present in the coronary arteries but with different distributions. The large coronary arteries are equipped mainly with α receptors, which mediate contraction.

In the present case, the patient’s heart rate was 94 beats per minute (bpm) before adrenaline administration, which reduced it to 82 bpm. Therefore, adrenaline appears less likely to be the cause of the patient’s excruciating chest pain in the absence of the above symptoms, such as tachycardia, which are typically induced by adrenaline. However, without coronary angiography or any evidence of left ventricular dysfunction, it is impossible to explain which came first—the egg or the chicken.

References