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Targeted temperature management in Kounis syndrome following cardiac arrest with anaphylaxis

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Hypothermia reduces brain metabolism, lowers intracranial pressure, reduces brain cell apoptosis, reduces brain inflammation, decreases local lactate and production of free radicals, reduces vascular and cell membrane permeability and is used today to improve survival with good neurological outcome [1]. Targeted temperature management is referred to interventions used to reach and maintain a specific level temperature for each individual.

In the very interesting report published in *the American Journal of Emergency Medicine* [1], a 63-year-old man allergic to peaches developed anaphylactic shock with pulseless electrical activity following eating of 2 pieces of peaches. With cardio-pulmonary resuscitation the patient experienced return of spontaneous circulation but he became comatose with fixed dilated pupils and metabolic acidosis. Following targeted temperature management arterial blood pressure dropped to 81/52 mm Hg with a heart rate of 64 per minute but with increasing epinephrine and midazolam, fentanyl rocuronium administration and rewarming, the patient recovered and was discharged on day 18.

Since this case is the first to apply targeted temperature management in anaphylactic shock, the following issues need to be considered.

1. Despite that hypothermia has beneficial effect on brain metabolism, it can increase thrombin generation and facilitate thrombus formation. Indeed, a recent study has shown that thrombin generation, as expressed by the endogenous thrombin potential, is significantly increased (by as much as 100%) at decreased temperature to 24–34 °C. The increase endogenous thrombin potential, at decreasing temperature, might be due to decreased thrombin inhibition during the propagation phase of thrombin formation [2]. Although, in the reported patient, cardiac enzymes and coronary angiography were not given, and acute anaphylaxis-associated thrombotic Kounis syndrome type III variant can not be excluded [3]. This can explain why the patient's arterial blood pressure dropped to 81/52 mm Hg with a heart rate of 64 per minute after starting targeted temperature management.
2. The patient's arterial blood gases showed metabolic acidosis with pH of 6.95. However, he was brought in the Emergency Department for shortness of breath and loss of consciousness which denotes that some degree of respiratory acidosis was present at least in the beginning of his ordeal. Based on the Henderson-Hasselbalch equation for

blood acid-base balance, when the pCO₂ is raised the pH values drop [4]. Acidosis decreases the activated partial thromboplastin time whereas the decrease in temperature contributes also, although less, to the decrease in activated partial thromboplastin time [2]. Clot lysis decreases under hypothermic and/or acidotic conditions, but increases with hyperthermia [5].

3. The authors correctly and wisely administrated for 24 h, midazolam, fentanyl, and rocuronium intravenously. However, all these 3 agents namely midazolam [6], fentanyl [7], vecuronium [8] have been incriminated as inducing mild or severe hypersensitivity reactions. It should be pointed out that there are clinical studies which indicate that atopic individuals, prone to allergy and simultaneously exposed to several anesthetics, as in the described case, have more symptoms than monosensitized individuals [9].

Indeed, small, even sub-threshold numbers of IgE antibodies with different specificities have additive effects and can join forces in order to trigger mast cells to release their mediators and induced anaphylactic shock. This can happen when the patient is simultaneously exposed to the corresponding antigens [10]. In the described case, the epinephrine that contains sulfite as preservative could have been acted as the fourth antigenic agent.

In severe cases of anaphylaxis, sulfite free epinephrine is preferable to be given intramuscularly because it has also fast onset of action and more sustained levels as compared with the other routes.

It seems likely that anaphylactic cardiac collapse associated with coma constitutes a distinct group of patients that need specific and meticulous management. Future studies will show if targeted temperature management will be routinely applied in cases involving cardiac arrest, anaphylaxis and anaphylactic shock with coma.

References

- [1] Lee WJ, Kim DH, Woo SH, Seol SH, Choi SP. Targeted temperature management after cardiac arrest with anaphylaxis. *Am J Emerg Med* 2017;35:807.e5–7.
- [2] Gorter KA, Stehouwer MC, Van Putte BP, Vlot EA, Urbanus RT. Acidosis induced by carbon dioxide insufflation decreases heparin potency: a risk factor for thrombus formation. *Perfusion* 2017;32:214–9.
- [3] Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med* 2016;54:1545–59.
- [4] Kunkler A, King H. Comparison of air, oxygen and carbon dioxide embolization. *Ann Surg* 1959;149:95–9.
- [5] Dirkmann D, Hanke AA, Gorlinger K, Peters J. Hypothermia and acidosis synergistically impair coagulation in human whole blood. *Anesth Analg* 2008;106:1627–32.
- [6] Bernardini R, Bonadonna P, Catania P, Passalacqua G. Perioperative midazolam hypersensitivity in a seven-year-old boy. *Pediatr Allergy Immunol* 2017;28:400–1.
- [7] Li Z, Yin P, Chen J, Li C, Liu J, Rambojan H, et al. Activation of the extracellular signal-regulated kinase in the amygdala modulates fentanyl-induced hypersensitivity in rats. *J Pain* 2017;18:188–99.
- [8] Parent B, Wearden P, Kounis NG, Chrysostomou C. Kounis syndrome or allergic coronary vasospasm in a two-year-old. *Congenit Heart Dis* 2011;6:499–503.
- [9] Nopp A, Johansson SG, Lundberg M, Oman H. Simultaneous exposure of several allergens has an additive effect on multisensitized basophils. *Allergy* 2006;61:1366–8.
- [10] Von Hundelshausen P, Weber C. Platelets as immune cells: bridging inflammation and cardiovascular disease. *Circ Res* 2007;100:27–40.

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