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Letter to the Editor

Anaphylactic Cardiovascular Collapse during Anesthesia: The Kounis Acute Hypersensitivity Syndrome Seems to be the Most Likely Cause

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With have read with a great interest the article published in J Korean Med Sci [1] concerning a 16-yr-old patient who developed severe anaphylactic reaction with cardiovascular collapse during anesthesia for incision and drainage of post operative femur fracture infection. The authors of this report thought that the culprit cause was the microemulsion propofol administration. However, this patient apart from microemulsion propofol [2], had received, during anesthesia, and for the subsequent cardiovascular arrest, another 10! substances such as midazolan [3], remifentanil [4], rocuronium [5], ephedrine [6], dexamethasome [7], epinephrine [8], as well as poloxamer 188 [9] and polyethylene glycol [10]. The latter 2 substances were components of propofol microemulsion. All these 11 substances can join forces in order to induce direct or indirect mast cell degranulation culminating in the development of the Kounis hypersensitivity associated coronary syndrome. Although the authors of this report thought that the patient's anaphylactic reaction was due to a non-IgE-mediated event, some of the substances this patient received for example fentanil can induce IgE-mediated anaphylaxis [4]. It is well known that mast cell degranulation is initiated by antigens cross-bridging their corresponding, receptor bound antibodies on the mast cell or basophil cell surface. The involvement of so many agents during anesthesia seems to be the cause of direct or IgE mediated mast cell degranulation. It is known that mast cell surfaces have between 500,000 and 1 million IgE molecules. These cells degranulate and release their mediators when the critical number of bridged antibodies reaches the critical order of 2,000 and make 1,000 bridges. It might be possible to accumulate the critical number of bridges by more than one non-crossreactive antigen and its corresponding antibody. Sensitive patients simultaneously exposed to several antigens have more symptoms than do mono-sensitized individuals. A recent study reported that antibodies with different specificities can have an additive effect, and even small amounts of corresponding antigens can trigger mediator release when the patient is simultaneously exposed to them [11]. These data suggest that a possible reaction to one anesthetic drug should not be clinically evaluated as a consequence of exposure to a single drug but rather viewed in the context of potential reaction to multiple anesthetic agents. These data could also explain why the patient's previous anesthesia with propofol, rocuronium, desflurane and remifentanil and the operation which took place one month prior to his present operation during which he received propofol and rocuronium were without any sequelae. We believe that anesthetic drugs acting as allergens can join forces in order to degranulate mast cells and induce anaphylactic reaction.

Kounis syndrome [12, 13] on the other hand, combines acute cardiovascular collapse with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells, and includes anaphylactic or anaphylactoid and allergic or hypersensitivity insults. It is caused by preformed and newly synthesized inflammatory mediators released during the anaphylactic process. A subset of platelets bearing FCεRI and FCεRII receptors is also involved in the activation cascade. The heart seems to be the primary site and the target of anaphylaxis resulting in the development of Kounis syndrome [14].

There are some strange, bizarre and astonishing events which raise therapeutic dilemmas when treating anaphylaxis. For example, epinephrine was given during resuscitation, but apart from its adrenergic action, it can also induce mast cell degranulation because it contains as a preservative, sodium metabisulfite. There are reports of hypersensitivity, anaphylaxis, and even death from Kounis syndrome from sulfite administration [15]. Anaphylactoid shock has been reported during epidural anesthesia and was attributed to metabisulfite, an additive agent of epinephrine-containing local anesthetic [16]. Epinephrine is still the primary drug for anaphylaxis, but we recommend avoidance of medications containing metabisulfites in such patients. Fortunately, preservative-free epinephrine (American Regent Inc, USA) is now commercially available for sulfite sensitive individuals [8].

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Dexamethasone which was given to this patient, has also been implicated as causative agent for anaphylaxis in some occasions and this should be taken into consideration when treating such sensitized individuals.

Tryptase levels were not measured in this patient, and assessment for reactivity to skin disinfectants and latex was not carried out.

All patient cases of perioperative anaphylactic reaction require detailed and scrutinized work-up in order to identify the offending agent and to avoid future reactions.

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