



Letter to the Editor

Kounis syndrome during general anaesthesia and administration of adrenaline

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To the Editor,

During the course of anaphylaxis, occurrence of myocardial ischaemia has been known, which have recently been named as Kounis syndrome [1]. Regarding treatment for this syndrome, early intravenous administration of adrenaline is the key points for managing anaphylaxis [2–4] but adrenaline can aggravate myocardial ischaemia. Moreover, whether adrenaline is effective or not is controversial [5,6]. We report a case of Kounis syndrome during general anaesthesia in which administration of adrenaline was effective in both anaphylactic shock and myocardial ischaemia, and discuss perioperative problems about diagnosis and therapy.

A 61-yr-old man was scheduled for varicose vein stripping. He had in good health, had no past history suggestive of allergy, and took no medications. The operation began uneventfully under spinal anaesthesia. Ten minutes after the start of surgery, the patient became confusional, severely hypotensive and tachycardic. Ephedrine, phenylephrine and noradrenaline were administered in addition to rapid infusion of normal saline but the patient remained hypotensive and tachycardic. Fifteen minutes after occurrence of hypotension, the ECG revealed ST segment elevation in a MCL₅ lead. We suspected that hypotension was caused by left ventricular dysfunction as a result of myocardial ischaemia, and started nitroglycerin and noradrenaline continuously. But the patient's condition remained unchanged. A few minutes later, the anaesthetist noticed a mildly or moderately erythematous rash at the patient's face for the first time and

diagnosed as Kounis syndrome. Chest auscultation revealed clear breath sound and no wheezing. Since the allergic reaction was classified as the Ring and Messmer's grade III, 0.2 mg of adrenaline was administered intravenously followed by an infusion. The systolic blood pressure increased immediately, and the heart rate decreased gradually. Within 30 min of administration of adrenaline, the ST segment was returned to baseline value. Diltiazem in addition to nitroglycerin was given for the prevention of coronary artery spasm. An echocardiography did not show any abnormal wall motion and contractility abnormalities. The procedure was canceled. Fifty minutes after administering adrenaline, the patient was transferred to the intensive care unit where troponin T was negative and a significant increase in tryptase was seen. The next day, cardiac enzyme measurements were within normal limits. The patient made an uneventful recovery. Six weeks later, allergy testing was performed using the prick method, which revealed strongly positive to latex and negative to all the drugs used. Cardiac catheterization revealed the presence of angiographically normal lesion-free coronary arteries.

During the course of anaphylaxis, hypotension and tachycardia commonly occur, which are detrimental to the balance of myocardial oxygen supply and demand. Moreover, administration of adrenaline, which is the first line therapy for anaphylaxis [2–4], can further impair myocardial oxygen supply–demand relationships. In case of Kounis syndrome, since coronary artery spasm or occlusion occurs under such clinical situation, the myocardium faces in a serious crisis. Thus, the balance of myocardial oxygen supply and demand must be improved as promptly as possible. For that purpose, anaphylaxis should, first of all, be diagnosed and controlled. However, in this patient, it took about 20 min until we identified a cause of severe hypotension as anaphylaxis. Clinical manifestations in anaesthetised patients often differ from those in awake patients [2,3]. Among classical triad of clinical signs of anaphylaxis, respiratory manifestation is less common during anaesthesia and cutaneous symptom is often difficult to detect because of opaque surgical drapes. Moreover, cardiovascular symptoms are not uncommon during anaesthesia and have numerous etiologies. The diagnosis of anaphylaxis during anaesthesia is often difficult [2,3]. In case of Kounis syndrome, if anaphylaxis is not noticed when myocardial ischaemia occurs like this case, the anaesthetists can commit an error because of a difference in therapies between anaphylaxis and acute coronary syndrome [5]. Thus, anaphylaxis should be taken into consideration whenever unexplained cardiovascular collapse suddenly occurs during anaesthesia.

Although simultaneous treatment for both acute coronary syndrome and anaphylaxis is necessary in patients with Kounis syndrome, there is a difficult therapeutic dilemma between both pathological

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conditions [5]. Some drugs for anaphylaxis can be harmful in patients with acute coronary syndrome, and other drugs for acute coronary syndrome may exacerbate the anaphylactic reaction. In particular, adrenaline can aggravate myocardial ischaemia and induce arrhythmias. Ridella et al. [6] reviewed the literature on Kounis syndrome caused by beta-lactam antibiotics and clarified that adrenaline was used in only 23% of the cases. However, early intravenous administration of adrenaline is the key points of perioperative management of anaphylaxis [2–4]. Previous investigators have demonstrated that poor outcomes during anaphylaxis are associated with either late or absent administration of adrenaline or inappropriate dosing [3]. In this patient with the Ring and Messmer's grade III allergic reaction, we gave priority to the treatment of anaphylactic shock over that of acute coronary syndrome, and administered adrenaline, which was effective in both shock and myocardial ischaemia. Whether adrenaline is effective or not in patients with Kounis syndrome is unknown [5,6]. At the present time, guidelines for treatment of Kounis syndrome have not been established. However, we believe that the highest priority should be given to early control of the systemic allergic reaction in case of severe allergic reaction (e.g. the Ring and Messmer's grade III or IV reaction) and administration of adrenaline with careful titration is essential.

Since we did not consider latex as the culprit agent for anaphylaxis even after diagnosing as Kounis syndrome, the patient was not treated in a latex-free environment. This might be continuously exposed to the allergen, which could contribute to extended haemodynamic instability. As anaphylaxis caused by most of allergens that are commonly used during anaesthesia progresses within minutes, the time span between exposure to such allergens and noticed manifestations is important information in determining the etiology of anaphylaxis [2–4]. However, latex anaphylaxis is not always rapid in onset and can occur anytime during anaesthesia and surgery [2]. This delay in presentation of latex allergy means that the etiology of anaphylaxis cannot be determined even when anaphylaxis occurs immediately after other medications are administered. During anaesthesia and surgery, not only the diagnosis of anaphylaxis but also identification of the etiology of anaphylaxis may be difficult. In addition, latex allergy can occur without obvious risk factors like this case. Therefore, it is important to convert to a latex-free environment whenever sudden cardiovascular collapse of unknown etiology is encountered during surgery and anaesthesia.

In summary, there are difficult problems with regard to diagnosis and therapy during general anaesthesia in patients with Kounis syndrome. Although adrenaline is controversial for the treatment of these patients, the anaesthetists should not hesitate to administer adrenaline for haemodynamic instability because the highest priority should be given to early control of the systemic allergic reaction even with myocardial ischaemia. Also, if anaphylaxis, which is often difficult to diagnose during anaesthesia, is not noticed when myocardial ischaemia occurs, the anaesthetists can commit an error in therapy. Thus, they should pay attention to occurrence of anaphylaxis whenever myocardial ischaemia occurs during anaesthesia.

Conflicts of interest

All authors declare no conflict of interest.

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