Case Report

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New Fatal Case of Kounis Syndrome Triggered by Metamizole: A Case Report

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Abstract

Kounis syndrome is the concurrence of acute coronary syndromes with conditions associated with mast cell activation, such as allergies or hypersensitivity, and anaphylactic or anaphylactoid insults. In this report, we present a case of a patient who suffered a Kounis syndrome after a metamizole infusion in post-surgery time. NSAIDS are the most frequent causes of drug associated anaphylactic reactions in literature. The cardiac manifestations of systemic mastocytosis may be life-threatening, and for this reason is important to consider their presence and to predefine the way to treat it.

Keywords: Metamizole; Dypirone; Anaphylactic shock; Anaphylactic reactions; Kounis syndrome; Acute coronary syndrome

Introduction

Anaphylactic reactions are often induced by drugs. Kounis syndrome (KS) is defined as the concurrence of acute coronary syndromes including coronary spasm, acute myocardial infarction and stent thrombosis, with conditions associated with mast-cell and platelet activation and involving interrelated and interacting inflammatory cells, such as macrophages and T-lymphocytes, in the setting of allergic or hypersensitivity and anaphylactic or anaphylactoid insults [1]. This situation leads to cardiovascular symptoms and signs, including acute coronary events, which may result in the nosologic entity Kounis syndrome. Vasospastic allergic angina, allergic myocardial infarction and stent thrombosis with occluding thrombus infiltrated by eosinophil's and/or mast cells are the 3 reported variants of this syndrome [2]. Current data come from nearly 300 cases published in the literature [3]. Most of them are isolated drug-related case reports. The number of reported cases is growing, especially in southern Europe [4]. The awareness of KS is rising. Thorough reviews have shown causes incriminated of inducing KS and these can be assorted [5]. It has been stated that KS is not a rare disease but is a rarely suspected and diagnosed clinical condition [6]. It is necessary to know how to treat a Kounis syndrome or at least, identify it. There is no specific diagnostic test for this syndrome and it is probably under-diagnosed because of the variable manifestations of an allergic reaction [7]. KS has mostly been reported in southern Europe, especially in Spain, Italy, Greece and Turkey. This different geographic distribution could be attributed to climate and environmental conditions resulting in pollen cross-reactivity, hymenoptera exposures, overconsumption of medicines and/ or inadequacy of preventative measures but, in addition, this could respond to a different awareness of physicians of the existence of KS, even a different suspicion of it, when occurs [2].

Patient Report

A fatal case of an acute coronary syndrome has been reported, where a metamizole infusion induced an anaphylactic shock. A 43-year-old North-African woman without any drug allergy known was treated by metamizole in post-surgical period for Bartholin abscess. She had no previous history of drug allergies and her medical history only included some spontaneous abortion with positive anticardiolipin antibodies in a laboratory determination and antiphospholipid syndrome in studio. No regular medications.

Seconds after the first metamizole infusion, she developed an anaphylactic shock with bronchospasm, extreme bradycardia (35 bpm) and upper extremity and chest skin reaction. The patient suffers a cardiac arrest in operating room. She received intravenous epinephrine, atropine, and hydrocortisone and was transferred to the intensive care unit after a cardiac massage and defibrillation, with fluid perfusion and oxygen. It was necessary her endotracheal intubation. In the critical care unit, she suffered a new sudden cardiac arrest which required epinephrine and cardiac massage.

Epinephrine was administered intravenous and not intramuscular route.

Thereafter patient developed a bilateral pulmonary embolism and ischemic hepatitis. Computed axial tomography showed an extensive cerebral oedema.

Histopathological confirmation of the presence of eosinophil and mast cells in the thrombus was required. She never recovered consciousness. The patient died four days later. All symptoms pointed at Kounis syndrome type I.

Discussion

This variant of Kounis syndrome is observed in patients with no previous heart condition [8]. The prognosis is usual better in patients with this variant [7]. Mahmoud A et al., in a recently review showed that serious complications are rare in type I KS with a death rate of 2,9%, 2,2% in females and 3% in males. In all of the complicated cases with fatal consequences, with an only one exception, an allergic reaction to a medication was the trigger [5].

The use of metamizole may develop Kounis syndrome, apart from the case currently under discussion, more cases have been reported [3]. A recent study of 51 cases of Kounis syndrome reported to the international pharmacovigilance Agency during the period 2010-2014 showed that non-steroidal anti-inflammatory medications were the most frequent trigger drugs [8,9]. We suggest that Kounis syndrome should be considered in the differential diagnosis of acute coronary syndrome. We can anticipate that more cases will appear in the future. Therefore, a high index of suspicion seems to be important. Anesthesiologists should be familiar with mastocytosis and Kounis syndrome because they are both life-threatening conditions that may present during intraoperative anaphylaxis or myocardial ischemia, and they have specific management implications [10]. Management of KS consists of restoring myocardium revascularization in conjunction with the treatment of the allergic reaction. The difficulty lies in the fact that the treatment of either of the two associated entities may worsen the other injury [8]. Drugs administered to treat cardiac manifestations can worsen allergy and drugs given to treat the allergic symptoms can aggravate cardiac dysfunction. Treatment is aimed at coronary artery vasodilators and allergic reaction amelioration. For the treatment of the allergic reaction, both H1 and H2 antihistamines, such as diphenhydramine (1 to 2 mg/kg) and ranitidine (1 mg/kg) can be used. The use of H1 receptor blockers has been suggested in Kounis syndrome but in a low flow rate because these drugs can precipitate hypotension and compromise coronary flow [11]. Corticoids are an important part of the treatment of anaphylaxis but they may impair wound healing causing myocardial wall thinning and cardiac aneurysms. Despite, their use in KS is probably safe and appropriate [8]. In the same way, fluid resuscitation is the mainstay treatment in the management of distributive shock. It is necessary take into consideration with patients' specific clinical conditions such as ejection fraction, acute pulmonary oedema, and hemodynamic instability.

Epinephrine is the medication of choice to relieve the life-threatening symptoms of anaphylaxis par excellence; but, it may aggravate myocardial ischemia and induce coronary vasospasm and arrhythmias in KS especially if administrated intravenously. Epinephrine was administered intravenous in our patient. Thus, an intramuscular route is preferred in a dose of 0.2 to 0.5 mg each 5 to 15 minutes, until the resolution of symptoms or the appearance of epinephrine side effects [8].

Primary percutaneous coronary intervention is the preferred reperfusion strategy when it is possible. Otherwise, fibrinolytic therapy should be considered [8].

Pharmacological treatment of myocardial revascularization includes adjunctive antithrombotic therapy: acetylsalicylic acid (ASA) has a risk and that it can induce or worsen an anaphylactic reaction and P2Y12 receptor inhibitor that do not have a harmful effect on the associated anaphylactic reaction [8]. The unstable hemodynamic situation of our patient made impossible any of this approach.

Calcium channel blockers and nitrates, intravenous or sublingual nitroglycerin, seem reasonable and safe in patients with KS if the blood pressure is satisfactory [1]. Intravenously administered nitroglycerin is indicated in the first 48 hours after an acute coronary syndrome for treatment of persistent ischemia, heart failure, or hypertension. Although nitrates may induce an allergic reaction, this molecule seems safe in KS when the hemodynamic status is satisfactory. Furthermore, beta-blockers may interfere with the use of epinephrine which is the basis of treatment of anaphylaxis and they can cause a subsequent coronary spasm due to an unopposed activity of α-adrenergic receptors. Consequently, beta-blockers are contraindicated in KS [8]. Finally, opioids, as powerful analgesic and anxiolytic agents, are indicated but their use may induce massive mast cell degranulation which may aggravate the anaphylactic reaction. They should hence be given carefully in patients with KS to relieve the chest pain [8]. However many questions about the optimal treatment of KS remain unanswered.

Conclusion

Actually, there is no consensus on treatment for KS, and most of the data on it are from case reports but an agreed approach should be defined for future cases. All health professionals, pharmacist included, need to get trained on this syndrome to ensure a better syndrome recognition and appropriate management of these patients, in a direct or indirect way, e.g. contributing to protocols development.

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