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TYPE 1 KOUNIS SYNDROME AND MULTIORGAN FAILURE SECONDARY TO METAMIZOLE

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ABSTRACT
Kounis syndrome is defined as acute coronary syndromes secondary to allergic insults.Various drugs, conditions and environmental exposure has been shown to cause Kounis syndrome. We report a 40 year-old male patient otherwise healthy who suffered of acute coronary syndrome and multiorgan failure after one tablet of metamizole consumption. Severe anaphylactic shock and multiorgan failure was treated by high dose vasopressor support, mechanical ventilation and plasmapheresis. He was discharged as healthy at the end of three weeks intensive therapy. This case highlights the occurence of acute coronary syndrome and multiorgan failure following drug induced anaphylaxis. Kounis syndrome should be kept in mind in case of an acute cardiac complication.

INTRODUCTION

Various coronary syndromes, including Kounis syndrome, have been described during anaphylaxis. Kounis syndrome describes one of the mechanisms that could possibly take place under circumstances where there are concurrent occurrence of acute coronary syndrome and allergic reaction, resulting in a sudden cardiovascular collapse [1]. There are two variants of this syndrome. Type I variant includes subjects with normal coronary arteries without cardiac morbidities, while type II variant includes subjects with previous coronary artery disease in whom acute allergic events manifest into plaque rupture leading to acute coronary artery spasm or acute myocardial infarction [1].

The syndrome suggests that coronary artery spasm or atheromatous plaque rupture is related to the release of allergic mediators [1]. Various drugs, animals, and insect bites associated with allergic reaction have been reported to develop Kounis syndrome [2]. We describe an otherwise healthy male patient who developed acute myocardial infarction and multiorgan failure after the anaphylactic reaction to metamizole and directed us to the diagnosis of Kounis syndrome.

Case report

A 40 year-old male patient otherwise healthy applied to Emergency Service with complaints of acute generalized erythema in body and dizziness. He declared that he had a local nevus extraction on cheek today and afterwards consumed one tablet of metamizole 500 mg. His complaints started two hours later and progressively worsened. On first evaluation he was conscious and cooperative. Whole body erythema was obvious. Hypotension (76/52 mmHg) and mild tachycardia (104/min) was detected. Other physical evaluation was normal. He was monitorized, blood samples taken for examination and saline solution started intavenously. An hour later he complained of a severe chest pain. Hemodynamic collapse was experienced in minutes. Electrocardiogram findings revealed acute ST-elevated anterolateral myocardial infarction (Figure 1).

Vasopressor support was started (noradrenalin infusion 0.1 mcg/kg/min). He immediately was consulted with Cardiologists and transferred to angiography laboratory. In coronary angiography thrombus was extracted from mid-distal portion of left anterior descending artery but retrograde flow was not achieved (Figure 2.). Only a small portion of anterolateral septum was observed to be hypokinetic but global ejection fraction was measured to be %55-60. Since still hypotensive despite noradrenalin support an intra-aortic balloon pump was inserted at the end of the procedure and clopidogrel was started. Despite maximal (3 mcg/kg/min) noradrenalin and intra-aortic balloon pump support he was severely hypotensive (60/30 mmHg) and adrenalin infusion was added. Distributive anaphylactic shock and Kounis syndrome were considered to be responsible of this clinical state. The patient was transferred to medical intensive care unit. Mean arteriel pressure was hardly maintained 60 mmHg with supportive adrenalin and noradrenalin infusions at maximal dose.

Meanwhile urinary output declined and respiration deteriorated and the patient was intubated and mechanical ventilation support started. The fast deterioration in renal function and critical hemodynamic status directed us to continuous veno-venous hemodialysis. He tolerated this procedure well and urinary output started after 48 hours and the procedure was ceased on the third day. On the third day trombocytopenia and microangiopathic hemolytic anemia developped which was attributed to thrombotic trombocytopenic purpura. Plasmapheresis was started at a dose of 40 ml/kg and continued for 7 days with day by day amelioration in clinical and laboratory status. Vasopressor support was gradually decreased and stopped and intraaortic balloon pump was extracted by the end of plasmapheresis. Respiratory mechanics also gradually ameliorated and after successful weaning he was extubated on eight day. On the fourteenth day of hospitalization he was discharged from intensive care unit. The rest of the hospital course of this patient was unremarkable, and he fully recovered.

Figure 1. Electrocardiogram taken at the time of chest pain showing ST-segment elevation in leads D1, AVL,V1-5

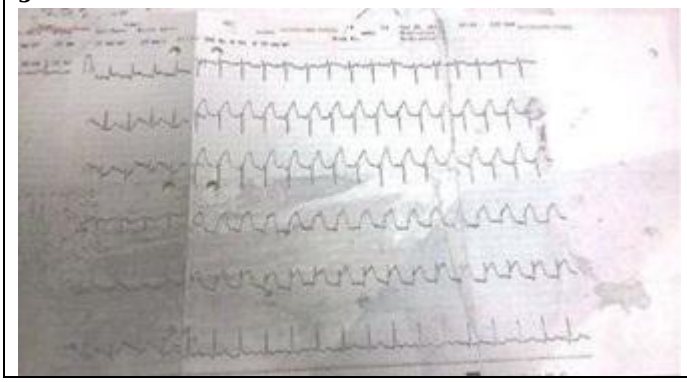
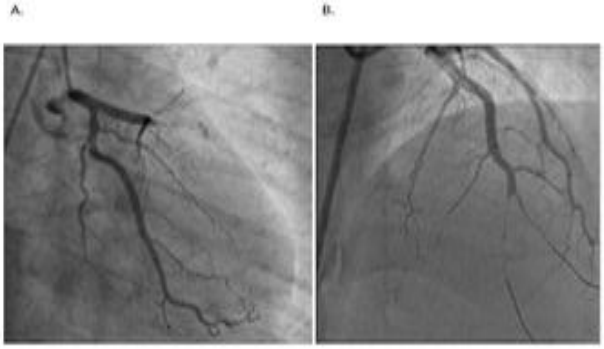


Figure 2. Coronary angiography views before (A) and after (B) percutaneous transluminal coronary angioplasty



DISCUSSION AND CONCLUSION

We presented a case of life-threatening anaphylactic reaction to metamizole, which concurrently developed with myocardial infarction and multiorgan failure. The patient developed acute myocardial infarction hours after metamizole consumption but despite generalized hyperemia no classical features of anaphylaxis or hypersensitivity reactions were detected.

Kounis syndrome was first described in 1991 as ‘acute coronary syndrome caused by inflammatory mediators during an allergic insult’ [1]. Pathophysiologically, Kounis syndrome typically results from mast cell degranulation in the setting of an allergic insult with the subsequent release of numerous inflammatory mediators such as histamine, neural proteases, arachidonic acid products, platelet activating factors and variety of cytokines [3]. Histamine is able to implicate platelet activation, thickening of intima, coronary vasoconstriction, platelet activation and tissue factor expression [4].

The number of causes that have been implicated to induce Kounis syndrome is increasing rapidly. These include various drugs (antibiotics, analgesics, antineoplastics, contrast media, corticosteroids, intravenous anaesthetics, non steroid anti inflammatory drugs, skin disinfectants, thrombolytics, anticoagulants, proton pump inhibitors), environmental exposures (stings by ants, bees, wasps, jellyfish, grass cutting, millet allergy, poison ivy, latex contrast, shell fish eating, viper venom envenoming), and several conditions (angio-oedema, bronchial asthma, urticaria, food allergy, exercise induced allergy, mastocytosis, serum sickness) [2].

Metamizole sodium (dipyrone) is a worldwide used non-steroidal anti-inflammatory drug. Since 1974, metamizole sodium was banned in more than 30 countries as a result of the association of this agent with the potentially lethal but rare adverse reaction agranulocytosis [5]. In addition, metamizole sodium may cause cutaneous

and allergic idiosyncratic reactions, anaphylactic shock and severe hypotension.

To our knowledge, there are three cases to date describing metamizole-induced cardiac complications due to Kounis syndrome [6-8].

In our present case, the patient likely suffered from the type 1 variant of Kounis syndrome due to young age and no history of chronic diseases before. Coronary angiography revealed acute thrombotic occlusion in mid-distal portion of left anterior descending artery. Although intervened early hypotension due to anaphylactic shock further decompensated blood flow to renal arteries and this was the possible reason of acute renal failure. Thrombotic trombocytopenic purpura, may be due to allergic mediators of anaphylaxis or even clopidogrel [9]. Cases of anaphylactic or allergic reactions associated with coronary events are frequently encountered in clinical practice. It is therefore crucial to suspect the possibility of individual hypersensitivity reactions especially in patients who develop coronary events. Acute coronary syndrome with allergic symptoms should raise suspicion for the possibility of Kounis syndrome.

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CONFLICT OF INTEREST: NIL

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