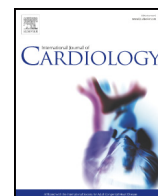




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Letter to the Editor

Kounis syndrome following cold urticaria: The swimmer's death

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Kounis syndrome is a hypersensitivity coronary disorder induced by conditions, environmental exposures, drugs, and coronary stents. So far, conditions that have been reported to be associated with Kounis syndrome include angio-edema, bronchial asthma, exercise induced anaphylaxis, food allergy, idiopathic anaphylaxis, mastocytosis, serum sickness and urticaria [1]. We report a unique case of cold-induced urticaria complicated by Kounis syndrome during swimming in sea water (swimmer's death) [2] that survived but with severe and avoidable impairment of quality of life (QoL).

A 68 year-old female was brought by her friends to the emergency department complaining of itchy feeling, chest discomfort and difficulty in breathing. Her symptoms had started soon after touching the sea water when she went for swimming about 2 h previously. Her friends described that she fainted immediately after started swimming and recovered by external massage. On examination, in the emergency room, her body was covered by generalized erythematous rash and was cold. Her pulse was 90 regular, the blood pressure 140/80 and temperature 35 °C. Electrocardiogram was normal but the high sensitivity cardiac troponin was 1.33 (normal values 0.00–0.005). Echocardiography revealed global reduction of left ventricular contractility resembling myocardial stunning with reduced ejection fraction to 30%. She was treated with diphenhydramine corticosteroids and nitrates intravenously for an allergic reaction associated with myocardial ischemia. Her symptoms resolved gradually and she was

transferred to a coronary care unit for further investigations. Detailed past history revealed that six years previously she have had an acute nonST elevation myocardial infarction that had occurred again while swimming treated conservatively in another hospital. In that hospital coronary angiography had revealed normal coronary arteries. She reported also hospitalization to a dermatology clinic due to a dermal exanthema covering all over her trunk. At that time, she underwent dermal biopsy and allergic skin prick tests that showed reaction to several allergens and had been characterized as an atopic person. She also mentioned attacks of photodermatitis. During the second day, in our hospital, her condition improved and a coronary angiography showed again normal coronary arteries with normalized echocardiogram and increased ejection fraction to 45%. Laboratory investigations including rheumatoid factor, cryoglobulins, antinuclear antibody titers and checking for thrombophilia were all negative. She was diagnosed as Kounis syndrome type I variant induced by cold urticaria. We did not perform ice-cube-challenge test on ethical grounds. She was advised to avoid cold stimuli with water temperature preferably <25 °C and to use prophylactic antihistamines and corticosteroids.

Kounis syndrome is mast cell degranulation associated with acute coronary disorder resulting from the action of inflammatory mediators released during mast cell degranulation in allergic or anaphylactic episodes. Mast cell degranulation occurs when 2000 nearby antibodies attached to mast cell surface are bridged by corresponding antigens and make the critical number of 1000 bridges [3]. Such mediators can induce either coronary artery spasm which can progress to acute myocardial infarction or atheromatous plaque erosion or rupture culminating to coronary thrombosis [4]. This is a classical pathway to induce an allergic or anaphylactic episode. However, mast cells have also the ability to degranulate in response to cold and to release their mediators such as histamine [5]. Histamine can induce coronary artery spasm via H1 receptors situated in the coronary arteries. In general, mast cells can be activated, in susceptible patients, by physical stimuli such as exposure to cold, exposure to heat or vibration, a condition known as physically induced urticaria [6]. Despite the direct mast cell activation by physical exposures, a role for IgE mediated activation in the pathogenesis of cold urticaria has been also proposed. This is based on serum transfer studies [7] and successful treatment with the anti-IgE drug omalizumab [8]. The described patient developed an allergic reaction manifesting as urticaria on two occasions while attempting to swim in cold sea water that was associated with nonST elevation myocardial infarction. Cold urticaria is an uncommon form of physical urticaria that can cause life-threatening reactions. Death may occur

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directly from anaphylactic reaction or by drowning when swimming in cold water (swimmer's death). Cold urticaria is mostly idiopathic. It can be classified into familial and acquired type which is divided into primary and secondary. Secondary urticaria can follow conditions such as infections, especially hepatitis, drug use, cold agglutinins, vasculitis, and malignancy [9]. In a study of 62 patients suffering from cold urticaria [10] 21 (33.9%) were atopic, 32 (51.6%) were female, their mean age was 41.5 ± 15.6 years while the mean age at disease onset was 32.5 ± 15.6 years; half of the patients were ≤ 30 years old at disease onset. In the same study one third of patients experienced at least one severe systemic reaction with hypotension and/or respiratory distress. In another study cardiovascular symptoms were the most frequent, followed by respiratory symptoms [11]. So far, myocardial infarction associated with cold urticaria has never been reported. Cold urticaria as a chronic disease that may present even with near fatal anaphylaxis, strongly affects the QoL and patients feel that must obey to restrictions that decrease their personal activities. Patients with cold urticaria should be educated about the possible occurrence of severe anaphylactic reactions and be supplied with antihistamines, corticosteroids and an emergency kit including adrenaline auto-injector [11]. Since our case is the first that combines cold urticaria with Kounis syndrome, decision whether to use adrenaline in such cases is challenging due to lack of experience. However, in severe cases sulfite free epinephrine is preferable to be given intramuscularly because it has faster onset of action and more sustained levels as compared with the subcutaneous route. We recommend intramuscular doses of 0.2–0.5 mg (1:1000). Aqueous solution is preferable [12]. Additional studies are needed to identify possible risk factors for severe reactions, to standardize the diagnostic measures, to uncover the pathophysiology of cold induced Kounis syndrome and thus to improve therapy [11].

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Acknowledgments

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

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