



Letter to the editor

Recurrent Kounis syndrome. How should be the long-term treatment of Kounis syndrome?

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A 45-year-old female patient presented to the emergency room complaining of retrosternal chest pain and weakness accompanied by sweating that began after a bee sting and lasted for approximately half an hour. The patient was conscious, and she had pale and sweaty appearance. Arterial blood pressure was 70/50 mm Hg, pulse was 56 rpm, and oxygen saturation was 96%. The patient denied any complaints such as itching or skin problems that could be associated with an allergic reaction. The electrocardiogram showed ST elevation in DII, DIII, and aVF, and reciprocal changes in anterior leads. Transthoracic echocardiography showed hypokinesia in the inferior wall. It was realized from her past history that the patient had been admitted to a hospital one year prior with the same complaints following a bee sting, after which she underwent coronary angiography with the diagnosis of acute myocardial infarction that revealed normal coronary arteries. She had been told that acute myocardial infarction was due to the bee sting (Kounis syndrome) and was discharged from the hospital. No prophylactic therapy was administered. The patient was considered to have Kounis syndrome, and she was placed on a therapy involving acetylsalicylic acid 300 mg, epinephrine 1 mg iv, and infusion of isotonic solution (NaCl 0.9%) with which arterial blood pressure gradually increased. In the physical examination 15 min later, blood pressure was 118/85 mm Hg, chest pain subsided, and ST-segment elevations reciprocal changes in anterior leads on ECG disappeared. The laboratory tests conducted upon admission revealed mild leukocytosis (leukocyte count = 12.380/μl) and eosinophilia (1.2%). Immunoglobulin E level

was elevated (180 g/l). During the four days of hospitalization in the coronary intensive care unit, troponin I levels remained stable and chest pain did not re-occur. The patient was clinically and hemodynamically stable during the hospitalization period, and she was then discharged from the hospital and she was prescribed diltiazem 60 mg once daily, isosorbide mononitrate 20 mg once daily, and desloratadine 5 mg once daily to be taken perorally.

The current manuscript reports a case of type 1 Kounis syndrome caused by an allergic reaction that manifested with hypotension and acute ST-elevation myocardial infarction that occurred twice within a one-year interval after a bee sting.

Kounis syndrome is defined as acute coronary syndrome occurring in association with allergic, anaphylactic, or anaphylactoid reactions caused by the activation of mast cells [1]. This syndrome can be caused by exposure to environmental factors such as bee stings, pollen, and insect bites, but also exposure to such allergens as drugs, toxic substances, and food [2]. During allergic reaction, cardiac mast cells, as the mast cells in other tissues, release platelet-activating factor, histamine, leukotriene, and neutral proteases as serotonin and tryptase when they are activated. These mediators exert many effects on the cardiovascular system. For example, platelet-activating factor causes vasoconstriction, proteases result in plaque erosion and rupture, whereas histamine causes coronary vasoconstriction and platelet activation [3]. This syndrome was reported to have two types as originally defined by Kounis [4], and a third type, which is referred to as the type 3 variant, was defined with the addition of stent thrombosis [5]. Type 1 is characterized by angiographically normal coronary arteries, and coronary vasospasm occurs as a result of allergic reaction in the absence of atherosclerotic coronary artery disease. Type 2 is characterized by acute coronary syndrome caused by coronary vasospasm or plaque rupture occurring as a result of allergic reaction in the presence of atherosclerotic coronary artery disease. The present case is consistent with type 1 Kounis syndrome.

Presenting with allergic symptoms and chest pain are the basis of diagnosis in Kounis syndrome. Systemic allergic reactions can occur within minutes or hours following exposure to an allergen. This reaction can affect the respiratory system, cardiovascular system, gastrointestinal system, skin, and mucosa. This reaction can manifest as an isolated skin problem or as an anaphylactic reaction that threatens the patient's life. Among the clinical findings, hypotension is the single symptom that would alone lead to the diagnosis of anaphylaxis [6,7]. The present case

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had hypotension and ST-segment elevation myocardial infarction without skin involvement; however, neither electrocardiogram nor echocardiographic provided evidence for right ventricular involvement. Among the diagnostic tests, elevated serum histamine, tryptase, eosinophil count, and IgE antibody levels support allergic reactions. In the present patients, IgE antibody level and eosinophil count were elevated, and histamine and tryptase levels were not analyzed.

The treatment of Kounis syndrome in the acute phase involves the management of acute coronary syndrome and the suppression of an allergic reaction. In patients suspected to have type 1 Kounis syndrome, nitrates and calcium channel blockers can be preferred due to the fact that coronary vasospasm is the basic pathologic process; beta-blockers, however, must be avoided. Beta-blockers worsen coronary vasospasm and they may attenuate the effects of epinephrine [7]. Steroids and antihistamines must be used in the first line to suppress an allergic reaction. In addition to steroid therapy in patients with type 2 Kounis syndrome, coronary angiography can be performed to detect the presence of coronary artery disease and angioplasty can be performed when required [8]. The present case sustained acute ST-segment elevation myocardial infarction after a bee sting one year prior to the current presentation. A second coronary angiography was not considered due to the fact that she had been found to have normal coronary arteries on the previous coronary angiography, and recently, the patient had transient ST-segment elevation and the troponin value did not turn out to be positive.

Currently, the treatment guidelines for patients with Kounis syndrome have not been established, and most of the information about the treatment of this syndrome comes from individual case reports or case series. In a review of reported cases with Kounis syndrome, steroids, H1 receptor blockers, nitroglycerine, and H2 receptor blockers were found to be the most widely used medications in the treatment [9]. Although the condition is rarely encountered, allergic reaction is the basic pathological process for which treatment options have been described and employed and are still used in the acute phase. However, there are no reported data or experiences regarding treatment options to be adopted in order to minimize the harms or protect the patient upon re-exposure to a similar allergen in the long term as occurred in

the present case. The present case was prescribed calcium channel blockers, nitrate, and H1 receptor blockers and advised her to avoid exposure to allergens. Upon her exposure to a similar allergen in the future, it will be possible to know how beneficial this therapy would be and how sufficient it would be to protect the patient from Kounis syndrome. There is no data regarding this and there is a debate over the need to have intramuscular/subcutaneous adrenalin doses available or using continuously a prophylactic medication as H1 receptor antagonists in order to avoid the re-occurrence of such life-threatening conditions as severe hypotension. We recommend the establishment of an international registry to collect standardized information on these patients.

Conflict of interest

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

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