

Letter

Systemic mastocytosis presenting as kounis syndrome

Kounis syndrome is defined as coronary vasospasm associated with hypersensitivity reactions.¹ Multiple triggers have been associated with Kounis syndrome, including Hymenoptera venoms; drugs such as nonsteroidal anti-inflammatories, proton pump inhibitors, β -lactam antibiotics, general anesthetics, and iodine contrast media; foods; latex; and snake venom. The clinical presentation of Kounis syndrome includes a mixture of symptoms and signs of an allergic reaction and acute coronary syndrome.²

Mastocytosis is characterized by mast cell proliferation in different organs with clinical manifestations due to the release of mast cell mediators. Urticaria pigmentosa is the most common skin manifestation. Flushing, pruritus, abdominal symptoms, bone lesions, and neuropsychiatric disorders are other common presentations in systemic mastocytosis.³ We report a case of systemic mastocytosis presenting as Kounis syndrome after a bee sting.

A 60-year-old man with a history of depression and no other medical conditions was stung by a honeybee on the neck. After 15 minutes, he experienced generalized itching, erythema with associated dizziness, and loss of consciousness. On arrival to the emergency department, he was hypotensive (blood pressure, 83/45 mm Hg) with a Glasgow Coma Scale score of 7. He was intubated and received mechanical ventilatory assistance. Initial electrocardiography revealed ischemic changes with ST-segment elevation in the inferior leads and ST depression in the antero-lateral leads (Fig 1). Troponin levels and echocardiography results were normal. Tryptase levels were not measured. Intravenous fluids and vasopressors, including epinephrine, were administered. A few hours later, the patient recovered completely, and the electrocardiography changes returned to normal.

The patient, a beekeeper, was referred to the allergy unit for assessment of possible bee venom hypersensitivity. He explained that during the last 20 years he has had 3 similar episodes, but none of these episodes had been preceded by bee stings. The first 2 episodes had been attributed to a food allergy, but this had never been confirmed. The last episode was approximately 8 years previously without any apparent trigger. Furthermore, he had been stung by bees several times without any systemic reactions. He had not taken any drugs or ingested any foods before the reaction. The patient did not have any cardiovascular risk factors, and coronary angiography results were normal.

Physical examination revealed brown macular lesions on the chest with a positive Darier sign. The skin biopsy specimen was compatible with urticaria pigmentosa. His basal serum tryptase level was 140 ng/mL. The bone marrow biopsy specimen revealed extensive mast cell infiltrate with clusters of abnormal mast cells and the molecular biology a *c-kit* mutation. Four months after the acute episode, we performed skin prick tests (1 μ g/mL) and

intradermal tests (0.00001 to 1 μ g/mL) to bee and wasp venoms. All the results were negative. The total IgE level was 34.3 kU/L. Specific IgE levels were 0.40 kU/L (reference range, <0.35 kU/L) to honey bee and 0.11 kU/L to the major allergen Api m1.

According to these findings, the patient was diagnosed as having systemic mastocytosis. He was advised about possible triggers and prescribed oral sodium cromoglycate, antihistamines, and an adrenaline autoinjector to use in case of anaphylaxis. The presentation of acute coronary syndrome together with allergic symptoms after the bee sting is consistent with Kounis syndrome.

A case series of patients with different mast cell-related disorders revealed that 10 patients had Kounis syndrome triggered by drugs, foods, and, in 1 patient, a wasp sting.⁴ In contrast to our case, this patient was found to have high levels of specific IgE to Hymenoptera venoms. On the other hand, systemic mastocytosis is associated with severe anaphylaxis to Hymenoptera.⁵ In patients with systemic mastocytosis, the absence of urticaria or angioedema and the presence of dizziness and/or syncope during anaphylaxis⁶ are frequent observations. The patient, a beekeeper, had mild sensitization to bee venom, but he had been previously stung by bees without any reactions. Moreover, after this reaction, he had been stung in the arm and face again without any systemic reaction. The facts that the results of intradermal tests (1 μ g/L) and specific IgE tests to Api m1 were negative and that the specific IgE to whole apis was low (0.40 kU/L) make it probable that this sensitivity is due to his exposure as a beekeeper rather than a bee allergy.⁷ Moreover, the patient has left his activity as a beekeeper, so we have decided not to recommend bee venom specific immunotherapy.

Hymenoptera stings can induce acute coronary syndromes by different pathogenic mechanisms, including direct action of the venom on the coronary endothelium.⁸ In this case, the sting may have been a trigger for the coronary vasospasm in a patient with undiagnosed systemic mastocytosis.

Kounis syndrome was described in 1991 by Nicholas Kounis, although cases of coronary spasm after drug administration have been reported previously.⁹ There are 3 types of Kounis syndrome.¹ Type 1 is present in patients without cardiovascular risk factors or coronary lesions. Reaction induces coronary spasm and causes chest pain and electrocardiographic changes secondary to ischemia. Cardiac enzymes may be normal or reflect the progression to an acute myocardial infarction. Type 2 occurs in patients with preexisting atheromatous disease, and type 3 can occur in patients with drug-eluting stent thrombosis.

Mast cells in the human heart are located mainly between myocardial fibers, around blood vessels, and in the arterial intima. Kounis syndrome is associated with mast cell degranulation, and tryptase levels may be increased in some patients during the acute episode.¹⁰

In conclusion, we report the case of a patient who developed type 1 Kounis syndrome and was found to have systemic

Disclosures: Authors have nothing to disclose.

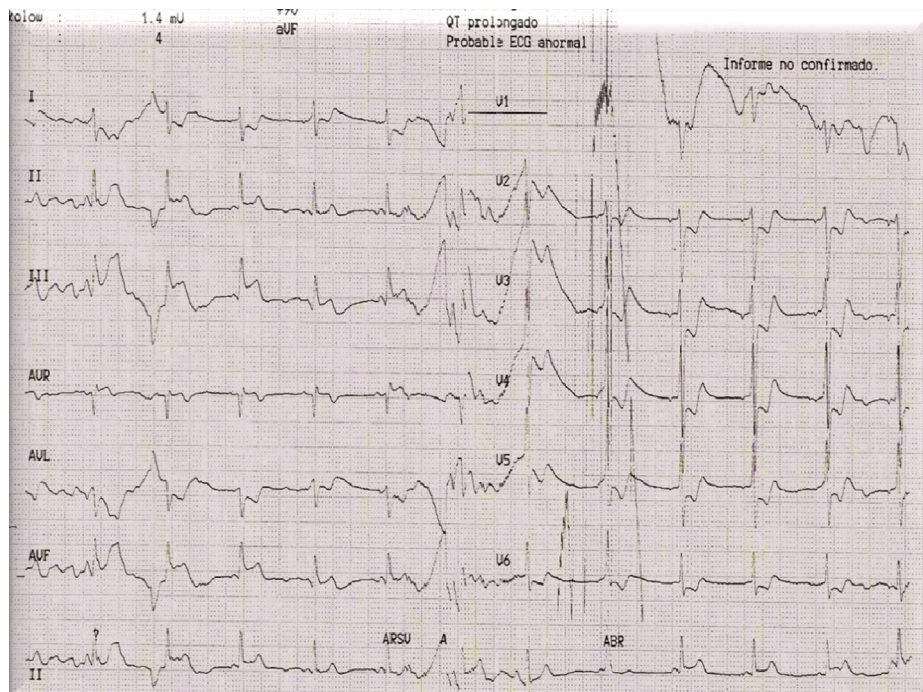


Figure 1. ST-segment elevation in the inferior leads and ST depression in the anterolateral leads.

mastocytosis. On the basis of these findings, we suggest that serum tryptase levels during the reaction and at baseline are measured in all patients presenting with Kounis syndrome to rule out possible underlying mastocytosis.

Ramon Leonart, MD*
 Blanca Andres, MD*
 Melina Makatsori, MRPC†
 Manuel Rubio-Rivas, MD*
 Ramon Pujol, PhD*
 Mercè Corominas, PhD*

*Allergy Section
 Internal Medicine Department
 Hospital Universitari de Bellvitge
 L'Hospitalet de Llobregat
 Barcelona, Spain

†Allergy Department
 Royal Brompton Hospital
 London, England
rlleonart@gmail.com

References

- [1] Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol.* 2006;110:7–14.
- [2] Gázquez V, Dalmau G, Gaig P, Gómez C, Navarro S, Mercé J. Kounis syndrome: report of 5 cases. *J Investig Allergol Clin Immunol.* 2010;20:162–165.
- [3] Bains SN, Hsieh FH. Current approaches to the diagnosis and treatment of systemic mastocytosis. *Ann Allergy Asthma Immunol.* 2010;104:1–10.
- [4] González-de-Olano D, Matito A, Sánchez-López P, et al. Mast cell-related disorders presenting with Kounis syndrome. *Int J Cardiol.* 2012;161:56–58.
- [5] Bonadonna P, Zanotti R, Müller U. Mastocytosis and insect venom allergy. *Curr Opin Allergy Clin Immunol.* 2010;10(4):347–353.
- [6] Alvarez-Twose I, González de Olano D, Sánchez-Muñoz L, et al. Clinical, biological, and molecular characteristics of clonal mast cell disorders presenting with systemic mast cell activation symptoms. *J Allergy Clin Immunol.* 2010;125:1269–1278.
- [7] Kalogeromitros D, Makris M, Gregoriou S, et al. Pattern of sensitization to honeybee venom in beekeepers: a 5-year prospective study. *Allergy Asthma Proc.* 2006;27:383–387.
- [8] Kogias JS, Sideris SK, Anifadis SK. Kounis syndrome associated with hypersensitivity to hymenoptera stings. *Int J Cardiol.* 2007;114:252–257.
- [9] Cisteró A, Urías S, Guindo J, et al. Coronary artery spasm and acute myocardial infarction in naproxen-associated anaphylactic reaction. *Allergy.* 1992;47:576–578.
- [10] Kounis NG. Serum tryptase levels and Kounis syndrome. *Int J Cardiol.* 2007;114:407–408.