



Letter

Coronary spasm secondary to biphasic anaphylaxis after hymenoptera stings

Kounis syndrome was first described in 1991 by Kounis and Zavras¹ who defined it as the concurrence of acute coronary syndromes (ACSs) with allergic reactions. Although initially termed *allergic angina*, it has been shown that it can progress to acute myocardial infarction,² mainly in patients with pre-existing cardiomyopathy, but occasionally in patients without coronary lesions. Inducing factors are diverse and include the ingestion of certain drugs, food allergies, jellyfish stings, cut grass, millet, latex, etc. Occasionally, Kounis syndrome can be induced by an allergic reaction caused by a hymenoptera sting, as in the case presented in this report.³

We describe the case of a patient who presented with unstable angina several hours after having been stung by wasps. A 64-year-old man presented with headache, blurred vision, dizziness, sore throat, stridor, palpitations, rash, and generalized pruritus after being stung by 3 to 4 wasps. He was transferred to the emergency department, where he was treated with 60 mg of intravenous (IV) 6-methylprednisolone, 10 mg of IV dexchlorpheniramine, and 0.5 mg of subcutaneous (SC) adrenaline (AD). At admission, his blood pressure was 105/75 mmHg, his heart rate was 108 beats/min, and his arterial oxygen saturation was normal. The biochemistry and blood counts showed normal values, except for high creatinine (1.27 mg/dL) and leukocyte (12,640/ μ L) levels. Electrocardiogram showed sinus tachycardia (rate 109/min) with no other alterations. When the patient's blood pressure decreased to 87 mmHg, he was started on fluid resuscitation with crystalloid solutions. Then, he was moved to the intensive care unit and treated with 200 mg of IV hydrocortisone and 0.5 mg of SC AD, with good response and complete resolution of the rash and pruritus. Five hours later, the patient complained of oppressive precordial pain, which rapidly resolved after administration of IV nitroglycerin. Electrocardiogram showed ST-segment depression lower than 1 mm in leads II, III, and aVF and negative T waves in these leads and in leads V₄ and V₅. Cardiac biomarkers were normal. Serum tryptase and immunoglobulin E levels were high (22.4 ng/mL and 214 KU/L, respectively), with subsequent tryptase normalization. Coronary angiogram showed normal coronary arteries and ventricular function but showed a left main coronary artery spasm that resolved after intracoronary nitroglycerin administration. The patient was discharged from the intensive care unit to the ward completely asymptomatic and under treatment with amlodipine. Follow-up was carried out at the division of allergy, where skin tests and determination of hymenoptera venom-specific serum immunoglobulin E antibodies were performed. These confirmed the

patient's double sensitization to *Polistes dominula* and *Vespula* species, and he was started on specific immunotherapy for these venoms.

The reported incidence of allergic reactions to hymenoptera venom is approximately 5% in the general population.⁴ Symptoms vary from dermatologic manifestations such as rash and pruritus to gastrointestinal and respiratory disorders. In rare cases, patients with anaphylaxis can develop ACS. The present case suggests the even rarer event of a biphasic response.

Hymenoptera venom contains peptides, proteins, and vasoactive amines such as histamine, acetylcholine, dopamine, noradrenaline, and 5-hydroxytryptamine. Phospholipase A₂, hyaluronidase, and acid phosphatase are considered the main allergens. These constituents trigger physiologic reactions similar to the release of mast-cell mediators after an allergic reaction.

Kounis syndrome has been defined as the onset of an ACS, whether vasospastic angina or acute myocardial infarction, triggered by the direct action of the venom constituents on the vascular endothelium or by the release of inflammatory mediators that follows an allergic reaction. In fact, these allergens lead to vasospasm or atheromatous plaque erosion.² Variants of this syndrome exist.² Type I is observed in patients with neither risk factors nor coronary lesions; it presents with coronary spasm and normal values of cardiac biomarkers, although these occasionally can be high. This variant probably suggests some degree of endothelial dysfunction. Type II occurs in those with pre-existing atherosclerotic disease, whether known or not, and in which the release of mediators induces plaque erosion and/or rupture, triggering angina, or acute myocardial infarction. Type III, recently described, includes patients with drug-eluting stent thrombosis.

Our patient had type I Kounis syndrome, because cardiac catheterization showed only left main coronary artery spasm. The fact that the onset of the ACS was several hours after the wasp sting and after complete resolution of initial symptoms, together with the increase in serum tryptase and immunoglobulin E levels observed, suggests that the episode was caused by a biphasic allergic reaction. This phenomenon with controversial pathogenesis has been described to occur in up to 20% of anaphylactic reactions.⁵ Our case is unique because the coronary symptoms that developed later were not accompanied by the initial manifestations of anaphylaxis. These findings have been rarely described in the literature.^{6,7} Coronary artery spasm documented during angiography has been described in the literature, albeit only within minutes of administering SC AD.⁸ Other studies have measured time to peak plasma epinephrine concentration after SC administration, proving it can be up to 2 hours.⁹ In contrast, we believe that, given the delay from the AD

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injection to the manifestation of coronary symptoms (5 hours), it is unlikely that AD was involved in triggering the reaction in this case.⁷

Although there is no strict recommended observation period for anaphylaxis cases, it is reasonable to establish an 8-hour monitoring period. However, patients with a history of risk factors (eg, asthma, previous biphasic reactions, unknown inciting trigger, hypotension at presentation, or protracted anaphylaxis) should be observed for a longer period, perhaps at least 24 hours after the first symptoms.^{5,10} Prognosis is good once the acute phase has been overcome, and patients generally undergo immunotherapy to prevent future episodes, as in the present case.

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