

CASE FOR DIAGNOSIS

[Translated article] Kounis Syndrome, Mast Cells Beyond the Skin

Síndrome de Kounis, mastocitos más allá de la piel

Medical history

A 51-year-old male with a past medical history of hypertension, bronchial asthma, and allergies to aspirin and amoxicillin presented to the Dermatology ER with a 1-h history of a pruritic skin rash, which started 1 day after beginning treatment with cefuroxime 250 mg/12 h for cystitis. During his stay in the ER, the patient developed oppressive chest pain along with autonomic symptoms.

Physical examination

The physical examination revealed the presence of erythematous–edematous plaques with a pale yellow center and hyperemic periphery of axial (Fig. 1) and limb distribution, along with bilateral eyelid edema (Fig. 2).



Figure 1

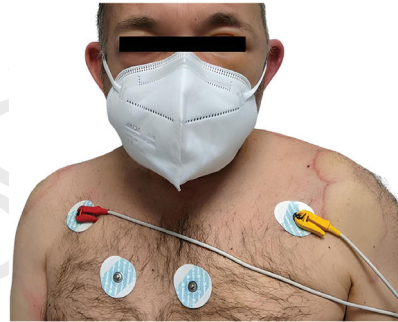


Figure 2

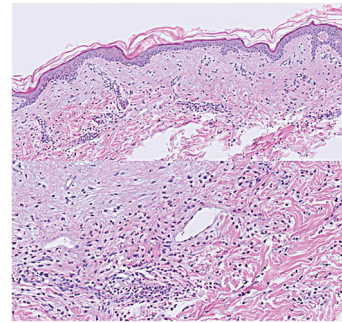


Figure 3

Supplementary tests

The electrocardiogram (ECG) revealed negative T waves in leads II, III, and aVF. The coronary computed tomography angiography of the chest ruled out pulmonary embolism, and the high-sensitivity troponin T myocardial injury marker was normal.

Histopathology

An incisional biopsy of one of the plaques revealed the presence of perivascular infiltrate including lymphocytes and neutrophils, as well as edema in the papillary dermis, which were findings consistent with acute urticaria (Fig. 3).

What is your diagnosis?

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34 Kounis syndrome type I.

35 Disease progression and treatment

36 IV methylprednisolone and dexchlorpheniramine were
37 administered, which resulted in the resolution of chest pain
38 and normalization of the ECG changes. The patient was dis-
39 charged with a tapering course of oral prednisone 30 mg and
40 loratadine 10 mg/12 h. He was referred to Cardiology for
41 coronary evaluation and to Allergy for beta-lactam allergy
42 testing. Unfortunately, the patient did not attend the rec-
43 ommended follow-up appointments.

44 Comment

45 Kounis syndrome (KS) is a myocardial ischemia-related phe-
46 nomenon triggered by allergic or anaphylactic stimuli. The
47 three main variants of this syndrome are allergic vasospas-
48 tic angina (KS type I), allergic myocardial infarction (KS type
49 II), and previous stent thrombosis (KS type III). Of these, KS
50 type I is the most common one, accounting for more than
51 70% of the cases.^{1,2}

52 KS is more prevalent in men aged 40–70 with a past medi-
53 cal history of allergies and cardiovascular risk factors.¹ Our
54 patient's profile matches the typical KS epidemiology: 51
55 years old, asthmatic, allergic to beta-lactams, and hyper-
56 tensive.

57 The pathophysiology of KS is based on mast cell
58 and platelet degranulation induced by the allergenic
59 stimulus.^{1,2} Mast cells are abundant in cardiac tissue; dur-
60 ing an allergic reaction, mast cell degranulation releases
61 substances that induce vasospasm (histamine, chymase,
62 cathepsin-D, leukotrienes) and/or cause plaque erosion and
63 rupture through fibrinogen degradation, which destabilizes
64 it (tryptase, neutral proteases).^{1,2} Symptoms primar-
65 ily include cardiac (angina, palpitations), dermatological
66 (hives, angioedema), and respiratory (dyspnea, wheezing)
67 signs.² The presence of the allergen is necessary to trig-
68 ger the episode, so once it has been removed, recurrence
69 of skin lesions or other symptoms is not expected in the
70 mid-term.^{2,3}

71 Antibiotics are the primary triggers of KS. Cephalosporins
72 are the most widely reported drug responsible for KS after
73 penicillins, with cases ranging from cefuroxime-induced
74 coronary spasm to allergic myocardial infarction.^{3,4}

75 In addition to the supplementary tests performed in this
76 case (electrocardiogram, CCTA, high-sensitivity troponin I,
77 and skin biopsy), serum tryptase and IgE levels are rec-
78 ommended to support a KS diagnosis.^{2,5} However, these
79 parameters are not available in our center ER.

80 Regarding treatment, KS type I usually resolves with
81 standard hypersensitivity reaction treatment: systemic cor-
82 ticosteroids and antihistamines.^{1,2,5} In contrast, KS types II
and III require therapies such as those used to treat other

83 acute coronary syndromes, which will be managed specif-
84 ically by Cardiology.^{1,2,5} There are specific considerations
85 for managing KS: aspirin can trigger anaphylactoid reac-
86 tions and exacerbate the condition, while epinephrine may
87 worsen vasospasm-induced events (KS type I).^{2,5} The utility
88 of the two drugs in KS requires further evidence, and their
89 use should be individualized.^{2,5}

90 In addition to skin and airways, mast cells may affect
91 other target organs, requiring multidisciplinary intervention
92 in the emergency setting.^{1,2,5} KS should be considered in any
93 patient who develops chest pain during an allergic reaction,
94 with a thorough review of drug allergy history and recent
95 drug administration.

96 Conflicts of interest

97 None declared.

98 References

- 99 1. Abdelghany M, Subedi R, Shah S, Kozman H. Kounis
100 syndrome: a review article on epidemiology, diagnos-
101 tic findings, management and complications of allergic
102 acute coronary syndrome. *Int J Cardiol.* 2017;232:1-4,
103 <http://dx.doi.org/10.1016/j.ijcard.2017.01.124>.
- 104 2. Barrionuevo Sánchez MI, Corbí Pascual MJ, Córdoba Sori-
105 ano JG, Ramírez Guijarro C, Calero Nuñez S, Gallego
106 Sánchez G. Kounis syndrome or allergic infarction: a rel-
107 atively unknown entity. *Med Intensiva.* 2018;42:506-9,
108 <http://dx.doi.org/10.1016/j.medin.2017.06.003>.
- 109 3. Mitsis A, Christodoulou E, Georgiou P. Coronary spasm secondary
110 to cefuroxime injection, complicated with cardiogenic shock
111 – a manifestation of Kounis syndrome: case report and litera-
112 ture review. *Eur Heart J Acute Cardiovasc Care.* 2018;7:624-30,
113 <http://dx.doi.org/10.1177/2048872617701885>.
- 114 4. Mazarakis A, Koutsojannis CM, Kounis NG, Alexopoulos
115 D. Cefuroxime-induced coronary artery spasm manifest-
116 ing as Kounis syndrome. *Acta Cardiol.* 2005;60:341-5,
117 <http://dx.doi.org/10.2143/AC.60.3.2005015>.
- 118 5. Ollo-Morales P, Gutierrez-Niso M, De-la-Viuda-Camino E,
119 Ruiz-de-Galarreta-Beristain M, Osaba-Ruiz-de-Alegria I,
120 Martel-Martin C. Drug-induced Kounis syndrome: lat-
121 est novelties. *Curr Treat Options Allergy.* 2023:1-18,
122 <http://dx.doi.org/10.1007/s40521-023-00342-9>.

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