



Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Acute ST elevation myocardial infarction due to allergic reaction, Kounis syndrome: A case report and review of the emergency management

Eva Rajha^{a,*}, Ahmad Didi^b, Habib Dakik^b, Afif Mufarrij^c

^a Department of Emergency Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

^b Department of Cardiology, The American University of Beirut Medical Center, Beirut, Lebanon

^c Department of Emergency Medicine, The American University of Beirut Medical Center, Beirut, Lebanon

ARTICLE INFO

Article history:

Received 26 September 2019

Received in revised form 1 October 2019

Accepted 7 October 2019

Available online xxxx

Keywords:

Kounis syndrome

Allergic myocardial infarction

Coronary artery vasospasm

ABSTRACT

Kounis syndrome is defined by the occurrence of an acute coronary syndrome (ACS) in the setting of an allergic, hypersensitivity or anaphylactic condition. Degranulation of mast cells and platelet activation leading to the release of multiple inflammatory mediators are thought to make the arterial circulation susceptible to acute cardiac events. It is an often underdiagnosed entity in the emergency setting, due to lack of awareness among emergency providers. Identifying Kounis syndrome is critical, since managing ACS differs from that of a classical acute myocardial infarction. We present the case of a 72-year old male patient with a history of stable coronary disease who presented to the emergency department with a diffuse pruritic rash and chest pain. Electrocardiogram showed ST elevation myocardial infarction. Urgent coronary angiography revealed total occlusion of the mid left anterior descending coronary artery which was treated with a drug eluting stent with an excellent outcome. The pruritic rash responded to treatment with intravenous corticosteroids and antihistamines; No allergens were identified. The patient's symptoms resolved and he had an uneventful hospitalization.

The diagnosis of Kounis syndrome can complicate the management of acute allergic reactions. Special precautions should be taken by emergency physicians with regards to the administration of beta blockers, morphine and vasodilators, which may be detrimental in this setting.

© 2019 Elsevier Inc. All rights reserved.

1. Background

Cardiovascular complications of hypersensitivity reactions have been documented historically in the medical literature [1–3]. “Allergic myocardial infarction”, known as Kounis syndrome (KS), was first described by Kounis and Zavras in 1991 [4,5]. This entity was redefined as “acute coronary syndrome associated with mast-cell and platelet activation in the setting of hypersensitivity and allergic or anaphylactic insults” [6]. KS is thought to be frequently underdiagnosed [7]. Its emergency department (ED) reported incidence is 3.4% of allergy presentations [7]. KS is caused by the release of histamine, arachidonic acid products, platelet-activating factor, cytokines and chemokines during mast-cell degranulation leading to atheromatous plaque erosion or rupture

and/or coronary vasospasm [4,8]. Three types of KS have been described. Type I involves patients with normal coronary arteries in whom the acute allergic insult induces coronary artery vasospasm with or without progression to acute myocardial infarction and cardiac enzyme elevation. Type II involves patients with quiescent pre-existing atheromatous disease in whom the allergic episode induces plaque erosion or rupture, manifesting as an acute myocardial infarction. Type III refers to patients with coronary stent thrombosis (type III-a) or stent restenosis (type III-b) with histologic evidence of eosinophils and mast cells [3,4,9].

In this report, we describe a case of type II KS presenting with ST elevation myocardial infarction associated with urticaria. The management of Kounis syndrome will be briefly discussed.

2. Case presentation

A 72-year old male patient, known to have non-obstructive coronary artery disease (CAD), presented with a one-hour history of diffuse pruritic rash and retrosternal chest pain radiating to the left shoulder, associated with vomiting. The patient had a

Abbreviations: ACS, acute coronary syndrome; KS, Kounis syndrome; ED, emergency department; CAD, coronary artery disease.

* Corresponding author at: Department of Emergency Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA.

E-mail address: evarajha@gmail.com (E. Rajha).

<https://doi.org/10.1016/j.ajem.2019.10.006>

0735-6757/© 2019 Elsevier Inc. All rights reserved.

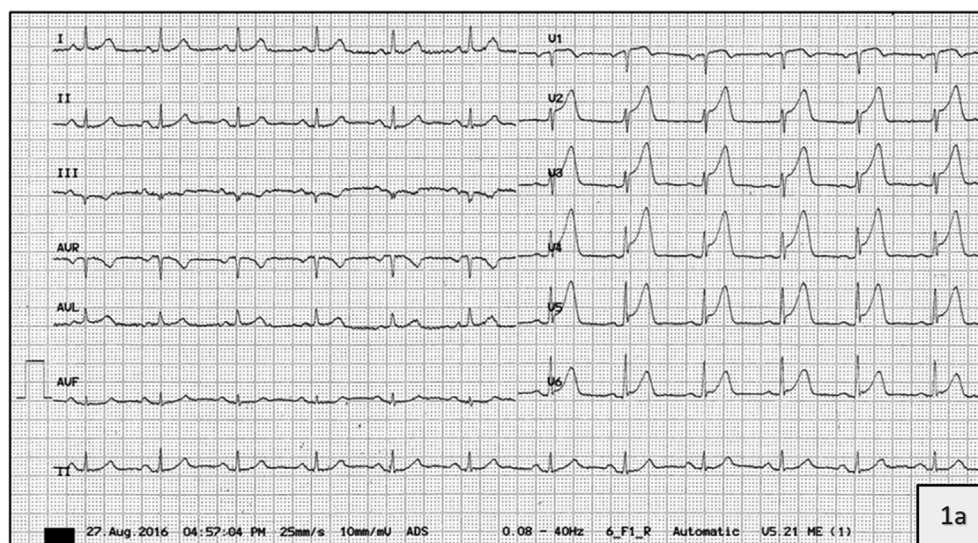


Fig. 1. (a) EKG with ST elevation on the anterior leads; (b) Erythematous rash over the chest and abdomen.

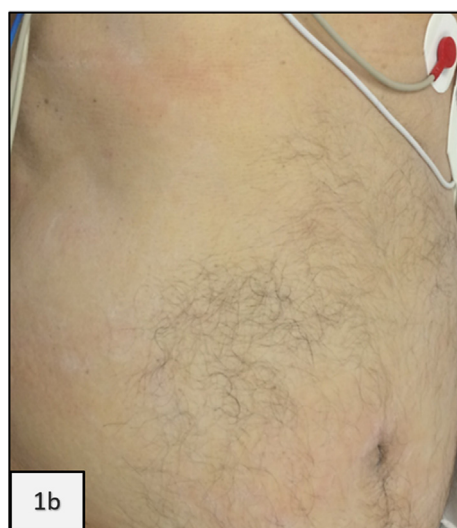


Fig. 1 (continued)

history of penicillin allergy that manifested as urticaria; however, he denied being exposed to penicillin, new drugs, foods or environmental allergens. On presentation, his vital signs were stable (temperature 37.1 °C, blood pressure 128/81 mmHg, heart rate 78 bpm, respiratory rate 20 breaths per minute). Physical examination revealed a well-developed man with a diffuse raised erythematous pruritic rash (Fig. 1a). He was diaphoretic and in pain. EKG showed ST segment elevation in the anterior leads (Fig. 1b). His basic laboratory studies were unremarkable except for a baseline troponin T of 0.018 ng/mL (0–0.03) that increased to 2.47 ng/mL after 12 h.

The allergic reaction was treated in the ED with intravenous hydrocortisone, diphenhydramine and ranitidine with resolution of the rash and pruritus.

Emergent coronary angiography demonstrated total occlusion of the mid left anterior descending coronary artery. Percutaneous coronary angioplasty was performed and a drug eluting stent was deployed (Fig. 2a and b). Echocardiography showed akinesia of the apex, and good contractility of the remaining segments. The patient had an uncomplicated hospitalization and was discharged on a medical regimen of aspirin 81 mg, clopidogrel

75 mg, valsartan 40 mg, bisoprolol 2.5 mg and atorvastatin 20 mg daily.

3. Discussion

Allergic reactions are associated with the release of inflammatory mediators and cytokines that can cause coronary vasospasm (type I KS), plaque erosion or rupture in subclinical CAD (type II KS) or coronary artery stent thrombosis (type III-a KS)/restenosis (type III-b KS) [8]. This rare entity is seldom mentioned in the Emergency Medicine literature [10,11]. KS is triggered by allergens such as food, drugs (predominantly analgesics, antibiotics and iodine contrast) and environmental agents [6,12]. It most commonly affects individuals between the ages of 40 and 70, with history of atopy, hypertension, smoking, diabetes or hyperlipidemia [13]. KS should be suspected in patients with or without cardiovascular risk factors or pre-existing CAD who present to the ED with chest pain or angina-equivalent symptoms accompanied by symptoms of systemic allergic reactions [6,14]. Diagnosis is supported by laboratory (serum histamine, tryptase, eosinophils, immunoglobulin E, cardiac biomarkers), electrocardiographic, echocardiographic and angiographic findings [11].

Management of type I and II KS consists of treating the allergic reaction with H1 and H2 antihistamines with or without intravenous corticosteroids, as well as the ACS [11]. Epinephrine may worsen coronary spasm and should be used for anaphylaxis with extreme caution [6,15]. ACS management guidelines (antiplatelet and anticoagulant therapy, reperfusion guidelines) should be followed with special attention to some medications: Beta-blockers may precipitate coronary spasm due to unopposed alpha agonism, especially if used concomitantly with epinephrine [15]. Vasodilators (nitrates, calcium channel blockers) help resolve vasospasm, but may worsen hypotension in patients with vasodilation from anaphylaxis [11]. Fentanyl and its derivatives are preferred for pain control since other opiates may worsen histamine release [6]. For type III KS, cardiac catheterization with aspiration of the stent thrombus is recommended, with histologic examination of aspirated contents and staining for eosinophils and mast cells [11]. The long-term medical management of CAD in patients at risk of anaphylaxis remains a challenge since some of the medications such as beta-blockers and ACE inhibitors complicate anaphylaxis treatment.

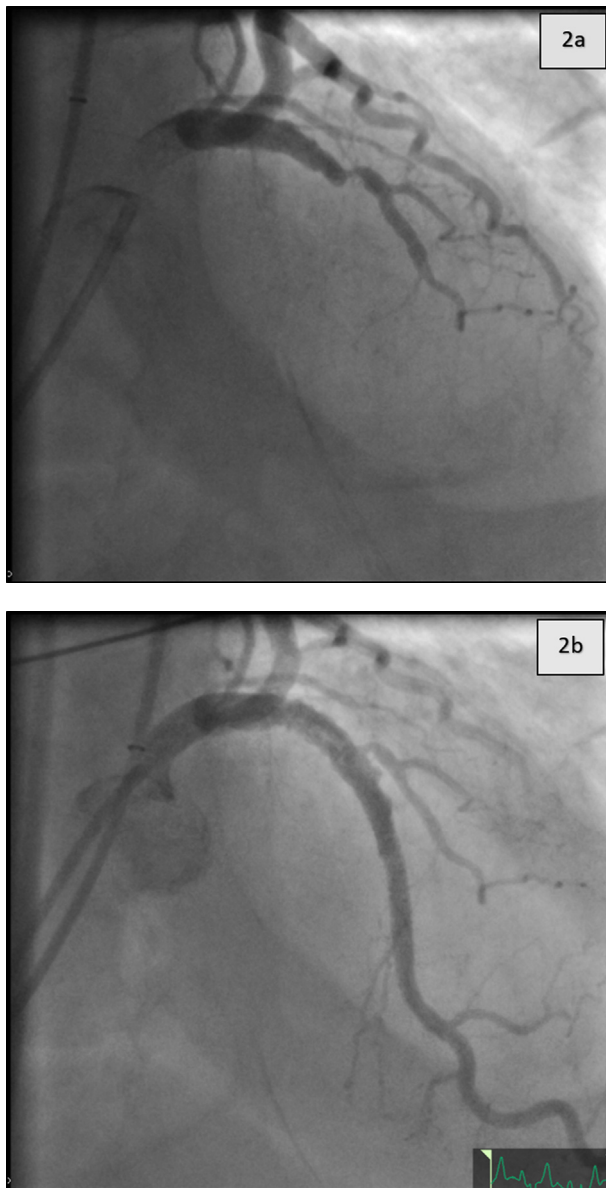


Fig. 2. (a) Total occlusion of the mid LAD; (b) LAD after revascularization with one drug eluting stent.

KS remains a challenging ED diagnosis and should be excluded in anaphylactic cardiovascular presentations. Early recognition and appropriate treatment are of paramount importance, however further management guidelines are still needed.

Authors' Contributions:

Eva Rajha, MD, Ahmad Didi, MD, Habib Dakik, MD, Afif Mufarrij, MD.

E.R. conceived and designed the project, contributed to the drafting and editing of the manuscript.

A.D. conceived and designed the project, contributed to the drafting of the manuscript.

H.D. and A.M. conceived and designed the project, contributed to the editing of the manuscript.

All authors read and approved the final manuscript.

Financial support

None.

Previous presentation

None.

Disclaimers

None.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

References

- [1] Wadsworth GH, Brown CH. Serum reaction complicated by acute carditis. *J Pediatr* 1940;17:801–5.
- [2] Pfister CW, Plice SG. Acute myocardial infarction during a prolonged allergic reaction to penicillin. *Am Heart J* 1950;40:945–7.
- [3] Kounis NG, Cervellin G, Koniari I, et al. Anaphylactic cardiovascular collapse and Kounis syndrome: systemic vasodilation or coronary vasoconstriction?. *Ann Transl Med* 2018;6:332.
- [4] Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm?. *Int J Cardiol* 2006;110:7–14.
- [5] Kounis NG, Zavras GM. Histamine-induced coronary artery spasm: the concept of allergic angina. *Br J Clin Practice* 1991;45:121–8.
- [6] Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med* 2016;54:1545–59.
- [7] Helbling A, Humi T, Mueller UR, Pichler WJ. Incidence of anaphylaxis with circulatory symptoms: a study over a 3-year period comprising 940,000 inhabitants of the Swiss Canton Bern. *Clin Exp Allergy: J Br Soc Allergy Clin Immunol* 2004;34:285–90.
- [8] Kounis NG. Coronary hypersensitivity disorder: the Kounis syndrome. *Clin Ther* 2013;35:563–71.
- [9] Abdelghany M, Shah S, Subedi R, Kozman H. New classification of Kounis Syndrome. *Int J Cardiol* 2017;247:14.
- [10] Caglar FN, Caglar IM, Coskun U, Ugurlucan M, Okcun B. Kounis syndrome: myocardial infarction secondary to an allergic insult—a rare clinical entity. *Acta Cardiol* 2011;66:559–62.
- [11] Abdelghany M, Subedi R, Shah S, Kozman H. Kounis syndrome: A review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. *Int J Cardiol* 2017;232:1–4.
- [12] Orion K, Mack J, Kullak-Ublick GA, Weiler S. Kounis syndrome: A retrospective analysis of individual case safety reports from the international WHO database in pharmacovigilance. *Int J Clin Pharmacol Ther* 2019;57:240–8.
- [13] Cortes JE, Kim DW, Pinilla-Ibarz J, et al. Ponatinib efficacy and safety in Philadelphia chromosome-positive leukemia: final 5-year results of the phase 2 PACE trial. *Blood* 2018;132:393–404.
- [14] Cox L, Larenas-Linnemann D, Lockey RF, Passalacqua G. Speaking the same language: The World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System. *J Allergy Clin Immunol* 2010;125(569–574):574.e561–567.
- [15] Lieberman P, Simons FE. Anaphylaxis and cardiovascular disease: therapeutic dilemmas. *Clin Exp Allergy: J Br Soc Allergy Clin Immunol* 2015;45:1288–95.