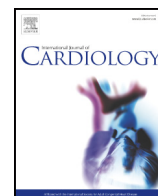




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International Journal of Cardiology

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

Letter to the Editor

Anaphylaxis mediated myocardial infarction in a coronary graft: A new variant of Kounis syndrome (a case report)[☆]Kristen Dazy^{a,*}, Daniel Walters^{a,1}, Christine Holland^{b,1}, James Baldwin^{b,1}^a University of Michigan Department of Internal Medicine, USA^b University of Michigan Department of Allergy and Immunology, USA

ARTICLE INFO

Article history:

Received 21 June 2013

Accepted 3 July 2013

Available online xxxx

Keywords:

Kounis syndrome

CABG

AERD

Aspirin desensitization

The “syndrome of allergic angina”, otherwise known as Kounis syndrome (KS), was first introduced into the medical lexicon in 1991 by Kounis and Zavra as the “coincidental occurrence of chest pain and allergic reactions accompanied by clinical and laboratory findings of classical angina pectoris [1].” To date, various allergic mediators including kiwi, ibuprofen, beta-lactam antibiotics, contrast media, and insect venom have been identified as triggers [2]. Since the initial description, it has been categorized into three distinct types [3]. The original variant, Type I, describes patients with normal coronary arteries and no pre-existing atherosclerotic disease risk factors who develop coronary artery spasm with resultant ischemia and/or myocardial infarction (MI) following release of inflammatory mediators during an allergic insult. The Type II variant results from coronary spasm or plaque erosion/rupture in patients with pre-existing atherosclerotic disease. The Type III variant occurs in the setting of a pre-existing drug eluting stent. To the best of our knowledge, we present the first reported case of KS in a coronary artery bypass graft (CABG) which suggests a potential Type IV variant of this syndrome.

[☆] Description: In today's literature, Kounis syndrome, or the association between allergic and/or hypersensitivity reactions and acute coronary syndromes, is becoming increasingly documented within clinical practice. We present a case of a 69-year-old male with a history of aspirin-exacerbated respiratory disease (AERD) and coronary artery disease (CAD) status post coronary artery bypass graft (CABG) who developed acute thrombosis within a bypass graft following aspirin anaphylaxis. To our knowledge, this is the first case of Kounis syndrome occurring in a bypass graft and suggests a type IV variant of the syndrome.

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¹ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

A 69-year-old gentleman with history of aspirin-exacerbated respiratory disease (AERD), severe asthma (FEV1 59%), allergic rhinitis, and coronary artery disease (CAD) status post percutaneous coronary intervention (PCI) and three-vessel CABG presented to an outpatient Allergy Clinic for aspirin desensitization. His past reaction to both aspirin and ibuprofen included rhinorrhea, sneezing, throat tightness, difficulty breathing, and emesis within 30 min of ingestion. At 8:21 AM on Day #1 of desensitization, he tolerated the initial dose of 20 mg of aspirin. At 11:25 AM, he was given a 40 mg dose and observed per protocol. Two hours later, the patient complained of wheezing, nasal congestion, and ocular tearing for which he received an albuterol nebulizer treatment, cetirizine (10 mg), and montelukast (10 mg) with good response. Serial spirometry did not demonstrate respiratory compromise via Forced Expiratory Volume (FEV1) measurement. One hour later, he continued to complain of nasal congestion and intranasal phenylephrine was administered. At approximately 16:00 PM, the patient was asymptomatic and discharged from clinic. On Day #2 of desensitization, the patient received a 40 mg dose of aspirin at 8:52 AM followed by an 81 mg dose at approximately 12:30 PM. Both doses were tolerated and he was discharged after a standard three hour observation period.

One hour after leaving clinic, he developed swelling of his hands and feet with eruption of a pruritic, maculopapular rash across all extremities. Within the next 60 min, his symptoms progressed to include both tongue and lip swelling. At 19:38 PM, he presented to the Emergency Department complaining of throat swelling, shortness of breath, ocular tearing, and palpitations. Initial vital signs included a respiratory rate at 26 per minute, blood pressure 124/57 mm Hg, pulse 125 beats per minute, and oxygen saturation 91% on room air. Physical examination revealed respiratory distress with wheezing and stridor along with injected conjunctiva and diffuse urticaria on extremities. ECG on arrival showed sinus tachycardia with no ischemic findings. Laboratory work was notable for troponin I <0.10 ng/mL (0.00–0.29 ng/mL), CK-MB 2.7 ng/mL (0.0–4.9 ng/mL), and CPK 150 IU/L (38–240 IU/L). Out of concern for rapidly developing anaphylaxis, he was immediately treated with 0.3 mg (1:1000) IM epinephrine injection followed by an albuterol nebulizer, diphenhydramine (50 mg IV), methylprednisolone (125 mg IV), and famotidine (20 mg IV). A tryptase level drawn 7 min after epinephrine injection was elevated at 41.2 ng/mL (<11.5 ng/mL). Following the above treatment, the patient had improved hemodynamics with subjective improvement in throat swelling.

Approximately 25 min after medication delivery, he developed severe, non-radiating, substernal chest pain. Repeat ECG (Fig. 1) revealed new ST-segment elevation in leads III and AVF with ST-depression in leads V2, V3 and AVL. Repeat labs showed an acute troponin elevation

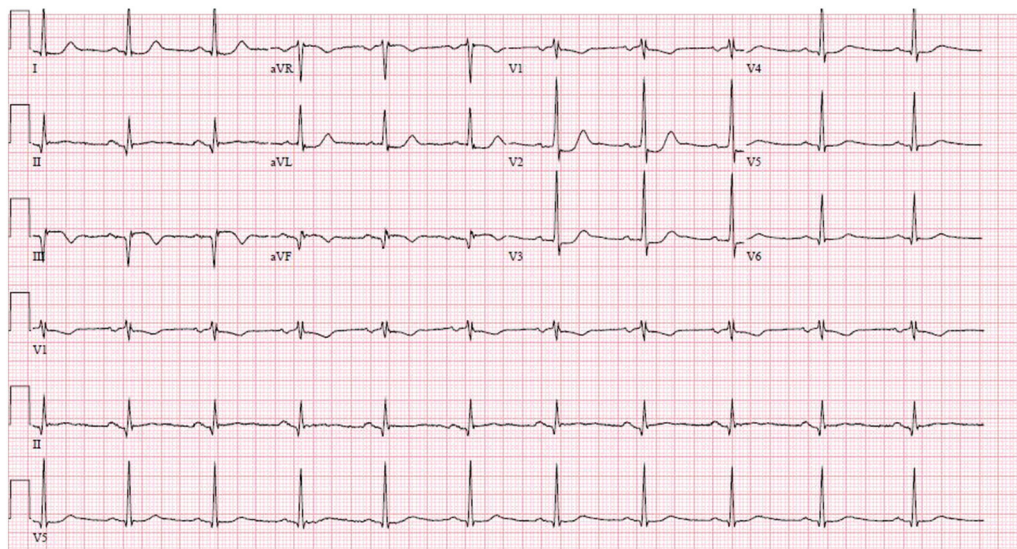


Fig. 1. ECG demonstrating new ST-segment elevation in leads III and aVF following epinephrine injection.

at 8.29 ng/mL with eventual peak to 34.19 ng/mL (0.00–0.29 ng/mL). The patient underwent immediate left heart catheterization with coronary angiography revealing an acute thrombus in the proximal segment of the saphenous vein graft (SVG) to the right posterior descending artery (rPDA) (Fig. 2). The two remaining grafts were patent. PCI was performed with deployment of two overlapping bare metal stents at the occlusion. ECG after intervention demonstrated resolution of the prior ischemic findings with new inferior Q-waves. Transthoracic echocardiogram revealed normal ventricular systolic function and segmental wall function. He was discharged after 72 h on an oral steroid taper and dual H1/H2 histamine blockade with plan for indefinite aspirin/NSAID avoidance. Prasugrel was prescribed for anti-platelet therapy. A baseline tryptase level obtained 6 months later returned normal at 6.0 ng/mL.

Adverse reactions to aspirin in patients with CAD are not commonly reported in the literature, but aspirin can cause non-IgE mediated anaphylaxis in patients with underlying AERD [4]. Our case of KS occurred in the setting of aspirin desensitization. Mast cell mediated coronary syndromes have been found to have increased levels of

several mediators, including histamine, thromboxane, leukotrienes, platelet activating factor, and tryptase compared to normal controls [5]. It has been postulated that the release of these mediators are the cause, rather than the result, of the acute coronary event [6]. During systemic anaphylaxis, inflammatory mediators can act directly on vasculature leading to vasodilation and large fluid shifts with subsequent reduction in venous return, cardiac output, and coronary perfusion [7]. Other mediators, such as histamine, can act directly on the heart and coagulation cascade by inducing coronary vasoconstriction, tissue factor expression and platelet activation [8]. In KS, epinephrine used for the treatment of anaphylaxis can further aggravate ischemia through coronary vasospasm and myocardial stunning [9].

Literature has advocated that a tryptase value greater than 25 ng/mL is indicative of an anaphylactic reaction [10]. Our patient had a tryptase of 41.2 ng/mL. We hypothesize that non-IgE mediated aspirin anaphylaxis in combination with increased cardiac demand from epinephrine exposure and a possible atherosclerotic graft led to the acute occlusion of the patient's graft and resultant STEMI. Our case highlights the first known case of Kounis syndrome occurring in a coronary bypass graft and argues for a Type IV variant of the syndrome.

References

- [1] Kounis NG, Zavras GM. Histamine-induced coronary artery spasm: the concept of allergic angina. *Br J Clin Pract* 1991;45:121–8.
- [2] Gazquez V, Dalmáu G, Gaig P, Gomez C, Navarro S, Merce J. Kounis syndrome: report of 5 cases. *J Investig Allergol Clin Immunol* 2010;20(2):162–5.
- [3] Nikolaidis LA, Kounis NG, Grandman AH. Allergic angina and allergic myocardial infarction: a new twist on an old syndrome. *Can J Cardiol* 2002;18(5):508–11.
- [4] Feng CH, White AA, Stevenson DD. Characterization of aspirin allergies in patients with coronary artery disease. *Ann Allergy Asthma Immunol* 2013;110(2):92–5.
- [5] Takase B, Maruyama T, Kurita A, et al. Arachidonic acid metabolites in acute myocardial infarction. *Angiology* 1996;47:649–61.
- [6] Kovanen PT, Kaartinen M, Paavonen T. Infiltrates of activated mast cells at the site of coronary atheromatous erosion or rupture in myocardial infarction. *Circulation* 1995;92:1083–8.
- [7] Mazarakis A, Almpanis GC, Papathanasiou P, Kounis N. Kounis syndrome uncovers critical left main coronary disease: the question of administering epinephrine. *Int J Cardiol* 2012;157:e43–5.
- [8] Kounis N. Kounis syndrome (Allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol* 2006;110(1):7–14.
- [9] Izgi C, Cevik C, Nugent K. Severe myocardial infarction after concentrated epinephrine use for the treatment of anaphylaxis: Kounis syndrome or epinephrine effect? *Heart Lung* 2010;39(2):160–3.
- [10] Baldomà N, Cosmen CR, Galinski SF, et al. Serum tryptase levels in acute coronary syndromes with ST elevation. *Int J Cardiol* 2009;131(3):403–4.

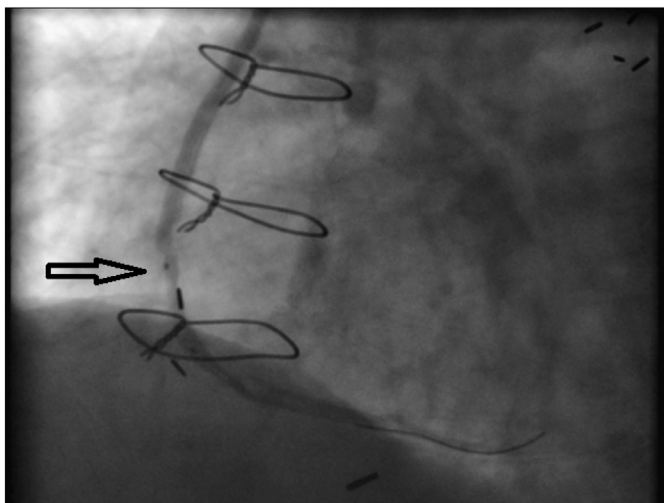


Fig. 2. Coronary angiography revealing acute thrombus in SVG to rPDA territory.