



Short communication

A rare case of Kounis syndrome provoked by mad honey poisoning

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ARTICLE INFO

Article history:

Received 26 April 2016

Received in revised form 22 May 2016

Accepted 22 May 2016

Available online 27 May 2016

Keywords:

Kounis syndrome

Mad honey

Grayanotoxin

ABSTRACT

Kounis syndrome, resulting in acute coronary syndromes, as a result of allergic or hypersensitivity reaction is triggered by several factors. Vasospasm which is mediated by mediators released after mast cell activation, is the responsible mechanism for comprising of type 2-myocardial infarction. Mad honey containing grayanotoxin is previously shown to be associated with gastrointestinal, neurological and cardiac disorders. In this case report, we presented a Kounis syndrome that has occurred after the mad honey intake and treated successfully, previously not mentioned in the literature.

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Introduction

Kounis syndrome which is described as the occurrence of acute coronary syndromes with allergic or hypersensitivity reactions, was first defined in 1991 by Kounis and Zavras.¹ Later in 1998 Braunwald reported that vasospastic angina might be induced by allergic mediators such as histamine or leukotrienes.² Several factors including drug use, foods, sedative and anesthetic agents are associated with Kounis syndrome.

Mad honey poisoning can occur after ingestion of honey, made of the nectar from flowers of the Rhododendron family.³ Clinically, grayanotoxin can cause gastrointestinal, neurological, and cardiac signs and symptoms as a result of toxic cellular effect on the sodium channels.⁴

Herein, we report a case of patient who presented with acute myocardial infarction after consuming mad honey for reasons of gastrointestinal disorder.

Case presentation

A 58-year-old male patient was admitted to our Emergency Service with nausea and chest pain lasting for 1 h. His medical history was unremarkable except for smoking history. On his physical examination, arterial blood pressure was 90/70 mmHg and pulse rate was 45/min. Unexplained abnormal skin findings were noted during general examination. Electrocardiography (ECG) of the patient that was performed in the Emergency Service revealed 47/min sinus bradycardia and 2 mm ST

elevation on the leads D1, aVL and V7–9 accompanied by reciprocal ST depression on the leads D2–3, aVF and V4R–6R (Fig. 1A–C).

The patient was transferred to the catheter laboratory with the diagnosis of acute posterolateral myocardial infarction. He received 300 mg acetylsalicylic acid (ASA) and 600 mg clopidogrel load via oral route and 8000 IU heparin via intravenous route. We performed right and left selective coronary angiography which revealed no significant stenosis (Fig. 2A–D). Later, the patient was transferred to intensive care unit for routine follow up. His control electrocardiograms showed no improvement in ST elevation and his echocardiographic evaluation did not demonstrate apical ballooning pattern that support Takotsubo Cardiomyopathy. On his biochemistry analyses, leukocyte count was 6.762/mm³, hematocrit was 44%, neutrophil was 61%, lymphocyte was 18.5%, eosinophil was 18.8%, troponin T level was 474.7 pg/mL (reference: 0.03–14 pg/mL), creatinine kinase-MB was 7.82 ng/mL (reference: 0.00–4.9 ng/mL), postprandial blood glucose was 115 mg/dL, low-density lipoprotein level was 115 mg/dL, and creatinine level was 0.95 mg/dL.

Because of severe hypotension and bradycardia, iv atropine and saline infusion treatment was provided. When his medical history was reevaluated, it was learned that he had received honey from eastern black sea region of Turkey in order to heal his digestive disorder. Moreover, his unexplained skin findings were confirmed as allergic rash by dermatology. After much deliberation the patient was considered to have Kounis syndrome as a result of mad honey poisoning. Following administration of intravenous antihistamines (pheniramine maleate 22.75 mg, administered intravenously) his chest pain was improved and the ST segments normalised (Fig. 1D). In addition, plasma histamine, beta-tryptase, C4 and IgE levels were investigated in order to confirm our diagnosis. Results of blood biochemistry analyses revealed that plasma beta-tryptase, C4 and IgE levels were over the upper limit of

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Peer review under responsibility of The Society of Cardiovascular Academy.

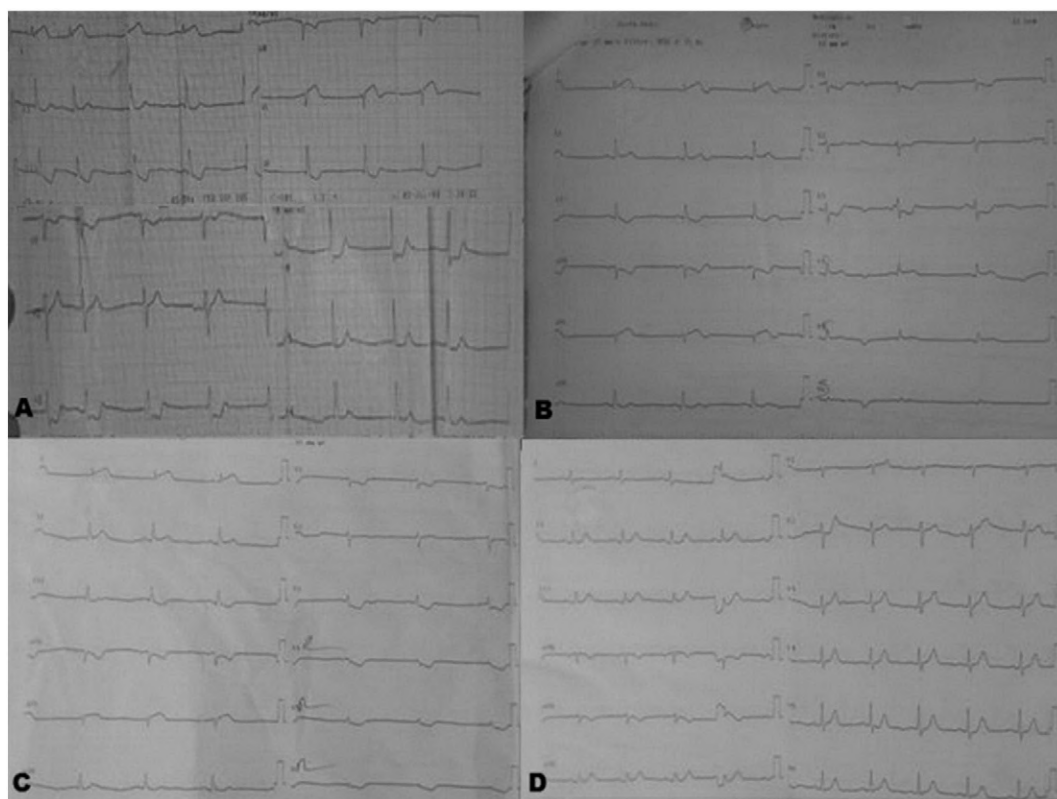


Fig. 1. A–D: 1A: Electrocardiogram (ECG) at admission to emergency service, 1B: ECG of posterior derivations, 1C: ECG of right derivations, and 1D: ECG after administration of intravenous antihistamines.

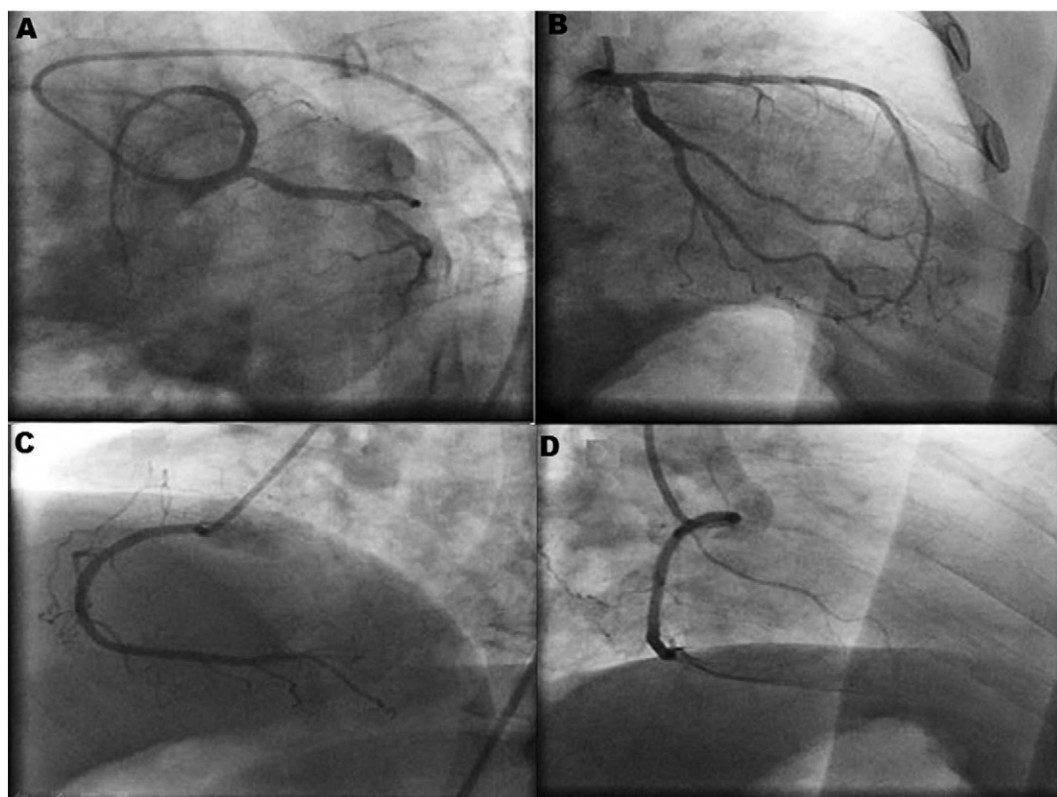


Fig. 2. A–D: Images of coronary angiography 2A: Left anterior oblique (LAO) caudal view of left coronary system, 2B: Right anterior oblique (RAO) caudal view of left coronary system, 2C: RAO cranial view of right coronary artery (RCA), and 2D: LAO view of RCA.

normal serum value. On his control transthoracic echocardiographic examination, left ventricular ejection fraction was measured to be 65%. No regional wall motion impairment or any other pathology was observed. During routine follow up his physical examination revealed no complaint or sign of allergic reaction. His cardiac enzymes decreased and the patient was discharged on the 4th day of hospital admission.

Discussion

Kounis syndrome is described as the occurrence of acute coronary syndrome as a result of mast cell activation provoked by the release of inflammatory mediators. Histamine and leukotrienes are major culprit mediators which cause coronary events via vasoconstriction. Moreover, serum proteases trigger coronary events not only via metalloprotein activation but inducing atheromatous plaque erosion.^{5,6} According to current classification three types of Kounis syndrome are identified. Type I is observed in patients with the absence of cardiovascular risk factors. The underlying mechanism is allergic mediators that provoke endothelial dysfunction or microvascular angina. Type II is observed in patients with history of coronary artery disease in whom allergic mediators induce coronary vasospasm or erosion/rupture of the atheromatous plaque, resulting in acute myocardial infarction. Type III is observed in patients presented with drug-eluting stent thrombosis in whom aspirated thrombus material obtained from the culprit coronaries stain positive for mast cells and eosinophils.^{7,8} Variety of factors have been identified in the literature that cause Kounis syndrome such as environmental toxins, antibiotics, contrast media, intravenous anesthetics, analgesics, skin disinfectants, steroids, thrombolytics, anti-inflammatories and antineoplastics.⁹

Mad-honey intoxication may be observed after ingestion of Grayanotoxin, also known as andromedotoxin, acetyl-andromedol, or rhodotoxin,¹⁰ is found in the nectar of *Rhododendron ponticum*, a plant that is endemic to the Black Sea region of Turkey, Nepal, Japan, Brazil, and some regions of North America.¹¹ In endemic regions these plants can be used as alternative remedy for infections and gastrointestinal disorders even for sexual disorders. There are several reports in literature which demonstrate the association between mad honey poisoning and conduction disorders such as ST elevation, sinus bradycardia, sinoatrial block, QT prolongation, nodal rhythm, and asystole.^{11–13}

It is well known that the mismatched oxygen supply and demand due to impaired myocardial perfusion lead to involvement of type 2 myocardial infarction. In our patient, we observed acute posterolateral MI, 4 h after ingestion of honey. In addition his vital signs improved after iv saline infusion and supportive medical therapy. Due to patient's symptoms that did not associate with stress and no apical ballooning was seen on echocardiographic evaluation, we ruled out stress-induced cardiomyopathy. Moreover, coronary vasospasm considered as a differential diagnosis. In our patient, coronary vasospasm due to allergic reaction and development of a thrombus formation which dissolved spontaneously might be a result of other conditions. Although intravascular ultrasonography

(IVUS) or OCT (optical coherence tomography) might be useful to distinguish these situations, but we did not use these instruments because of patient's worsening clinical status during procedure.¹⁴ In addition, hypercoagulability syndromes such as antiphospholipid antibody syndrome, activated protein C resistance, antithrombin III and protein C or S deficiency should bear in mind as differential diagnosis. Consequently, the most possible diagnosis was type I Kounis Syndrome. Allergic skin reactions, normal coronary arteries and rapid recovery after supportive therapy also support this decision.

To our knowledge, no case of Kounis Syndrome as a result of mad honey poisoning has been reported in the literature. Typically, patients with mad honey poisoning presented with excessive hypotension and bradycardia which usually responds to atropine and saline infusion treatment. However intravenous antihistamine and in some cases more aggressive therapy with steroids are not common under these circumstances. Although we provided supportive medical care, clinical improvement was observed following administration of iv antihistamine therapy.

In conclusion, physicians should keep in their minds that patient with mad honey poisoning may present with acute myocardial infarction. In addition, those patients may develop Kounis Syndrome which requires alternative therapies.

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