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Kounis Syndrome: A More Commonly Encountered Cause of Acute Coronary Syndrome

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Abstract

Kounis syndrome (KS) has been defined as cardiovascular symptoms that occur secondary to allergic or hypersensitivity insults. It was thought to be a rare condition but is now being more commonly identified as the cause of acute coronary events in patients without previous history of coronary artery disease (CAD). The most identified KS cases have been provoked by medications on elderly male patients.

The purpose of this case report is to describe an unusual case of KS, triggered by a food allergen in a young female patient. This case reminds us that it is important to have a high index of suspicion, particularly in MI patients presenting without previous history of CAD. In this manner, an appropriate management, considering both cardiac and allergic components of KS, can be given without further delay and progression of symptoms.

Keywords: Acute coronary artery syndrome, allergic reactions, chest pain, hypersensitivity, Kounis syndrome, type 2 myocardial infarction, vasospasm

INTRODUCTION

Coronary artery spasm and myocardial injury in the absence of evident preexistent coronary artery disease (CAD) have been documented in the setting of a severe allergic reaction. Histamine released by degranulation of mast cells is usually associated with severe allergic and anaphylactic reactions that can also result in severe coronary artery spasm or atheromatous plaque erosion with rupture, in some cases. [[1,2,3,4,5,6](#)]

This previously considered rare hypersensitivity reaction resulting from allergen exposure likely occurs more commonly; however, is not being accurately recognized. Consequently, health-care providers in general not only need to be aware of this clinical entity but also be cognizant of presentations in which a potential allergen exposure triggers symptom requiring prompt recognition and treatment. We report the case of a 23-year-old woman who developed an intense allergic coronary vasospastic presentation after accidental ingestion of a known allergic trigger.

CASE PRESENTATION

A 23-year-old woman with bronchial asthma and Arnold-Chiari Type 2 receiving physical and occupational rehabilitation, after undergoing placement of a ventricular-pleural shunt after a prolonged hospitalization, developed sudden onset of dyspnea, chest discomfort, and palpitations after accidentally consuming milk, a well-known allergen to her.

She was a nonsmoker, who has not used illicit drugs and has no previous history of hypertension, diabetes, or family history of premature CAD.

On physical examination, blood pressure was 110/64 mmHg, P = 96 bpm, RR = 18/min, and T = 96.7° Fahrenheit. Furthermore, she had no generalized urticarial or facial swelling. Cardiac examination revealed normal S₁ and S₂ without any gallop murmur or rub appreciated. Lungs were clear to auscultation, and tracheostomy was in place.

Her initial electrocardiogram (ECG) showed sinus rhythm with early repolarization ST-segment changes [Figure 1].

With the acute flare allergic reaction, she developed chest discomfort. Cardiac troponin I was elevated (1.34 ng/ml). Subsequent ECG showed ST-segment depressions in leads V2, V3 that later change to ST-segment elevations with reciprocal inferior leads (II, III, AVF), suggesting an anterior wall myocardial infarction [Figure 2].

At this time, the patient was treated with intravenous corticosteroids and diphenhydramine and received normal saline. An echocardiogram performed at the time showed mild anterior wall hypokinesis with somewhat reduced left ventricular systolic function. The patient was then taken for an emergent coronary angiogram. No epicardial coronary artery stenosis was identified [Figures 3 and 4].

DISCUSSION

From a mechanistic point of view, mast cell activation is responsible for the release of numerous inflammatory mediators with the potential of causing either coronary artery vasospasm or atheromatous plaque erosion with rupture.[1] These released mediators can be pre-formed such as in the case of histamine, neutral proteases-chymase and tryptase, platelet-activating factor, or they could be newly synthesized such as cytokines, chemokines, arachidonic acid products leukotrienes, and prostaglandins. Even though histamine, serotonin, and leukotriene are the most important vasoactive mediators, histamine, the main amine released during allergic reactions, is the one known to stimulate both H1- and H2-receptors resulting in Kounis syndrome (KS).[2]

KS was first described in 1991. It is the concurrence of acute coronary events due to either an allergic or anaphylactoid reaction caused by inflammatory mediators released mainly from activated mast cells.[3]

From its initial inception, KS has evolved to involve the following three recognized variants: Type 1: the acute coronary event is secondary to spasm; Type 2: where coronary thrombosis is the main culprit, and Type 3: the coronary event occurs secondary to drug-eluting stent thrombosis.[1]

Our patient was diagnosed with the Type 1 variant, in which myocardial ischemia or infarction occurs with normal coronary arteries because of coronary artery vasospasm. Even though one prior type I KS has been reported in the English literature on a 65-year-old female who had an anaphylactic reaction 30 min after eating shellfish with severe discomfort associated to transient ST-segment elevation as well as gradual prolongation the atrioventricular interval en route to the hospital.[4] To the best of our knowledge, this is the first KS Type I variant case being reported in such a young patient.

The initial treatment of these patients requires the administration of intravenous steroids, antihistamines, and fluid replacement, as in our patient. In some cases, depending on the magnitude and extent of the allergic reaction, epinephrine, oxygen, and antithrombotics might be required prior to taking the patient for a coronary angiogram.

These initial interventions are primarily intended not only to suppress the allergic reaction but also to dilate the coronary arteries. The latter is mainly accomplished using vasodilators such as nitrates and calcium channel blockers.[5]

It is important to be reminded that morphine, a drug commonly used to treat patients presenting with acute coronary artery syndromes, should be avoided in KS, as it may potentially stimulate histamine release and exacerbate the pathologic cascade paradoxically worsening the acute event.[6]

Similarly, beta-blockers should also be avoided in this setting if KS is highly suspected as it also may potentiate coronary vasospasm due to an unopposed alpha-adrenergic action.

When epinephrine is used for the acute treatment of anaphylaxis, careful monitoring is indicated as epinephrine may potentially worsen coronary vasospasm, aggravating coronary ischemia in KS patients.[7]

Although medical treatment can aid in the symptomatic recovery of the patient, ultimately, the primary intent of therapy should be directly aimed at removing the allergic insult that triggered the response.[8]

In summary, even though KS was once very uncommon, but now it is a more common explanation, particularly when patients present with an acute coronary event and no epicardial coronary artery stenosis is found on cardiac catheterization. [Table 1](#) illustrates various cases found in literature, which exemplifies the amount of cases reported, and puts into perspective that KS is not as uncommon as we might think. In these cases, an allergic trigger needs to be identified. Surely, our case presentation not only reminds us to keep a high level of suspicion but also to institute appropriate treatment measures once an allergic reaction is thought to be the offending agent.

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Conflicts of interest

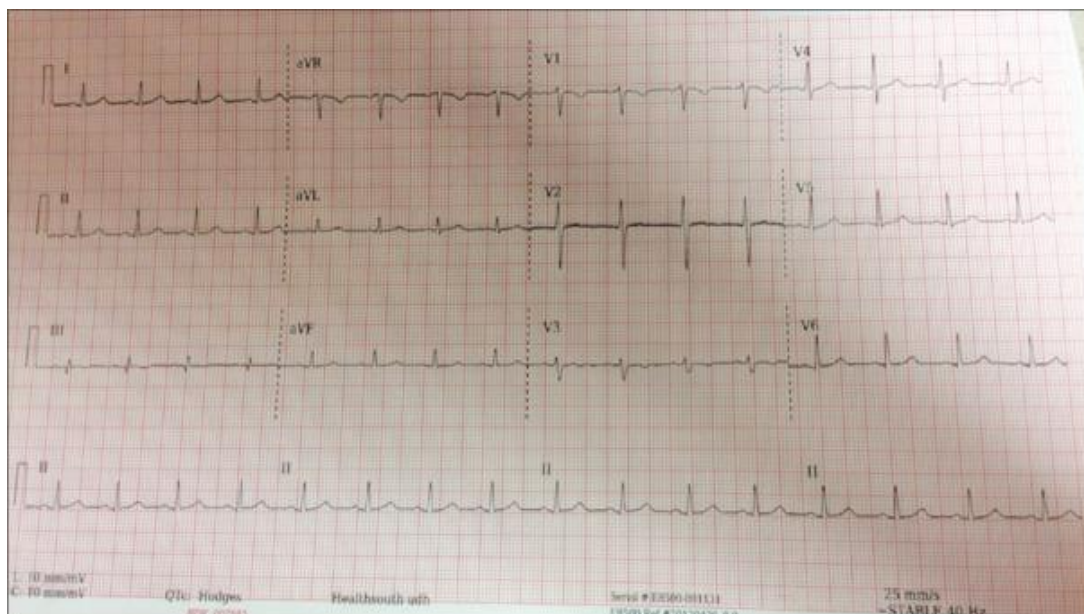
There are no conflicts of interest.

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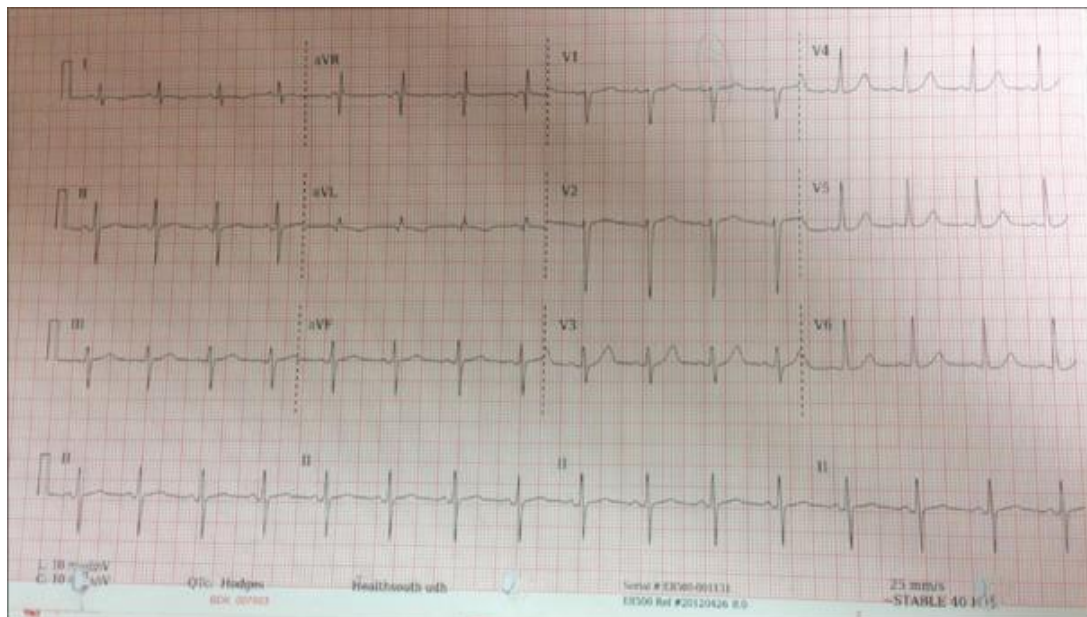
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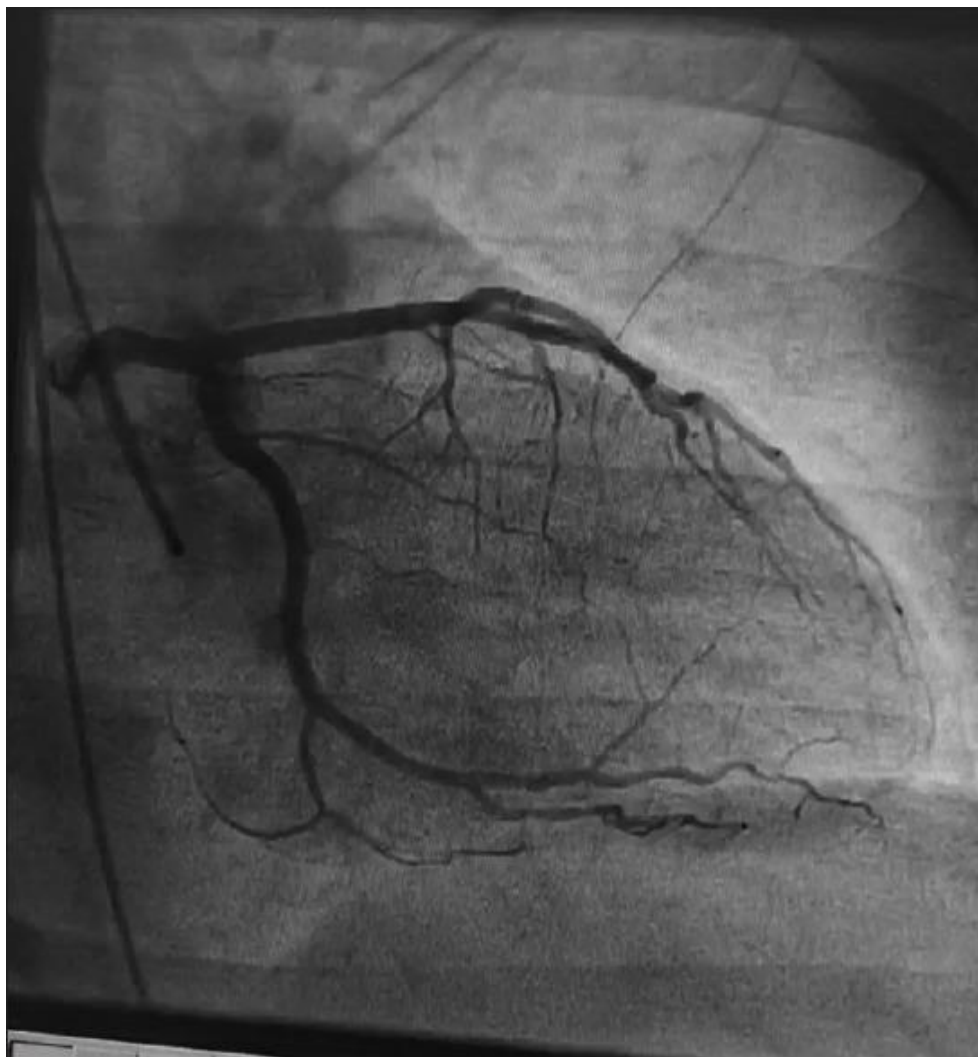
Figures and Tables

Figure 1

Initial electrocardiogram, sinus arrhythmia with nonspecific T-wave changes in anteroseptal leads

Figure 2

Repeat electrocardiogram, sinus tachycardia, ST depression in leads V3-V6 indicating dynamic changes, representative of an acute myocardial infarction in the adequate clinical setting

Figure 3

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Coronary angiogram right anterior oblique caudal view: normal unobstructed left main artery, left circumflex artery, and left anterior descending artery

Figure 4

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Coronary angiogram right anterior oblique view: normal unobstructed right coronary artery

Table 1

Summary of articles reporting Kounis syndrome

Authors, journal, year	Study design	Main exposure	Main outcomes	Key findings
Kounis, International Journal of Cardiology[1]	Literature search	Anaphylaxis	KS	Histamine, leukotrienes, interleukins, and tryptase are key mediators of KS. Mast cell stabilizers and antibodies against cytokines are potential therapeutic and preventive strategies for this syndrome
Wada <i>et al.</i> , Heart Vessels[4]	Case report	Food-induced anaphylaxis	Allergic vasospasms	Ergometrine maleate provocation test can be used to reproduce KS symptoms
Cevik <i>et al.</i> , International Journal of Cardiology 143[5]	Literature search	KS	Treatment	The treatment of KS should consider both cardiac and allergic components. Follow-up in cardiology and allergy clinics should be part of KS management
Kounis, Clinical Therapeutics[7]	Literature search	KS	Pathophysiology, causality, clinical appearance, variance, prevention and treatment	Mast cell degranulation inhibitors can be used to prevent acute coronary and other arterial events in allergic or hypersensitive patients
Memon <i>et al.</i> , Proceedings[8]	Case series	CAD versus no CAD (pure vasospasm)	ST elevation MI	IV steroids and diphenhydramine improved symptoms and resolved ST elevations in patients with both underlying CAD or no previous history of CAD
Rayner-Hartley <i>et al.</i> , Canadian Journal of Cardiology[9]	Case report	Samter's triad	Allergic vasospasms	Young woman with Samter's triad developed Kounis syndrome after ingestion of NSAIDs or acetaminophen, which improved with calcium channel blockers
Garcia <i>et al.</i> , Revista Cubana de Cardiología y Cirugía Cardiovascular[10]	Case report	Bee sting anaphylaxis	KS	48-year-old man who developed type I Kounis syndrome after bee sting. Patient's symptoms resolved after treating exclusively allergic symptoms
Nachmias and Leibowitz, British Journal of Hospital Medicine (2014)[11]	Case report	Salad with mustard dressing	KS	59-year-old woman with no previous history of ischemic heart disease who developed KS following ingestion of salad with mustard dressing
Meiía-Rentería <i>et al.</i>	Case	Undercooked	KS	44-year-old man with previous history of

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KS: Kounis syndrome, CAD: Coronary artery disease, MI: Myocardial infarction, IV: Intravenous, NSAIDs: Nonsteroidal anti-inflammatory drugs