



KOUNIS SYNDROME - A RARE DIAGNOSIS.

Cardiology

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ABSTRACT

Background: Kounis Syndrome is a rare but clinically significant condition at the crossroads of allergic reactions and acute coronary syndromes (ACS). Also known as “allergic myocardial infarction.” The incidence of Kounis syndrome varies study by study but is reported to be approximately -> 1.1 to 3.4% of patients with allergic reactions. 5 The syndrome is mediated by mast cell degranulation leading to the release of histamine, leukotrienes, and other inflammatory mediators, which can result in coronary vasospasm, plaque rupture, or stent thrombosis. 1 Kounis syndrome (KS) is an acute coronary syndrome that occurs in the setting of allergic or hypersensitivity reactions, it was first described by Nicholas Kounis. It encompasses a spectrum of allergic reactions leading to acute coronary events. The mechanism involves the release of inflammatory mediators during an allergic response, which can trigger coronary artery spasm or plaque rupture, leading to angina or myocardial infarction. 1 Kounis syndrome is defined as the concurrence of acute coronary syndromes or anginal pain in conditions associated with mast-cell and platelet activation involving interrelated and interacting inflammatory cells in the setting of allergic or hypersensitivity and anaphylactic and anaphylactoid insults. Factors capable of causing Kounis syndrome include numerous drugs, environmental exposures, some foods products, and idiopathic anaphylaxis. 1-2

KEYWORDS

Kounis Syndrome, Vasospastic Allergic Angina, Coronary Artery Spasm, Allergic Myocardial Infarction, Allergic Reaction, Anaphylaxis.

INTRODUCTION

Kounis syndrome represents the concurrence of acute coronary syndromes or anginal pain with allergic, hypersensitivity, and anaphylactic reactions. It can be associated with a normal coronary angiogram or pre-existent coronary pathology. Idiopathic anaphylaxis is defined as anaphylaxis without any identifiable precipitating agent or event. Kounis syndrome is not a rare aetiology, but remains overlooked due to focus on the main complaint at the moment of presentation.

Common Triggers for KS:¹

- Drugs: NSAIDs, penicillins, cephalosporins, contrast media etc.
- Insect stings: Bee/wasp venom etc.
- Food allergens: Nuts, shellfish, gluten, dairy etc.
- Environmental agents: Latex, pollen etc.

Case Report:

We report a rare case of a 70-year-old male who presented to the emergency department with complaints of itching all over the body, rash, flushing, uneasiness, profuse sweating, chest heaviness, and acute shortness of breath. Patient had no comorbidities, and no history of substance use.

Two days prior, he had developed an ear infection and he was prescribed some oral medications by his doctor. After taking the third dose of the medication, he developed the aforementioned symptoms and had to be brought to the ER.

Incidentally, ECG showed ST-segment elevation in anterior leads with reciprocal ST depression.

On Examination:

Pulse : 77/min, regular
BP : 110/70mmHg
RR : 18 cycles/min
Spo2: 97% on room air

Systemic Examination :

CVS: s1 & s2 present, no added sounds
RS: Clear.
CNS: GCS- 15/15.
ABDOMEN: Soft, Non-tender

Troponin I: Negative on admission

2D Echocardiography: Normal ejection fraction with no regional wall motion abnormality (RWMA), and normal valves.

Clinical Suspicion: As per the history given, we suspected Acute Coronary Syndrome (ACS) v/s Allergic coronary vasospasm (Kounis type 1).

MANAGEMENT

The patient was managed as a case of ACS with loading doses of antiplatelets and low molecular weight heparin. Simultaneously, anti-histaminic and corticosteroids were administered for suspected drug-induced allergic reaction.

Remarkably, the ST elevations reduced within an hour, and the patient remained hemodynamically stable and asymptomatic throughout hospitalization.

Patient was advised ICU admission, Serial ECG and troponin level monitoring was done.

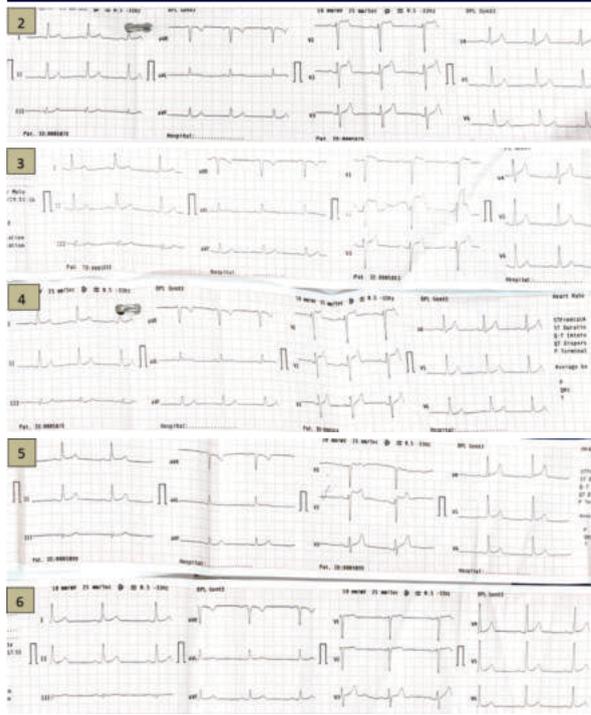
Repeat ECG after 6 hours showed normal sinus rhythm, Serial troponins remained consistently negative. The patient refused coronary angiography, but a focused allergy workup revealed a hypersensitivity to Amoxicillin, which had been part of his recent antibiotic course.

Blood Investigations:

Hb(g/dL)	12
Troponin I on admission	0.02
Troponin I x 2 hrs	0.02
Trop I x 6 hrs	<0.01
CKMB	18
BNP	72

Serial ECGs: ECG Suggestive of acute ST elevation myocardial infarction (according to ESC 2023 ACS criteria). ST elevations in leads v1-v4, and reciprocal changes in leads 2,3,aVF can be seen in the ECG.





On serial ECG monitoring, progressive normalisation of ST segment can be seen.

Patient had no cardiac symptoms or complaints throughout the course of admission.

Repeat 2D Echo:

LVEF-60%, No RWMA
Normal Valves and chambers.
No obvious clots or vegetations seen.

Treatment and Outcome

Patient was admitted and treated as a case of acute coronary syndrome with antiplatelets and low molecular weight heparin, and supportive management with steroids, anti-histaminic medications and pain killers was given for anaphylaxis, later patient was advised to undergo invasive coronary angiography in view of history, presenting symptoms and age, however patient denied any further investigations.

DISCUSSION

KS is a Hypersensitivity coronary disorder originally described by Kounis as “acute coronary syndrome associated with allergic reaction”.⁵

It is also known as “allergic angina”, “allergic myocardial infarction”, or “coronary hypersensitivity disorder”, the vasospastic changes seen in Kounis syndrome do not always lead to infarction.

It is induced by various conditions, drugs, environmental exposures, foods and coronary stents. The most common recognised triggers are antibiotics (28%) and insect bites (23%).⁶⁻⁷

KS is considered a relatively rare condition, and its true prevalence is not well established due to under-recognition and under-reporting. Recent reports suggest that KS has been observed across all races, age groups (from 2 to 90 years old), and geographic locations. It has mostly been reported in Southern Europe, particularly in Turkey, Greece, Italy, and Spain.

This geographical variation may be attributable to physician awareness, climate, environmental conditions, overconsumption of medicines, or inadequate preventative measures.⁷⁻⁹

Brief History of KS

In 1950 Plice and Pfistler - published first report of acute myocardial infarction during a prolonged allergic reaction to penicillin. In 1991 Kounis & Zavras - published first complete description of the pathophysiology, aetiology and clinical symptomatology of

histamine-induced coronary artery spasm, and the 'syndrome of allergic angina'. Later in 1998 Braunwald - categorized allergic angina in a subgroup of dynamic coronary occlusion lesions by stating that “allergic reactions with mediators such as histamine or leukotrienes acting on coronary vascular smooth muscle” can induce vasospastic angina. And in 2008 Biteker et al - published the first of four cases of children presenting with Kounis syndrome.⁴⁻⁶

Type	Cardiac history	Pathological changes
I	Normal coronary arteries, No risk factors for IHD	Coronary artery vasospasm
II	Inactive preexisting atheromatous disease	Plaque erosion of rupture causes vasospasm or infarction
III	Previous coronary artery stenting	Stent thrombosis secondary to platelet activation

Pathophysiology of Kounis Syndrome:

- The exact underlying mechanism is not fully understood, and there are two proposed mechanisms. Allergic, hypersensitivity, anaphylactic and anaphylactoid reactions are associated with Kounis syndrome.
- Ischaemia is thought to be due to release of inflammatory cytokines and inappropriate platelet activation through mast cell activation, which leads to coronary artery vasospasm and/or atheromatous plaque erosion or rupture.
- Apart from coronary arteries, it affects the cerebral and mesenteric arteries.⁶⁻⁸

Other proposed mechanisms are that global myocardial hypoperfusion occurs as a result of systemic vasodilatation and decreased venous return in the context of anaphylaxis.⁹⁻¹⁰

Kounis Syndrome Variants: Kounis describes three reported variants in his 2013 paper “Coronary Hypersensitivity Disorder” – vasospastic allergic angina (type I), allergic myocardial infarction (type II) and stent thrombosis (type III)

Kounis syndrome is a ubiquitous disease which represents a magnificent natural paradigm and nature's own experiment in a final trigger pathway implicated in cases of coronary artery spasm and plaque rupture.

Kounis syndrome seems to be not a rare disease but an infrequently diagnosed clinical entity which has revealed that the same mediators released from the same inflammatory cells are also present and in acute coronary events of non -allergic aetiology. These cells are not only present in the culprit region before plaque erosion or rupture but they release their contents just before an actual coronary event.¹⁰⁻¹³

Clinical Significance

- Diagnosis and treatment requires attention to both cardiac and anaphylactic pathophysiology
- Morphine must be avoided in Kounis Syndrome as it may stimulate histamine release and exacerbate mast-cell induced vasospasm.
- Some authors advocate that adrenaline should be used with caution as it may aggravate coronary ischaemia by worsening vasospasm.
- ECG changes often resolve upon treatment and withdrawal of underlying allergic insult.¹⁴
- Patients who undergo angiography will have improvement of vasospastic changes with administration of intracoronary nitroglycerine.
- The diagnosis of kounis syndrome should be entertained when acute onset chest pain is accompanied by allergic symptoms, electrocardiographic changes, and/or elevated cardiac enzymes.¹⁴

CONCLUSION

Vasospastic allergic angina, allergic myocardial infarction and stent thrombosis with occluding thrombus infiltrated by eosinophils and/or mast cells constitute the three reported variants of this syndrome.

This case highlights Type I Kounis Syndrome, where coronary vasospasm occurred in a structurally normal heart due to an amoxicillin-induced allergic reaction, mimicking STEMI. Early recognition and dual-focused treatment targeting both the allergic response and potential myocardial ischemia are key.¹²

Clinicians should maintain a high index of suspicion in patients presenting with ACS-like symptoms following recent exposure to

known allergens, especially in the absence of troponin rise or wall motion abnormalities.

In general, the prognosis of KS is better than the “conventional” acute coronary syndrome. This can be explained by several reasons including the known history of allergy to the trigger, the presence of other allergic manifestations and the early administration of the medical therapy which is effective in most of the cases.¹⁰⁻¹²

The diagnosis of this unique disease should be entertained when acute onset chest pain is accompanied by allergic symptoms, electrocardiographic changes, and elevated cardiac enzymes. All patients admitted to the emergency departments with chest pain and ST elevation on electrocardiography should also be interrogated for allergic insults, a history which we all many a times don't consider in a setting of ACS.¹⁵

Kounis Syndrome Emergency Treatment Suggestions:¹⁻⁸

Component	Type I (Vasospasm)	Type II (Plaque Rupture)	Type III (Stent Thrombosis)
Epinephrine (IM)	Yes, if anaphylaxis (caution if ischemia).	May worsen the ischemia.	Not recommended, Use cautiously only if needed for anaphylaxis.
IV Steroids (Methylprednisolone)	125 mg IV stat	Yes	Yes
H1 Antihistamines (Fexofenadine/ Diphenhydramine)	Fexofenadine 180 mg or IV Diphenhydramine	Yes	Yes
H2 Blockers (Ranitidine/ Famotidine)	Yes	Yes	Yes
Oxygen	High-flow if hypoxic	Yes	Yes
IV Fluids	Yes If hypotensive	Carefully, after ruling out heart failure/ pulmonary oedema.	Carefully, after ruling out heart failure/ pulmonary oedema.
Nitrates	Can be given For vasospasm relief	Can be given	Can be given
Calcium Channel Blockers	Diltiazem/ Verapamil	Use if vasospasm suspected	Can be given after ruling out heart failure/ pulmonary oedema.
Aspirin	Yes, with caution (may worsen allergy)	Yes	Yes
Heparin	Can be given	Yes As per ACS protocol	Yes. Mandatory
Dual Antiplatelet Therapy	Can be given	Yes	Yes
Stent Management	N/A	N/A	Urgent PCI/thrombus removal
Desensitization (long-term)	Consider if allergen essential	Yes	Yes

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