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Review Article

The Prevalence of Kounis Syndrome and COVID-19 Vaccination: A Comprehensive Review

Bhavya Ekambaram*, Swetha Suresh, Jerphene Franklin John, Nithish Kumar Jothi Kamaraj

Department of Pharmacy Practice, Saveetha College of Pharmacy, Saveetha Institute of Medical and Technical Sciences, (SIMATS-Deemed to be University), Chennai, Tamil Nadu, INDIA.

ABSTRACT

Background: Kounis Syndrome (KS) or allergic myocardial infarction is a rare, complicated Coronary Artery syndrome (CAD) which develops concurrently with an allergy or hypersensitivity reaction. It is also termed as Allergic Angina or Allergic Myocardial Infarction. The Coronary Artery Disease (CAD) is caused by Atherosclerotic plaque accumulation, a condition in which the coronary arteries that deliver blood, oxygen and nutrients to the heart muscle constrict or become clogged due to this, blood supply to the heart is reduced which can cause angina (chest discomfort) and dyspnea. The syndrome has well-defined clinical and diagnostic significance highlighting the involvement of inflammatory mediators in cardiovascular pathology. **Objectives:** To provide an overview on the pathophysiology, classification, triggers, clinical presentation, diagnosis, treatment and prognosis of Kounis Syndrome. **Materials and Methods:** A review of current literature on the mechanisms, clinical features and management strategies for KS, focusing specifically on the need for simultaneity in the recognition of allergic and coronary symptoms. **Results:** Kounis Syndrome (KS) is a rare condition where Acute Coronary Syndromes (ACS) is linked to allergic reactions. This happens because substances like histamine and tryptase are released. There are 3 types: vasospasm without Coronary Artery Disease (CAD), plaque disruption with existing CAD and hypersensitivity causing stent thrombosis. Triggers can be drugs, foods, insect bites, or environmental allergens. Symptoms include chest pain, ECG changes and allergic signs like rash and anaphylaxis. Diagnosis involves looking at the patient's history, identifying the allergen and checking for signs of ischemia and allergic reaction. Treatment includes antihistamines, corticosteroids, epinephrine (used carefully) and standard ACS treatments. The outcome depends on how much the coronary arteries are affected and the severity of the reaction. **Conclusion:** Kounis Syndrome is an allergy and cardiovascular pathology which indicates their connection. More public awareness through the medical community and the provision of better reporting are surely crucial in order to have more information of its epidemiology and adequate patient care. More studies should be carried out to elucidate the mechanisms and to prescribe effective treatments in the case of Kounis Syndrome.

Keywords: Acute coronary syndromes, COVID-19 vaccination, Hypersensitivity reaction, Kounis Syndrome.

Correspondence:
Dr. Bhavya Ekambaram
M.Pharm, Ph.D., Professor and Head, Department of Pharmacy Practice, Saveetha College of Pharmacy, Saveetha Institute of Medical and Technical Sciences, (SIMATS-Deemed to be University), Chennai-602125, Tamil Nadu, INDIA.
Email: bhavyae.scop@saveetha.com; bhavyavivek24@gmail.com

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INTRODUCTION

Kounis Syndrome, allergic myocardial infarction. This syndrome manifests as vasospastic angina or can lead to acute myocardial infarction; it is generally seen with allergic reaction.

Kounis Syndrome (KS) is the co-occurrence of an Acute Coronary Syndrome (ACS) with hypersensitivity actions after an allergenic event. It was first described by Kounis and Zavras in 1991 as an allergic angina syndrome (Kounis *et al.*, 1991).

Now, allergic angina and allergic myocardial infarction are common diseases that can affect patients of all ages, have multiple and ever-growing causes with widening clinical manifestations and constitute a broad range of mast cell-activation disorders referred to as Kounis Syndrome. However, none of these studies described the allergic angina syndrome, which could progress to the acute allergic myocardial infarction (Amro M *et al.*, 2020).

Kounis Syndrome is an acute coronary syndrome precipitated by the release of inflammatory mediators such as histamine, leukotrienes and cytokines during an allergic reaction, leading to coronary artery spasm or atheromatous plaque erosion and rupture (Kounis *et al.*, 1991).

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Kounis Syndrome has three variants

Type I: Patients without predisposing factor of coronary artery disease and normal coronary arteries where coronary artery spasm is induced by allergic mediators (Kounis *et al.*, 2011) (Figure 1).

Type II: Individuals with underlying stable atheromatous background, in which, allergic mediators could potentially induce plaque erosion or rupture.

Type III: Patients with stent thrombosis of the coronary arteries related to allergic reactions (Kounis, 2006).

Triggers: There are many allergens that can induce Kounis Syndrome, including:

- Antimicrobials, Anti-Inflammatories (NSAIDs), chemotherapeutic agents.
- Foods, especially nuts, shellfish and some fruits.
- Environmental exposures, e. g. insect stings and latex (Kogias *et al.*, 2010).

Clinical Presentation

Commonly experienced with chest pain and associated allergy signs including rash, itch, or anaphylaxis. Electrocardiography findings may mimic those of myocardial infarction and cardiac biomarkers may be elevated (Tsigkas *et al.*, 2010), (Lakshmipriya T *et al.*., 2025).

Diagnosis

Kounis Syndrome is based on a combination of clinical history, the identification of the potential allergen, features of an allergic reaction and evidence of myocardial ischemia. Other tests such as coronary angiography can be performed to look for spasm or rupture of atheromatous plaque (Kounis *et al.*, 2008) (Figure 2).

Pathophysiology

Management

The management of Kounis Syndrome requires treatment for the allergic response as well as the myocardial ischemia (Figure 3).

Antihistamines, corticosteroids and epinephrine for the allergic component

Conventional acute coronary syndrome treatments, including nitrates, calcium channel blockers, antiplatelet drugs and occasionally, Percutaneous Coronary Intervention (PCI) referred to as angioplasty with stent implantation, is a minimally invasive technique for opening blocked or constricted coronary arteries. It is a common therapy for Coronary Artery Disease (CAD), including acute myocardial infarction (heart attack) and it increases blood flow to the heart.

Prognosis

The outcome of Kounis Syndrome depends on the severity of the allergic reaction and the degree of coronary involvement that exists. It is in the early possible stages and need proper management to enhance the prognosis (Biteker *et al.*, 2011).

Epidemiology

Estimates of the incidence of Kounis Syndrome are unavailable because the condition likely goes underdiagnosed owing to its varied manifestations and its relation to several cardiovascular and allergic disorders. It has estimated that, awareness and reporting only are crucial to improve understanding its epidemiology data (Mazarakis *et al.*, 2011).

COVID-19 induced Kounis Syndrome

Possible Kounis Syndrome with death has been described in COVID-19 vaccinations showing that the syndrome links acute

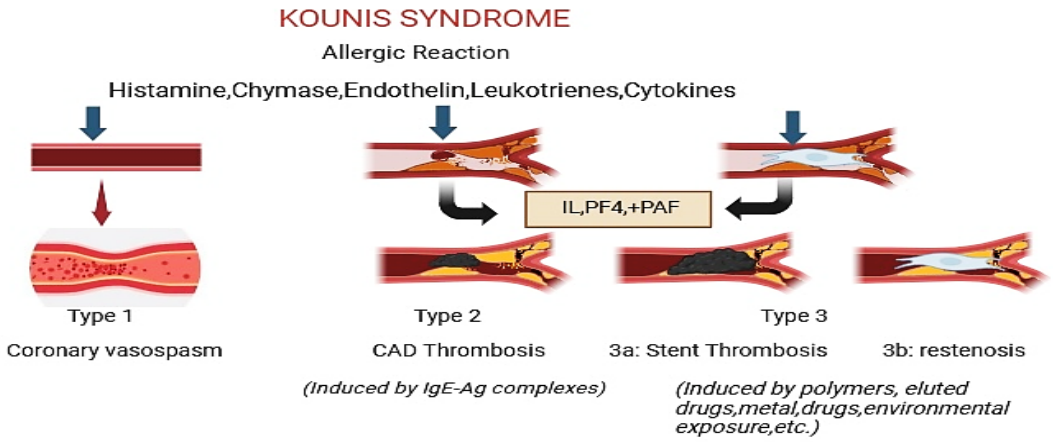

Figure 1: Overview of the triggers associated with Kounis Syndrome.

coronary events to allergic reactions. Here's a detailed overview of Kounis Syndrome in the context of COVID-19 vaccination, supported by references (Navaradnam P *et al.*, 2021):

Association with COVID-19 Vaccination

Kounis Syndrome, therefore, has appeared as a possible but not very frequent side effect of COVID-19 vaccination. The mechanism is an alleged allergic or hypersensitivity to components in vaccines, which can cause acute coronary syndromes (Fassio *et al.*, 2012).

Mechanism

The proposed mechanism entails the generation of histamine, tryptase and cytokine that are inflammatory mediators in reactions to the vaccine excipients or the immunologic response caused by the vaccine. Kounis has demonstrated that these mediators can lead to coronary artery spasm, plaque rupture, stent thrombosis, giving way to the manifestations of this syndrome (Abdelghany *et al.*, 2019).

Reported Cases

The current case reports show evidence of Kounis Syndrome after COVID-19 vaccination. These cases were associated with diverse vaccines-including mRNA vaccines like Pfizer-BioNTech and Moderna-and vector vaccines like AstraZeneca and Johnson and Johnson (Kounis *et al.*, 2021).

Clinical Presentation

These patients are mostly complaining of chest pain but some of them may have signs of allergy like rash, itching or angioedema. In most of the cases, electrocardiographic changes along with elevated levels of Cardiac biomarkers suggestive of myocardial ischemia are noted (Cagli *et al.*, 2021).

Diagnosis

❖ Diagnosis of Kounis Syndrome after COVID-19 Vaccination has temporal association between:

- Vaccine Administration,
- Onset of Myocardial Ischemia,
- Allergic Reaction.

❖ During Coronary Angiography, following may be observed:

- Coronary Artery Spasm,
- Atheromatous Plaque Disruption (Tajstra *et al.*, 2021).

Management

Management of Kounis Syndrome after COVID-19 Vaccination includes:

❖ Myocardial Ischemia Treatment (Rameez *et al.*, 2021).

- Nitroglycerin,
- Beta Blockers,
- Antiplatelet Agents,
- Percutaneous Coronary Intervention (PCI).

❖ Risk Mitigation Strategies (Singh *et al.*, 2021).

- Monitoring individuals receiving COVID-19 Vaccination,
- History of Cardiac Problem Patients screened before Vaccination,
- Prompt response to symptoms and providing protocols to manage adverse drug reaction.

❖ Allergic Reaction Management.

- Antihistamine or Antiallergic drugs,
- Corticosteroids,
- Epinephrine (rarely).

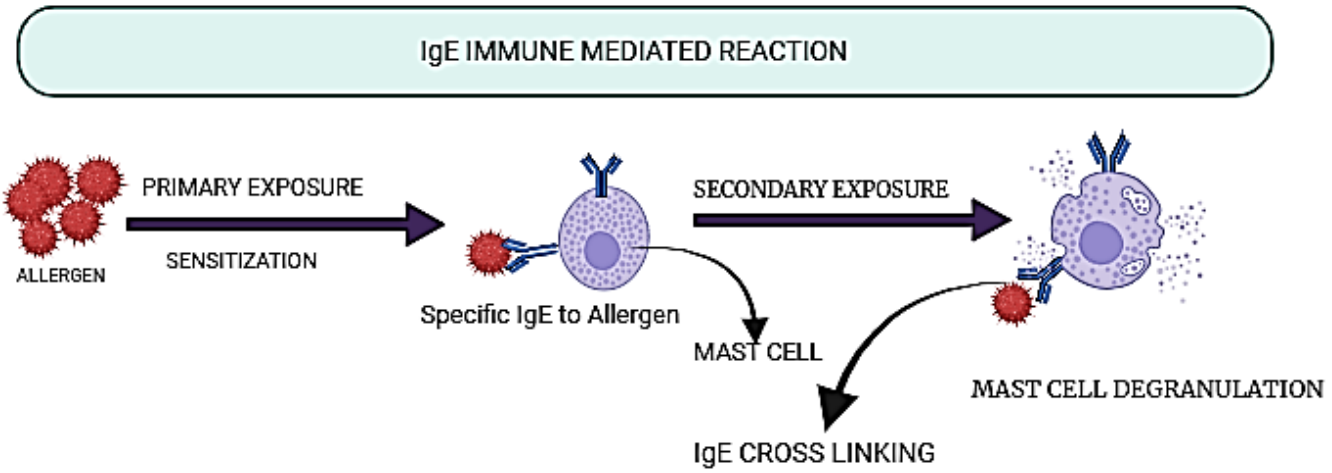

Figure 2: Pathophysiology of allergic myocardial infarction.

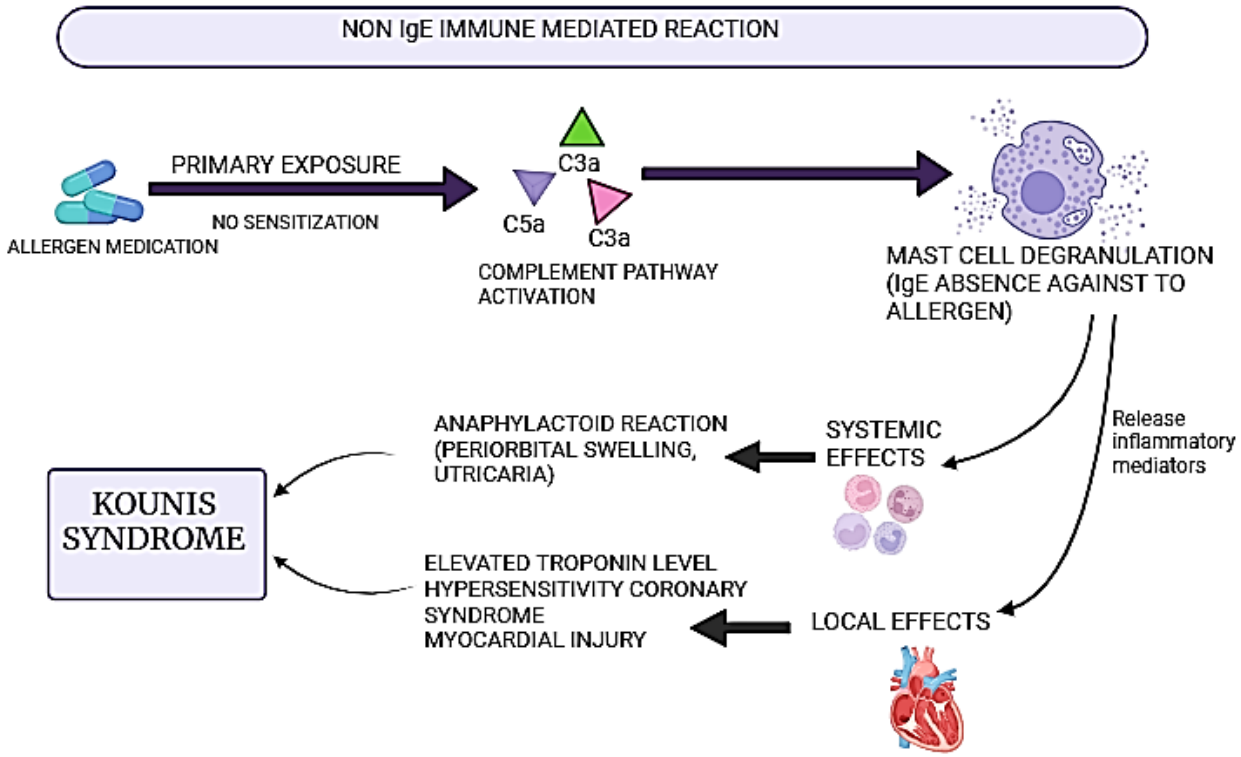

Figure 3: Management approach to Kounis Syndrome.

Prognosis and Outcomes

However, given the fact that Kounis Syndrome appears to be a self-limiting condition, whose patients usually do not develop any serious adverse outcome if the condition is well diagnosed and adequately managed early enough post-vaccination, the prognosis is rather good. However, the condition points to the need to be closely observing the individuals who receive the vaccines especially if they have allergies or heart diseases (CDC COVID-19, 2021).

CONCLUSION

Kounis Syndrome as a cardiac hypersensitivity after the COVID-19 vaccination is a rare side effect that targets patients with chest pain, an allergic attack and myocardial ischemia. It is a clinical diagnosis characterized by demonstrable myocardial ischemia and an allergic reaction. Available treatment options include antihistamines, corticosteroids and epinephrine and, in addition to this, nitrate, calcium channel blocker, antiplatelet agents and in severe cases, the revascularization tool, Percutaneous Coronary Intervention (PCI). The measures includes tests before administration of vaccine and follow up of vaccinated individuals so as to diagnose severe reactions. Kounis Syndrome following vaccination is rather benign, but incidence of the condition highlights the need to closely observe subjects who received vaccines, especially those with prior allergies or heart disease. The condition raises the need to continue closely observing vaccine recipients especially those with allergies or cardiovascular diseases.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ACS: Acute Coronary Syndromes; **NSAIDs:** Non-Steroidal Anti-Inflammatory Drugs; **KS:** Kounis Syndrome; **CAD:** Coronary Artery Disease; **ECG:** Electrocardiogram; **PCI:** Percutaneous Coronary Intervention; **mRNA:** Messenger Ribonucleic Acid; **COVID 19:** Corona Virus Disease 19.

ETHICAL STATEMENT

This review article entitled "Kounis Syndrome Prevalence in Context of COVID-19 Vaccination" does not involve any studies with human participants or animals performed by any of the authors. The research is based solely on the analysis and synthesis of previously published studies. All sources used have been appropriately cited, ensuring academic integrity and respect for intellectual property.

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