International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Gentamicin-Induced Kounis Syndrome: A Case Report and Review of Literature

Georgia Angeliniadis[1], Suad Srour Helal Owais[1], Trogkanis Efstratios[2]

[1]Medical School, University of Nicosia

[2]Department of Cardiology, General Hospital of Limassol, Cyprus

Citation: *Georgia Angeliniadis, Suad Srour Helal Owais, Trogkanis Efstratios. Gentamicin-Induced Kounis Syndrome: A Case Report and Review of Literature. Int Clinc Med Case Rep Jour. 2025;4(3):1-7.*

Received Date: 17 March, 2025**;** **Accepted Date:** 20 March, 2025**;** **Published Date:** 26 March, 2025

***Corresponding author:** Trogkanis Efstratios, Department of Cardiology, General Hospital of Limassol, Cyprus

ABSTRACT

Kounis Syndrome (KS) is an allergic or hypersensitivity reaction that manifests with cardiovascular symptoms. Once considered rare, it is now increasingly recognized as a cause of acute coronary spasm, even in patients without pre-existing coronary artery disease.

We present a case of pre-operative gentamicin-induced KS, highlighting its pathophysiology, clinical manifestations, epidemiology, diagnosis, and management. This case is particularly notable as it involves a young female patient who developed symptoms primarily after the third dose of gentamicin - a rare occurrence, as gentamicin-induced KS has not been well-documented in literature.

This case challenges the conventional perception of KS, demonstrating that it can occur in younger female patients rather than the traditionally expected demographic. The patient was managed symptomatically and kept under observation. She remains in stable condition, with a strict recommendation to avoid future exposure to gentamicin.

Keywords: Acute coronary syndrome; Allergic reactions; Chest pain; Hypersensitivity; Kounis syndrome; vasospasm

INTRODUCTION

KS is a rare condition in the context of severe allergies and anaphylactic reactions, causing myocardial damage and coronary artery spasm without obvious pre-existing CAD. KS involves a pathophysiological mechanism where histamine release from mast cell degranulation can occasionally cause atheromatous plaque erosion with rupture or severe coronary artery spasm [1].

The origins of KS date back to 1938, when Eugene Clark first described reactive arteritis and carditis following anti-pneumococcus serum administration. The first reported case of acute myocardial infarction (MI) associated with an allergic reaction was in 1950 by Pfister and Plice. However, it was not until 1991 that Kounis and Zavras identified a link between allergic angina and coronary spasms, which can progress to allergic acute MI. While it can occur at any age, it predominantly affects individuals aged 40–70 years, with risk factors including a history of allergies, hypertension, smoking, diabetes, and hyperlipidemia [2].

We report the case of a 30-year-old woman who developed an intense allergic coronary vasospastic presentation after third dose injection of gentamicin.

CASE REPORT

A 30-year-old woman was admitted to the ER with right-sided abdominal pain and fever. A urologist diagnosed her with pyelonephritis and prescribed Gentamicin (80 mg). The patient had no known history of allergies. After the first administration of Gentamicin (80mg), the patient had no immune reaction. 12 hours later the patient was administered a second dose of Gentamicin (80mg). Within thirty minutes after the second administration of the antibiotic, she experienced 15 minutes of sudden chest pain, which was self-terminated, with a normal blood pressure and no additional clinical findings. No further investigations took place. The following day the patient was administered a third dose of Gentamicin (80 mg) and thirty minutes later the patient developed sudden chest pain, similar to the previous day's episode, dyspnea and slight hypotension (80/60 mmHg), as her baseline BP is 100/70 mmHg. The 12-lead surface ECG revealed changes compared to her baseline ECG consistent with diffuse repolarisation abnormalities and more specifically slight ST depression (0.5 mV) in leads I, II, aVF and V2-V6 and biphasic T waves in leads I, II, aVR and V3 (refer to Figures 1 and 2). Additionally, the bedside cardiac echo revealed mild mitral regurgitation, normal left ventricular size, and an ejection fraction of 55%, with no regional wall motion abnormalities. The patient was then transferred to the ICU for monitoring after her anaphylactic reaction with a possible diagnosis of KS and was treated with Hydrocortisone, Loratadine, Pheniramine maleate, Aspirin and Low-molecular weight heparin (refer to table 1 for treatment and dosage). Initial troponin T levels taken in the ICU were high (316 ng/mL, normal value < 14 ng/mL), and that justified leading the patient to the cath lab for a coronary angiogram, which was unremarkable, with no signs of atherosclerotic plaques or coronary spasm.

Troponin T dropped to 74 ng/mL the following day. Two days later the troponin T levels continued to decrease to 22.30 ng/mL until the levels reached 8.92 ng/mL five days following the initial reaction, confirming myocardial injury with normal coronary arteries.

Blood tests showed elevated white blood cell count (13.54 x 10^3/µL) and neutrophils (12.08 x 10^3/µL), along with high glucose (121 mg/dL), mild hyponatremia (134 mmol/L), and mild hypokalemia (3.4 mmol/L). Liver and renal function tests were normal. The final diagnosis was gentamicin-induced KS.

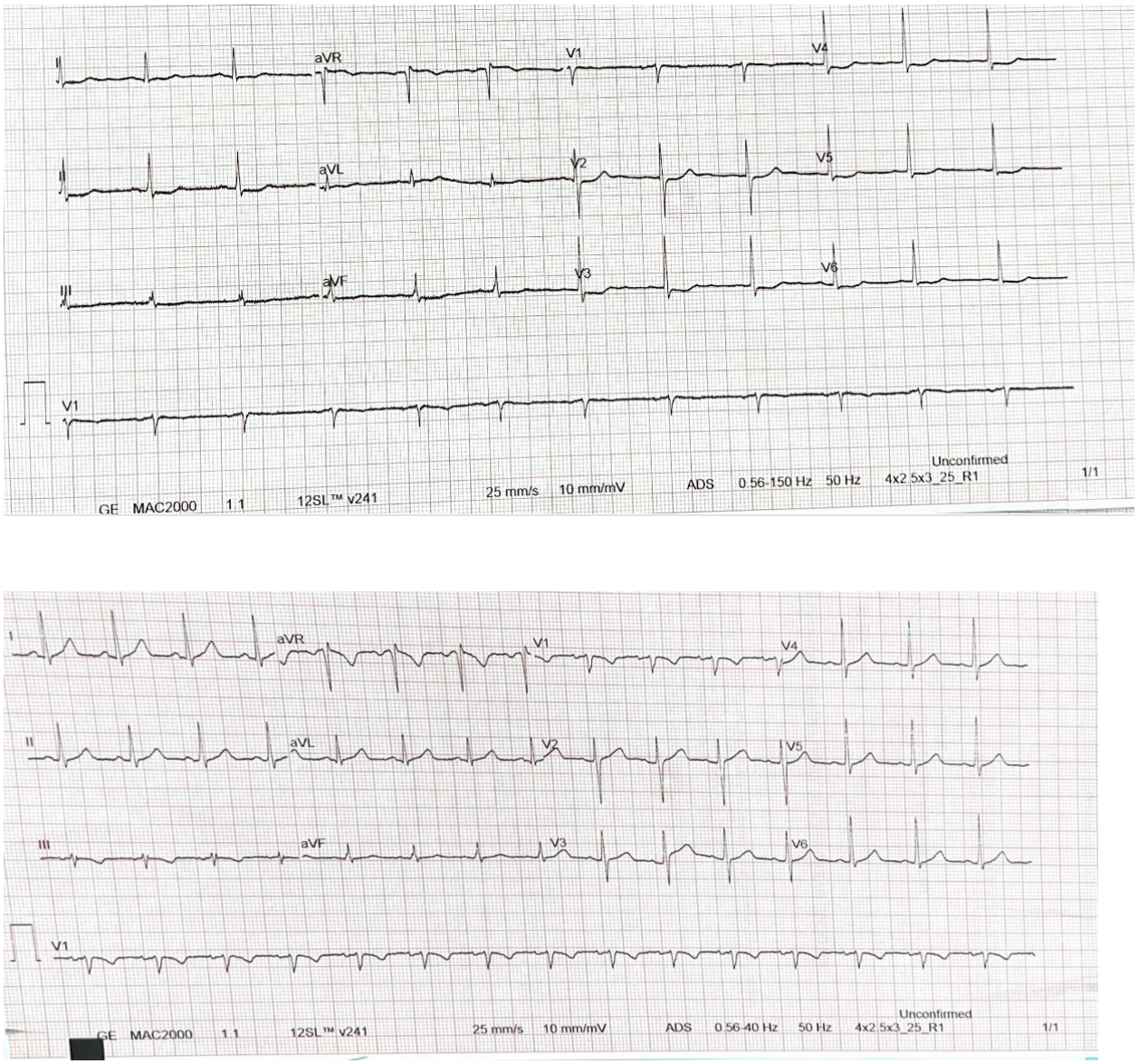

Figure 1: Image 1: Patient's ECG during acute phase reaction (third dose of Gentamicin).

Figure 2: Patient's baseline ECG

Table 1: Medications administered in the ICU after the second episode.

Drug	Dose
Loratadine (PO)	10 mg OD
Aspirin (PO)	75 mg OD
Enoxaparin sodium (SC)	0.4 mg BD
Rosuvastatin (PO)	10 mg OD
Hydrocortisone (IV)	200 mg OD
Pheniramine maleate (IV)	20 mg BD

DISCUSSION

Epidemiology

KS is a critical medical emergency characterized by acute coronary syndrome (ACS), including conditions such as coronary spasm and acute MI. There are various triggers that have been known to cause this allergic/ anaphylactic reaction, particularly medications that are widely used. These drugs include non-steroidal anti-inflammatory drugs (NSAIDS), analgesics, antibiotics, anti-neoplastics contrast media, proton-pump inhibitors, corticosteroids and anti-hypertensives [3]. Additional triggers include environmental exposures, foods, insect stings and stents [4]. In this case we have an antibiotic (gentamicin) which has not been reported in research most cases were beta-lactam antibiotics (pencillins & cephalosporins), macrolides, fluoroquinolones and vancomycin (refer to table 2 for further causes).

KS is more common in middle-aged men (40 to 70 years old) but has been reported across all age groups and ethnicities. Cases have been documented worldwide, with higher prevalence in Turkey, Greece, Italy, and Spain [5].

Different mechanisms can trigger acute coronary syndrome (ACS) during an allergic reaction, leading to its classification into four types.

- Type I occurs due to coronary spasm in normal coronary arteries.
- Type II involves either plaque rupture or coronary spasm in patients with pre-existing atheromatous disease.
- Type III is characterized by stent thrombosis.
- More recently, Type IV was introduced by Giovannini et al., referring to coronary artery bypass graft thrombosis [6].

It is suggested that the patient in this case experienced a type I reaction as she had no pre-existing disease prior to the administration of Gentamicin.

Table 2: Causes of KS that have been reported [3].

Drugs	Conditions	Foods	Exposures
Analgesics acetaminophen, aspirin, dipyridamole **Anesthetics** etomidate, isoflurane, midazolam, propofol, remifentanil, rocuronium bromide, succinylcholine, suxamethonium, trimethaphan **Antibiotics** ampicillin, ampicillin/sulfactam, amoxicillin, amikacin, cefazolin, cefoxitin, cefuroxime, cephradine, cinoxacin, lincomycin, penicillin, cefoperazone/ sulbactam piperacillin/tazobactam, trimethoprim, sulfamethoxazole, vancomycin **Anticoagulants** heparin, lepirudin **Anti-neoplastics** 5-fluorouracil, capecitabine, carboplatin, denileukin, interferons, paclitaxel, vinca alkaloids) **Contrast media** gadolinium, Iohexone, loxagate, meglumine diatrizoate, sodium indigotindisulfonate **Glucocorticoids** betamethasone, hydrocortisone **Nonsteroidal anti-inflammatory drugs** alclofenac, diclofenac, naproxen **Proton pump inhibitors** lansoprazole **Skin disinfectants** chlorhexidine, povidone iodine **Thrombolytics** streptokinase, tissue plasminogen activator urokinase **Others** allopurinol, bupropion, clopidogrel, dextran, enalapril, esmolol, fructose, gelofusin, insulin, iodine, iron, losartan, protamine, tetanus antitoxin, glaphenine, mesalamine, quetiapine	**Angioedema** **Anisakiasis** **Bronchial asthma** **Churg-Strauss syndrome** **Exercise-induced anaphylaxis** **Hay fever** **Idiopathic anaphylaxis** **Intracoronary stenting** **Mastocytosis** **Nicotine** **Scombroid syndrome** **Serum sickness** **Skin pricking** **Stents** (bare metal, bioresorbable, drug eluting)	**Actinidia chinensis** **Canned food** (tuna) **Eggs** **Milk** **Fish** **Fruits** **Mushroom poisoning** (Coprinopsis atramentaria) **Shellfish** **Vegetables** **Tomato salad**	**Animal licking** **Grass cutting** **Hirudotherapy (leech therapy)** **Hymenoptera stings** **Insect bites** **Jellyfish stings** **Latex contact** **Metals** **Millet allergy** **Octopus bite** **Poison ivy** **Scorpion sting** **Viper venom**

Pathophysiology

Several pathophysiological mechanisms have been proposed to explain how anaphylactic reactions affect the heart. Mast cells are activated either through antigen-antibody interactions or by the allergen itself, triggering their degranulation. Mast cell degranulation triggers the release of inflammatory mediators, including histamine, leukotrienes, platelet-activating factor, thromboxane, and prostaglandins. These substances can lead to endothelial dysfunction and smooth muscle over activity, which may result in tachycardia, coronary vasoconstriction, increased heart contractility, and atrioventricular conduction blocks. Histamine-induced activation of endothelial cells and platelets may also contribute to the erosion or rupture of coronary plaques, leading to the formation of a thrombus. As a result, these combined factors during anaphylaxis can cause coronary vasospasm, potentially triggering MI [7].

Clinical presentation

In KS, the primary clinical manifestations typically reflect an allergic reaction (often anaphylaxis) that is acute, subacute, or chronic, alongside cardiac symptoms. In majority of cases, symptoms manifest within the first hour of exposure to the trigger [5]. Patients often suffer from cardiac symptoms, such as ischemic chest pain and discomfort, dyspnoea, and syncope induced by coronary vasospasm, angina pectoris, MI or acute heart failure. These symptoms are related to allergic reactions, whether they are acute or chronic, including itchy skin, rashes, erythema, pruritus or angioedema. When anaphylaxis advances rapidly, vasoconstriction can be induced by reduced cardiac output and hypotension, leading to further skin reactions. Therefore, the absence of skin manifestations does not exclude KS, but indicates a severe reaction. Additionally, constitutional symptoms, such as nausea and vomiting, have been reported. If left untreated, KS can lead to cardiorespiratory arrest and sudden death [4]. A study that was recently published came to the conclusion that the cardiac signs and symptoms most commonly experienced were hypotension (75%) and chest pain (60%); additionally, symptoms that were dermatological, respiratory, and gastrointestinal presented in 70%, 30% and 20% of patients, respectively [5]. The patient in this case complained of sudden chest pain, stomach pain and dyspnoea.

Diagnosis

The diagnosis of KS is challenging due to its wide range of clinical manifestations. Diagnosis is established by combining cardiovascular and allergic/ anaphylactic signs and symptoms with laboratory, electrocardiogram (ECG), echocardiogram, and angiogram results. Additionally, a thorough history of past atopy and allergic reactions is crucial in the diagnostic process. In order to confirm or exclude KS, the following tests should be performed: serum tryptase, IgE antibodies and cardiac enzymes (CK, CK-MB, and troponin) (Poggiali et al., 2022). The most common ECG findings are ST segment elevation in inferior and anterior leads, although normal or nonspecific results are also possible. Patients can be divided into two groups based on the ECG: 1.) Prolonged ST elevation (> 20 mins) with chest pain, indicating acute total or near-total coronary occlusion and necessitating immediate reperfusion through primary percutaneous coronary intervention (PCI). 2.) Without prolonged ST elevation or depression, or T wave inversion, deferred PCI is allowed. The patient in this case did not experience ST elevation and was therefore classified as group 2. Upon resolution of the acute event, allergy

studies should be performed, specifically IgE and basophil activating test (BAT), skin prick tests and drug provocation test (DPT) [5].

Treatment

Managing KS is complex, as it requires addressing both acute coronary syndrome (ACS) and the underlying allergic reaction. The majority of treatment recommendations are based on case reports. Therefore, patients should be treated according to ACS protocols, with modifications based on their KS type. For Type I KS, treating the allergic reaction may be sufficient to resolve cardiac symptoms. Corticosteroids (e.g., hydrocortisone 1–2 mg/kg/day) help reduce inflammation and arterial hyperreactivity, while H1 and H2 antihistamines (e.g., diphenhydramine, ranitidine) support allergy management. Epinephrine should be used cautiously as it can worsen MI and induce vasospasm. For Type II KS, treatment follows standard ACS management, combined with steroids and antihistamines. Avoid beta-blockers as they might exacerbate coronary spasms. Type III KS requires intrastent thrombus aspiration, as histological examination may confirm an allergic cause. Patients with allergic reactions to stents may benefit from mast cell stabilizers and desensitization therapy. If allergy to nickel-titanium (nitinol) stent is confirmed and desensitization fails, stent removal may be necessary [2]. Our patient was in ICU for 10 days under observation, where she received Hydrocortisone, Pheniramine maleate and Loratidine for the allergic reaction, as well as Aspirin, Low-molecular weight heparin and Rosuvastatin (refer to Table 1). She was then discharged with Aspirin and Rosuvastatin.

CONCLUSION

KS is likely under-diagnosed. Increased awareness and early recognition are crucial for timely intervention. Standard ACS management may not always apply, and specific guidelines for KS are needed. Overall, the prognosis of KS is more favorable than conventional ACS, as the underlying allergic trigger can often be identified and managed effectively. Further studies are needed to establish definitive treatment guidelines. As far as we are informed, this is the first case presentation of gentamicin-induced KS.

REFERENCES

1. Rodríguez-Ruiz C, Puig-Carrión G, Delgado-Nieves A. López-Candales A. Kounis Syndrome: A More Commonly Encountered Cause of Acute Coronary Syndrome. Heart Views. 2019;20(3):122-125.
2. Abdelghany M, Subedi R, Shah S, Bosman H. Kounis syndrome: A review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. Int J Cardiol. 2017:232:1-4.
3. Kounis NG, Koniari I, Velissaris D, Tzanis G, Hahalis G. Kounis Syndrome-not a Single-organ Arterial Disorder but a Multisystem and Multidisciplinary Disease. Balkan Med J. 2019;36(4):212-221.

4. Poggiali E, Benedetti I, Vertemati V, Rossi L, Monello A, Giovini M, et al. Kounis syndrome: from an unexpected case in the Emergency Room to a review of the literature. Acta Biomed. 2022;93(1):e2022002.
5. Ollo-Morales P, Gutierrez-Niso M, De-la-Viuda-Camino E, Ruiz-de-Galarreta-Beristain M, Osaba-Ruiz-de-Alegria I, et al. Drug-Induced Kounis Syndrome: Latest Novelties. Curr Treat Options Allergy. 2023:1-18.
6. Allam C, Kounis NG, Chlawit R, Saouma M, Badaoui G. Kounis syndrome following COVID-19 vaccination. Proc (Bayl Univ Med Cent). 2022;35(3):369-370.
7. Ali S, Athar M, Rahman R, Rehman F. Ceftriaxone-induced Kounis syndrome: A case report and review of the literature. Rev Esp Anestesiol Reanim (Engl Ed). 2024;71(2):129-133.