

## A case report on cefoperazone induced cardiogenic shock - kounis syndrome

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### Abstract

**Background:** Kounis Syndrome is a hypersensitive coronary artery disease caused by the body being exposed to allergens that can be triggered by various medications and environmental factors. The body's defense mechanism launches a surge of chemicals during an anaphylactic reaction that could cause a state of shock, drop in blood pressure and constriction of the breathing passage, which makes breathing difficult.

**Case presentation:** A 55-year-old woman presented in our department with edema and a growth over her right buccal mucosa. A punch biopsy performed was indicative of squamous cell carcinoma. Considering Chronic Kidney Disease (CKD), consultation with a nephrologist was scheduled and proceeded with the advised recommendations. Following the first injection dose of Cefoperazone and Sulbactam, within 5 minutes, the patient reported chest discomfort and difficulty in breathing. CPR was given according to ACLS protocol. Adrenaline injection was administered and was connected to defibrillator shock.

**Conclusion:** It is imperative for healthcare providers and pharmacists to recognize that, cephalosporins may result in fatal disorders such as Kounis Syndrome (KS) in order to appropriately prescribe the treatment and take preventative measures.

**Keywords:** Kounis syndrome; Cefoperazone; Sulbactam; Cephalosporins; Anaphylaxis

### 1. Introduction

Kounis syndrome (KS) is a severe form of coronary artery disease triggered by the body's reaction to allergens, which is brought on by reactions to certain foods, medications, environment and different health issues [1]. It is instigated by mast cells that engage with macrophages and T lymphocytes, leading to a significant release of inflammatory substances in heart muscle, blood vessels, and plaque erosion or rupture [2] The main indicators and symptoms of Kounis syndrome are related to allergic reactions that manifest as heart-related symptoms. While Kounis syndrome (KS) is not uncommon, it is often overlooked during diagnosis. Clinicians should take Kounis syndrome into account for any patient receiving cephalosporin therapy who exhibits allergic symptoms or acute chest pain, as these are serious side effects linked to cephalosporin infusion [3].

Cefoperazone belongs to third-generation category of cephalosporins, which are capable of fighting Pseudomonas [4]. The most frequent side effects of cefoperazone include diarrhea, hypoprothrombinaemia and disulfiram-like reactions

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[5]. The three most common antibiotics associated with Kounis Syndrome are Cefazolin, Amoxicillin and Cefuroxime whereas Cefoperazone, Sulbactam accounting for only a small number of cases [7]. In addition to being aware of this medical condition, medical professionals in general should be alert to circumstances in which exposure to a potential allergen result in symptoms that need to be promptly recognized and treated [8]. This case report details a female patient who developed a cardiogenic shock due to an anaphylactic reaction induced by Cefoperazone and Sulbactam.

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## 2. Case presentation

A 55-year-old female presented with complaints of swelling and growth over right buccal mucosa. Reports of punch biopsy performed at outside hospital suggested a well-differentiated squamous cell carcinoma. The patient was admitted here for further management. Physical examination revealed, Temp 98.6°F, PR 80/min, BP 110/80 mm Hg, RR 20/min, SPO<sub>2</sub> 98% at room air, bilateral air entry was adequate, chest examination revealed normal breath sounds and on examination the abdomen was soft with bowel sounds. She had a past medical history of coronary artery disease (CAD) and had undergone percutaneous transluminal coronary angioplasty (PTCA) and stenting in year 2016. Further she had chronic kidney disease CKD and on maintenance haemodialysis (MHD). In addition, the patient commenced treatment with IV antibiotics, antacids, pain relievers.

Considering elevated serum creatinine levels, suspecting chronic kidney disease (CKD), a consultation with a nephrologist was scheduled and proceeded with the necessary actions. After five minutes of administration of first dose of Cefoperazone and Sulbactam injection, the patient developed chest pain, facial flushing and shortness of breath. Immediately infusion was withheld and vitals were measured which showed, SpO<sub>2</sub>:46 and there was no pulse. In addition to performing cardiopulmonary resuscitation (CPR), an Adrenaline injection (1mg) was given and connected to defibrillator shock. After 5 minutes one more dose of Inj. Adrenaline (1mg) was administered. After going through 2 cycles of cardiopulmonary resuscitation (CPR), the patient achieved ROSC (Return of spontaneous circulation).

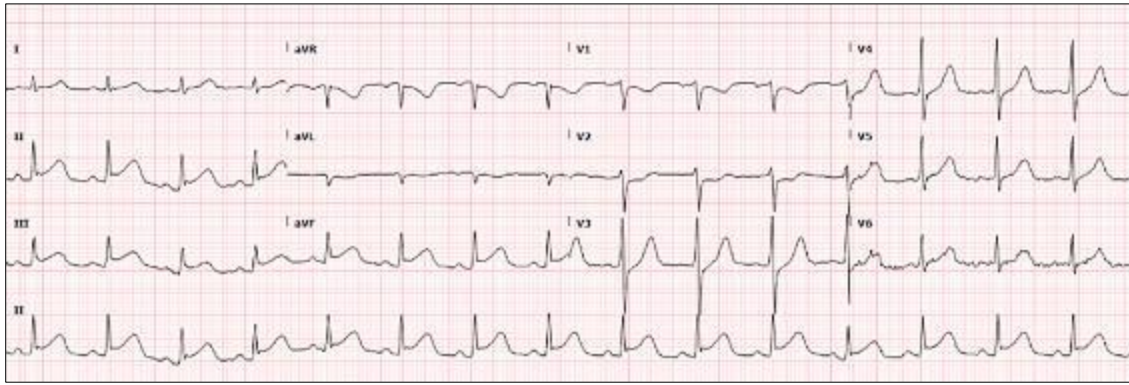
The patient was then shifted to Acute medical care unit for further management. The patient was intubated and started on inotrope and mechanical ventilator (MV) support. Laboratory investigations exhibited a serum cardiac Troponin I of 0.23 ng/mL and an elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) of 24313ng/L. 2D Echo performed was suggestive of left ventricular regional wall motion abnormality (LV RWMA) with mild to moderate left ventricular (LV) systolic dysfunction with an ejection fraction (EF) of 43% Figure 1, USG Doppler test for the blood flow in the left leg veins was inconclusive and showed no signs of deep vein thrombosis. The cardiologist's appointment was scheduled to discuss the patient's history of coronary artery disease (CAD) and previous episodes of cardiac arrest, after which the patient began treatment with diuretics and heparin(12units/kg/hr) as recommended.

The patient was planned for computed tomography coronary artery disease (CT CAD), but due to frequent VPCs (Ventricular Premature complexes), the scan was withheld. In view of recurrent Ventricular tachycardia, the patient was started on Inj. Cordarone (12 ml/24hr) and Lidocaine infusion of 50 mcg/kg per minute infusion for the first hour, then 25 mcg/kg per minute for the second hour, 12 mcg/kg per minute for the succeeding 22 hours. During hospital stay, the patient was treated with broad spectrum antibiotics, antacids, analgesics, inotropic support, MV support, diuretics, renal protectives, antiplatelets, anticoagulants, IV fluids and other supportive care. The patient's clinical condition showed significant improvement after 6days of admission. She stayed hemodynamically stable, afebrile and free of symptoms. Her NT-proBNP and blood Troponin I levels dropped to 923ng/L and 0.03ng/mL (Figure 2a. 2b) and echocardiogram showed LV function recovery up to 58% of EF. Gradually the patient's condition improved well and was discharged.

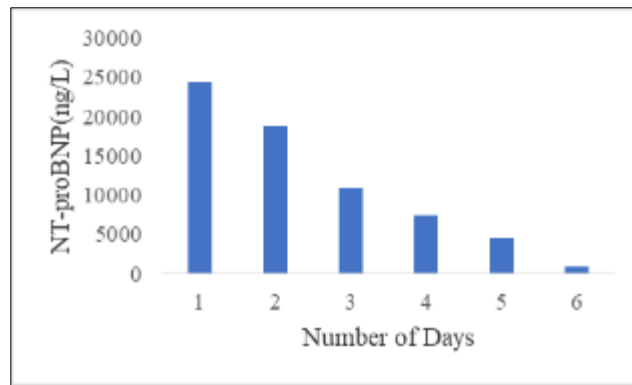
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## 3. Discussion

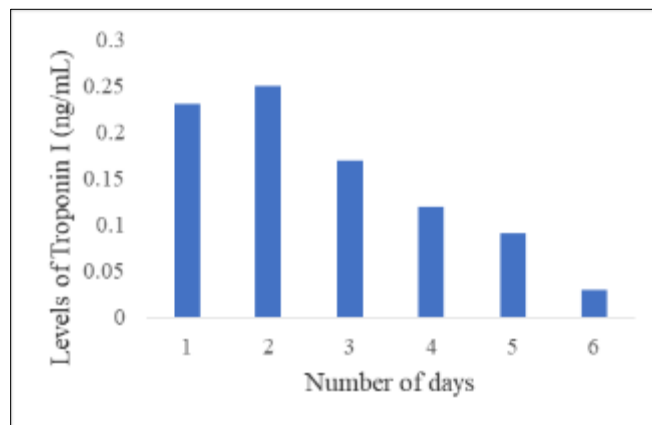
Kounis syndrome is a life-threatening disease, and therefore allergic reactions in patients with a history of cephalosporin allergy should be treated promptly. A recent large-scale study from the United States found that out of 235,420 patients hospitalized for anaphylaxis or hypersensitivity reactions, 2,616 (1.1%) developed acute coronary syndromes, and were diagnosed with Kounis syndrome [9]. It is widely understood that anaphylaxis results in spasms in coronary arteries either with or without tearing of atherosclerotic plaques, dilation of blood vessels throughout the body and an ablated venous return.



**Figure 1** 18-lead electrocardiogram (ECG) revealed a depression of 0.1–0.3 mV in the ST segment of lead I, aVL, V2–V6, and an elevation of 0.10–0.20 mV in the ST segment of lead II, III, avF, V3R–V5R



**Figure 2a** Levels of NT-proBNP from Day1 to Day 6



**Figure 2b** Levels of Troponin I from Day1 to Day 6

This can then lead to a reduced cardiac output, causing coronary hypoperfusion resulting in damage of myocardial tissue [10].

Even in the absence of a history of coronary heart disease, Kounis syndrome is likely to present in those who exhibit symptoms such as chest discomfort, shortness of breath and widespread allergic reactions such as a red rash and breathing difficulties. Different drugs, foods and environmental factors can cause this condition, with the most frequent causes being antibiotics (27.4%) and insect stings (23.4%) [11]. In our case the elevated rate of Cephalosporin-induced

Kounis syndrome (KS) might be attributed to the more common use of antibiotics and a possibility of cross-reactions with various  $\beta$ -lactams.

Cefoperazone-sulbactam, a combination drug made up of cephalosporin, cefoperazone and a  $\beta$ -lactamase inhibitor called sulbactam, Usually, there is no reaction to the cephalosporin by itself. But when it comes to contact with proteins or peptides in the body, it can act as a full allergen and prompt the body to produce IgE antibodies, which can cause allergic reactions [12]. Tests that are necessary to accurately diagnose Kounis Syndrome include serum tryptophan, histamine, cardiac enzymes, troponin, trypsin, electrocardiograms, echocardiograms, and angiography [13]. In the current study, the patient began to experience symptoms like wheezing, tightness in the chest, and facial flushing after receiving a cefoperazone-sulbactam injection. After evaluating the patient's medical history, laboratory report on Troponin, electrocardiogram, the condition was diagnosed as Kounis syndrome (KS) induced by cefoperazone-sulbactam.

Treatment of Kounis syndrome (KS) demands careful selection and application of several widely used medications. In cases of Kounis syndrome (KS), adrenaline, a common medication used to treat severe allergic reactions, should be administered cautiously because it may exacerbate coronary vasospasm and increase coronary ischemia [14]. In our case the patient returned to normalcy after receiving adrenaline injection in addition to CPR. Our study is in accordance with the previous studies of Rodriguez-Ruiz et al., on usage of intravenous steroids, antihistamines, fluid replacement for the initial treatment of KS patients and epinephrine, oxygen, antithrombotic upon the severity and longer duration of the allergic reaction [15].

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#### 4. Conclusion

Kounis syndrome is a serious medical condition that is difficult to diagnose and has a high mortality rate. Patients who have had renal disease or other cardiac surgical procedures in the past, as well as those who have previously experienced an allergic reaction to cephalosporins, should be properly identified and cared for. Antihistamines and steroids may be prescribed to treat allergic reactions.

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#### Compliance with ethical standards

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##### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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#### References

- [1] Kounis NG, Coronary hypersensitivity disorder: the Kounis syndrome. *Clin Ther.* 2013 May;35(5): 563-71.
- [2] 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: 212–21.
- [3] Fang W, Song L, Deng Z, Sun W, Li Z, Wang C. Analysis of Clinical Features of Kounis Syndrome Induced by Cephalosporin. *Front Cardiovasc Med.* 2022 Apr 26;9: 885438.
- [4] Petri WA. 2011. Penicillin, Cephalosporins, and other betaLactam Antibiotics. Brunton L, Chabner B, Knollman B. Goodman and Gilman's the Pharmacological Basis of Therapeutics. McGraw-Hill Inc. 12th edition. pp. 1493-9.
- [5] Khan DA, Banerji A, Bernstein JA, Bilgicer B, Blumenthal K, Castells M, et al. Cephalosporin allergy: current understanding and future challenges. *J Allergy Clin Immunol Pract.* (2019) 7: 2105–14.
- [6] Adachi H, Ihara M, Nojima Y, Kurimoto T, Nanto S. Kounis syndrome caused by anaphylaxis without skin manifestations after cefazolin administration. *J Allergy Clin Immunol Pract.* (2019) 7: 317–9.
- [7] Absmaier M, Biedermann T, Brockow K. Allergic myocardial infarction (Kounis syndrome) after cefuroxime with side-chain cross-reactivity. *J Allergy Clin Immunol Pract.* (2018) 6: 1781–3.

- [8] Pradhan S, Christ M, Trappe HJ. Kounis syndrome induced by amoxicillin following vasospastic coronary event in a 22-year-old patient: a case report. *Cardiovasc Diagn Ther.* (2018) 8: 180–5.
- [9] Desai R, Parekh T, Patel U, Fong HK, Samani S, Patel C, et al. Epidemiology of acute coronary syndrome co-existent with allergic/hypersensitivity/anaphylactic reactions (Kounis syndrome) in the United States: a nationwide inpatient analysis. *Int J Cardiol.* (2019) 292: 35–38.
- [10] Fassio F, Losappio L, Antolin-Amerigo D, Peveri S, Pala G, Preziosi D, et al. Kounis syndrome: a concise review with focus on management. *Eur J Intern Med.* (2016) 30: 7–10
- [11] Abdelghany M, Subedi R, Shah S, Kozman 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.
- [12] Sader HS, Carvalhaes CG, Streit JM, Castanheira M, Flamm RK. Antimicrobial activity of cefoperazone-sulbactam tested against Gram-Negative organisms from Europe, Asia-Pacific, and Latin America. *Int J Infect Dis.* (2020) 91: 32–7.
- [13] Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med.* (2016) 54:1545– 59.
- [14] Kemp SF, Lockey RF, Simons FE; World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization. *Allergy.* 2008 Aug;63(8): 1061-70.
- [15] Rodriguez-Ruiz C, Puig-Carrion G, Delgado-Nieves A, Lopez-Candales A. Kounis Syndrome: A More Commonly Encountered Cause of Acute Coronary Syndrome. *Heart Views.* 2019 Jul-Sep;20(3): 122-125