CASE REPORT

Kounis syndrome associated with benzathine penicillin G use: A case report

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A B S T R A C T

Kounis syndrome is a life-threatening medical condition that causes severe allergic reaction and acute coronary syndrome. Benzathine penicillin G is one of the most widely used antibiotics in clinical practice, but it can enhance both allergic and hypersensitivity complications. In this report, we describe the case of a 42-year-old man admitted to our hospital who presented with cryptic tonsillitis accompanied by angioneurotic edema, chest pain, and electrocardiographic variations. The patient was diagnosed with Kounis syndrome and treated with oral antihistamines and prednisolone. He was discharged following a complete recovery and regression of electrocardiographic abnormalities within 72 hours.

Introduction

Kounis Syndrome (KS) is characterized by the occurrence of acute coronary syndrome (ACS) with mast cell activation that is induced by inflammatory mediators released during allergic reaction. KS was first described by Kounis 2 as an allergic angina syndrome progressing to allergic myocardial infarction. Several causes of KS have been reported, including drug treatment (antibiotics, analgesics), various medical conditions (angioedema, bronchial asthma), and environmental exposure (ant, bee, and wasp stings). 3 The main mechanism proposed is the vasospasm of coronary arteries. Clinicians should be aware that various mediators of allergy lead to coronary spasm, plaque rupture, and thrombus formation, which seriously impact the course, prognosis, and management of the allergic reaction. 2 Here, we report the case of a 42-year-old man who developed ACS following an anaphylactic reaction to benzathine penicillin G.

Case report

A 42-year-old man visited our emergency hospital for an injection following treatment for cryptic tonsillitis, which was diagnosed by other clinicians. The injection procedure was performed after controlling his allergic status to benzathine penicillin G.Within minutes of the injection, the patient developed respiratory distress, facial cyanosis, fatigue, vertigo, and balance disorder. We assumed that the patient had developed an allergic reaction and oxygen inhalation was initiated after ensuring proper airway control. Chest pain and tightness developed simultaneously. On the electrocardiograph (ECG), ST elevation was observed in DII, DIII, and AVF derivations and ST depression and T negativity were observed in the DI and AVL derivations (Figure 1). The patient was questioned regarding hypertension, diabetes mellitus, smoking, and a family history of disease. The patient did not show any cardiac risk factors. Based on the physical examinations, the patient was conscious, oriented, and appeared frightened. His blood pressure and pulse were 60/40 mmHg and 70 beats/minute respectively. Uvula edema was observed upon oral examination. No abnormalities were observed during the examinations of other organs.

With respect to laboratory analyses, no abnormalities were detected in the hemogram. Biochemical analyses revealed normal levels of D–dimer, antithrombin III, lipoprotein (a), serum cholesterol, cardiac troponin I, and creatinine phosphokinase enzyme-myocardial bind (CK-MB). A minimal increase in creatine phosphokinase (CK) levels was detected (CK, 246 U/L; reference interval, 0–190 U/L). Cardiac markers remained normal over the proceeding 6 hours. Additionally, lupus antibodies and anticardiolipin immunoglobulin (Ig) G and IgM were negative. Fibrinogen levels and antithromophilic factors were within the normal range. Protein C or S deficiency was not detected. Based on the echocardiography, the ejection fraction was 60% and no abnormalities in wall motion were evident. Coronary angiography was...
performed to investigate the presence of coronary artery disease and normal coronary arteries were detected (Figures 2 and 3). Since no lesions were observed on the coronary angiograms, there was an absence of repetitive chest pain, and all laboratory analyses were normal, KS with coronary vasospasm triggered by an allergic reaction-associated discharge of histamine was proposed. Treatment with 0.9% NaCl serum infusion, 1 mg/kg prednisolone intravenous (IV), 50 mg diphenhydramine IV, and 50 mg ranitidine IV was initiated. The patient’s treatment was pursued for 3 days. After 3 days of treatment, cardiac enzymes were normal range. ST segment elevation was observed on the ECG regressed isoelectric line. The patient was discharged from the hospital following complete recovery.

**Discussion**

Following the first report of acute myocardial infarction during a prolonged allergic reaction to penicillin in 1950, the occurrence of allergic reactions and ACS, termed KS, has gained acceptance as a cause of coronary artery spasm. KS was first described in 1991 as an allergic angina syndrome that could progress to acute myocardial infarction, termed allergic myocardial infarction. Several causes have been reported to induce KS. These include drug treatment (antibiotics, analgesics, antineoplastics, contrast media, corticosteroids, intravenous anesthetics, nonsteroidal anti-inflammatory drugs, skin disinfectants, thrombolytics, anticoagulants, and proton pump inhibitors), various medical conditions (angioedema, bronchial asthma, urticaria, food allergy, exercise-induced allergy, and serum sickness), and environmental exposure (ant, bee, wasp, and jellyfish stings, grass cutting, poison ivy, latex contact, shellfish, and venom poison).

We evaluated of patients hospital records and we added the manuscript for other etiologies as you mentioned. Analyses of hemogram, D–dimer, antithrombin III, and cardiac enzymes were normal range. Additionally, protein C or S deficiencies were not detected. Fibrinogen levels and antihemophilic factor were within normal range. Also lupus antibody, anticardiolipin IgG and IgM were negative. Our patient had no risk factors for coronary artery disease. His symptoms had started 5 minutes after the injection of an IM of benzathine 1.2 million units benzathine penicillin G. According to these findings and the family history of our patient, the case was considered as KS type I variant. He was discharged with complete recovery and regression of electrocardiographic abnormalities in 72 hours. This case shows that allergic phenomenon may play a role triggering this kind of ACS.

Several reports have suggested that the onset of allergic phenomena in predisposed patients triggers an angina episode, with this association being described as KS. However, no previous reports have demonstrated a causal relationship between allergic reactions and ACS, and other possible mechanisms have not been excluded as causes of angina onset. Biteker et al reported the first case of KS in children. In their report, six patients were admitted or referred to their hospital over the previous 2 years with acute-onset chest pain accompanied by allergic symptoms, electrocardiographic changes, and elevated cardiac enzymes. Consistent with our case, the ECG revealed DII-III and aVF ST elevation, but cardiac markers were not elevated. Due to the rapid treatment of patients in the emergency department, this may have been due to the influence of other cardiac effects (Figure 3).

Previous cases of KS have been typically reported in the scope of emergency medicine and cardiology journals. The main clinical presentation of KS is urticaria and angioedema, suggesting that dermatologists are familiar with this syndrome. Numerous drugs may cause KS. In patients admitted to the emergency room with cardiac symptoms, the KS must be remembered in diagnosis of exclusion, so, the correct treatment can be started.
In our case, intramuscular injection (IM) benzathine penicillin G triggered KS. The emergency services department performed the injection. As a result, rapid intervention was possible. Therefore, the application of this injection outside of a hospital environment is dangerous. Injections should be performed in health institutions where the necessary conditions and treatment options are provided.

References


Figure 3 Left coronary arteries were normal based on coronary angiography. CX = circumflex artery; LAD = left anterior descending artery.