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GEMIFLOXACIN-INDUCED ALLERGIC MYOCARDIAL INFARCTION: A CASE REPORT

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□ **Abstract—Background: Gemifloxacin given once daily for 5–7 days has been shown to be non-inferior to, or in some instances superior to, comparator agents for the treatment of common lower respiratory tract infections. Gemifloxacin is generally well tolerated and is as safe as many frequently empirically prescribed antimicrobials. Case Report: We report a case of a 46-year-old woman given gemifloxacin for an upper respiratory tract infection who developed allergic myocardial infarction 15 min after taking an oral dose of 320 mg gemifloxacin. To our knowledge, this is the first case of allergic myocardial infarction associated with gemifloxacin. Why Should an Emergency Physician Be Aware of This?: Although anaphylactoid/anaphylactic reactions are rare adverse effects of fluoroquinolones, clinicians should be aware of this potentially fatal event. Electrocardiographic interpretation is a critical skill of the emergency physician. Awareness of Kounis syndrome and its specific electrocardiogram findings may help facilitate further testing that will aid in timely diagnosis and interventions. A diagnosis of Kounis syndrome should be considered in young, healthy patients with no atherosclerotic risk factors when they develop an acute coronary syndrome after administration of a potentially allergic agent.** © **2019 Elsevier Inc. All rights reserved.**

□ **Keywords—allergic myocardial infarction; gemifloxacin; Kounis syndrome**

INTRODUCTION

Gemifloxacin is a novel synthetic broad-spectrum fluoroquinolone that exhibits bactericidal activity primarily by inhibiting bacterial DNA gyrase (1). Gemifloxacin has excellent activity against both Gram-negative and Gram-positive organisms, including potent antibacterial activity against *Streptococcus* species and *Staphylococcal* species (1). Several fluoroquinolones have either been withdrawn from the market or had their use severely restricted because of adverse effects. However, gemifloxacin is one of the best-tolerated drugs in the quinolone group; the frequency of adverse events is low. Most adverse events are nausea, rash, diarrhea, and headache (2). Serious cardiovascular events associated with gemifloxacin use have not been reported previously. A slight prolongation in QT interval (2.56 ms) was reported in gemifloxacin-treated patients without any cardiac dysrhythmias (2).

Allergic myocardial infarction, known as Kounis syndrome, is characterized by the concurrence of acute coronary syndrome with mast cell activation induced by inflammatory mediators released during allergic reaction (3). There are several factors and diseases that can induce Kounis syndrome, including hymenoptera (e.g., bee) and viper venom, food allergens (e.g., shellfish), oral and

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parenteral drugs (e.g., insulin, antibiotics), stings by ants and jellyfishes, various conditions (angioedema, bronchial asthma, urticaria, mastocytosis), and a variety of environmental exposures (e.g., grass cutting, poison ivy, Latex contact) (4–6). Herein, we report the first case of allergic myocardial infarction secondary to gemifloxacin use.

CASE REPORT

A 46-year-old woman with no cardiovascular risk factors or a history of any chronic disease presented to our emergency department (ED) with chest pain, itchiness, facial rash, and palpitations after the first dose of gemifloxacin. According to her medical history, the patient had been diagnosed as having an upper respiratory tract infection and had been prescribed gemifloxacin mesylate 320 mg once daily. Fifteen minutes after the first dose, she developed typical chest pain and itching particularly localized in the extremities, followed by facial rush, palpitations, and shortness of breath. She was admitted to the ED. Upon ED arrival, physical examination demonstrated the following vital signs: respiratory rate 26 breaths/min, heart rate 105 beats/min, temperature 37.5°C, pulse oximetry 94% on room air, and blood pressure 90/50 mm Hg. She initially appeared to be in mild respiratory distress, with tachypnea, however, had no crackles to auscultation of bilateral lung fields. She had bronchospasm findings in lung auscultation. The patient had no lower-extremity pitting edema or jugular venous distention. She had erythematous appearance in face and extremities. Heart sounds were normal S1 and S2, no murmurs, and she reported typical chest pain. On admission, her electrocardiogram showed ST segment elevations in leads II, III, aVF; and ST segment depression in leads I, aVL, V1, V2 (Figure 1). She had no family history of coronary artery disease. Transthoracic echocardiography performed in the ED revealed inferior and posterior wall hypokinesia. Troponin-I estimated on arrival was 3.8 ng/mL (reference: 0–0.1 ng/mL), creatine kinase-MB fraction was 55 U/L (reference: 0–25 U/L). Intravenous ranitidine 50 mg, diphenhydramine 25 mg, methylprednisolone 80 mg, and rapid i.v. infusion of 0.9% saline, oxygen treatment, continuous salbutamol by nebulizer and epinephrine 0.3 mg intramuscular were administered in ED. In order to exclude coronary artery disease, coronary angiography was performed, which revealed normal coronary arteries. Fasting blood glucose, complete blood count, renal function tests, antithrombin III, D-dimer, and serum cholesterol levels were normal. Total immunoglobulin E was 225 IU/mL (reference: 0–100) and serum tryptase was 74 μg/L (reference: 5.6–13.5 μg/L). She was diagnosed with Kounis syndrome type I variant, secondary to gemifloxacin use. The patient was treated with oral antihistamines and 8 mg prednisolone every 6 h for 5 days. Four days later,

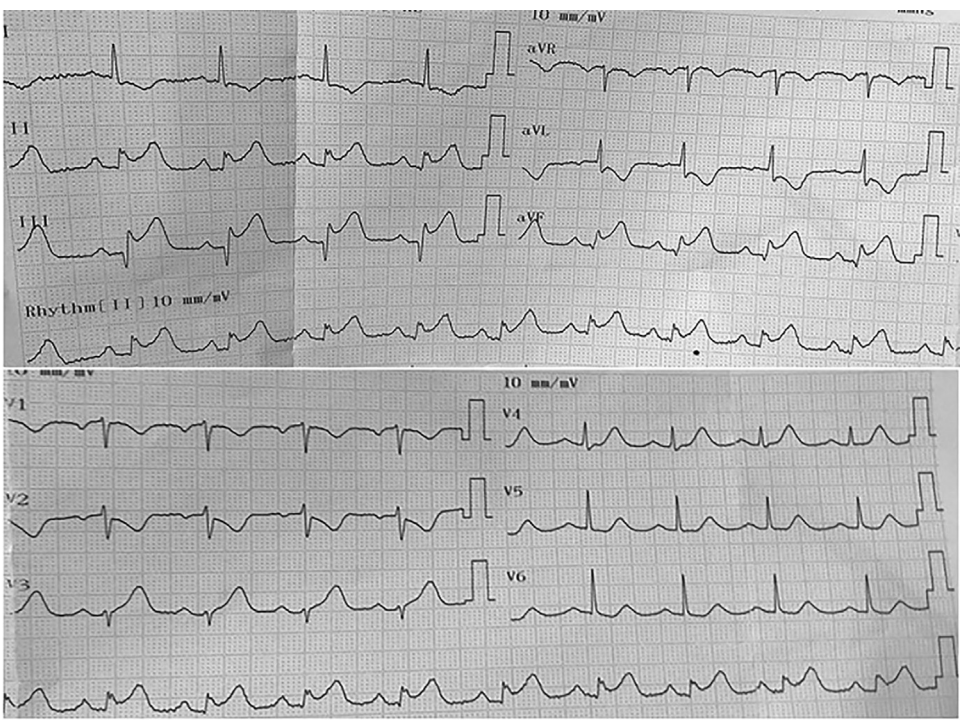

Figure 1. Electrocardiogram demonstrating inferior ST segment elevation and DI, aVL, V1, V2 ST segment depression.

repeated cardiac markers were within normal limits, with resolution of electrocardiographic abnormalities and regression of inferior and posterior wall motion abnormality on echocardiographic changes. The patient was discharged from hospital in excellent condition and after 10 days, at a follow-up visit, she was doing well.

DISCUSSION

Kounis syndrome is characterized by the concurrent presence of anaphylactic and cardiac components, which is caused by inflammatory mediators, such as a variety of cytokines, histamine, and chemokines released, during mast cell degranulation (3). Potentially, any kind of medication can trigger severe allergic reactions and multiple agents were associated with Kounis syndrome, although antibiotics are the most frequently involved drugs (4). However, there have only been four case reports involving a quinolone (ciprofloxacin, levofloxacin, and cinoxacin) (7–10).

Quinolones have been used for over many years to treat infections (1). These drugs can be classified into four groups by generation, and gemifloxacin is one of the fourth-generation members of this class of antibiotics (1,2). Although fluoroquinolones are generally safe antibiotics, life-threatening adverse events have been reported with fluoroquinolone use, and only one anaphylactic reaction has been reported to be due to gemifloxacin use (11,12). However, to the best of our knowledge, there have been no reports of Kounis syndrome secondary to gemifloxacin use in the literature.

Kounis syndrome has three variants, type 1–coronary spasm; type 2–coronary thrombosis; and type 3–drug-eluting stent thrombosis (13). It is important to distinguish the type, as it has management implications. Based on the clinical, laboratory, and electrocardiographic findings, the diagnosis of type I variant of Kounis syndrome induced by gemifloxacin use was made in our patient. No consensus exists regarding appropriate therapy for Kounis syndrome because the number of reported cases is low and the disorder is possibly underdiagnosed. Kounis syndrome has two aspects that need to be treated: acute coronary syndrome and allergic reaction. Treatment of allergic reaction can abolish type I variant alone but concomitant treatment of acute coronary syndrome is mandatory in type II and type III variants of Kounis syndrome. Supportive measures are the mainstay of management during the acute phase and antihistamines (H1 and H2 receptor blockers) provide symptomatic control of itching, hives, and angioedema (3).

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

Although anaphylactoid/anaphylactic reactions are rare adverse effects of fluoroquinolones, clinicians should be aware of this potentially fatal event. Electrocardiographic interpretation is a critical skill of the emergency physician. Awareness of Kounis syndrome and its specific electrocardiogram findings may help facilitate further testing that will aid in timely diagnosis and interventions. Kounis syndrome should be considered in young patients with acute coronary syndrome who have no history of risk factors for atherosclerotic cardiovascular disease after administration of a potential allergic agent. These patients need treatment with antihistamines, steroids, possibly adrenaline, oxygen, fluid resuscitation, and antithrombotic agents. An allergy workup should include the assessment of allergies to food, insect bites, and other environmental agents. Skin tests and other allergic tests may be useful in identifying the culprit agent.

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