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A Fatal Case of Kounis Syndrome Due to the Administration of Ceftriaxone

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Abstract: A seventy-one-year-old woman was administered ceftriaxone for pyelonephritis. The patient suddenly complained of breathing difficulty and electrocardiography (ECG) revealed pulseless electrical activity and ST segment elevation. Her initial rhythm, when she was transported to our department, was asystole. A return of spontaneous circulation was obtained after the administration of adrenaline. She was diagnosed with anaphylaxis with shock and Kounis syndrome. This is the fourth case and the first fatal case of Kounis syndrome induced by ceftriaxone. The therapeutic management of Kounis syndrome is challenging as it aims for myocardial revascularization as well as the treatment of the concomitant allergic reaction.
Keywords: Kounis syndrome, ceftriaxone, electrocardiogram, ST segment elevation, cardiac arrest.

INTRODUCTION

Kounis syndrome is defined as the concurrence of acute coronary syndromes (ACSs) associated with mast-cell and platelet activation in the setting of allergic or anaphylactic insult induced by various conditions, drugs, environmental exposure, foods and coronary stents [1]. Allergic, hypersensitivity, anaphylactic and anaphylactoid reactions are associated with this syndrome [1].

ACSs secondary to allergic reactions are associated with significant mortality. Three percent of allergy patients are reported to develop Kounis syndrome; thus, it should be excluded when physicians treat patients with anaphylaxis [2].

Ceftriaxone is a third-generation cephalosporin. The effects of ceftriaxone on severe infections, such as septicemia, bacterial meningitis, urinary tract infection, typhoid, bone infection, and sexually transmitted diseases have been described. Ceftriaxone is considered to have advantages in the treatment of some infections. These include the single daily dose and the short therapeutic course, which may modify therapeutic habits and have an additional cost benefit in some cases [3]. Although ceftriaxone is a generally well-tolerated antibiotic, serious and life-threatening adverse events such as anaphylaxis have been described in association with its use. However, there is a lack of data in the scientific literature regarding these events. This report describes a case of an anaphylactoid reaction that was likely to have been related to the administration of ceftriaxone, which manifested as shock, laryngeal edema and Kounis syndrome.

CASE REPORT

A seventy-one-year-old woman received an intravenous fusion of ceftriaxone sodium hydrate for pyelonephritis at a local medical facility. Her medical history included an allergy to iodine contrast medium and gastro-duodenal ulcer. After the administration of approximately 1–2 ml of the antibiotic, she suddenly complained of breathing difficulty, a chilly sensation, and her body started shaking. Her pulse and breathing declined with cyanosis. Her family doctor started cardiopulmonary resuscitation and called Emergency Medical Services but adrenaline was not administered. When the emergency medical technicians (EMTs) checked her, she showed pulseless electrical activity (heart rate, 70 beats per minute) and an ST segment elevation was observed on an electrocardiogram (ECG) (Figure 1). Within a few minutes, ECG showed ventricular fibrillation; consequently, the EMTs conducted a total of 3 defibrillations. The EMTs, who recognized laryngeal edema, performed tracheal intubation and transported her to our hospital. On arrival, she remained in a state of cardiopulmonary arrest. The initial rhythm was asystole. After the administration of adrenaline (1 mg, 3 times at 4-minute intervals), a return of spontaneous circulation was obtained. This was followed by the appearance of rash over her entire body (Figure 2). Methylprednisolone

sodium succinate (125 mg) and famotidine (20 mg) were administered. Computed tomography revealed a loss of cortico-medullary junction and a biochemical study showed an elevated troponin T level (0.042 [0.003–0.014] ng/mL). She was diagnosed with anaphylaxis with shock, laryngeal edema, hypoxic encephalopathy and Kounis syndrome, and was hospitalized in the intensive care unit of our hospital. Normothermia treatment was initiated in the first 24 hours; however, brain death occurred.

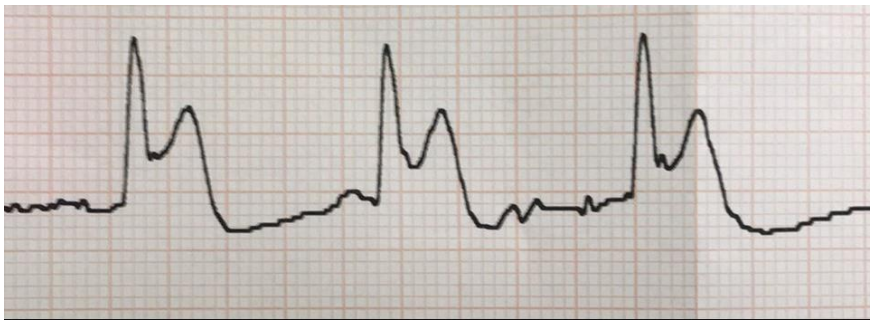

Fig-1: The electrocardiogram from the ambulance the electrocardiogram showed ST segment elevation

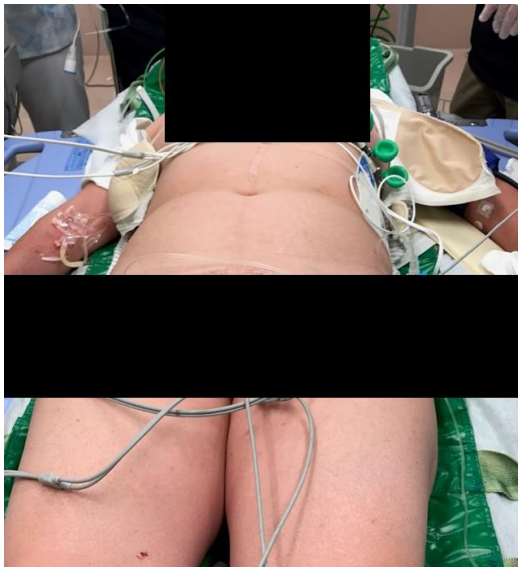

Fig-2: The skin findings after stable circulation was obtained the skin showed erythema

DISCUSSION

The most common causes of Kounis symptom are antibiotics, followed by insect bites. Renda *et al*. reported on 16 cases of Kounis symptom using the two largest pharmacovigilance databases from 2001 to 2016; 6 of the cases were associated with amoxicillin/clavulanic acid [4]. With regard to ceftriaxone, a 65-year-old man with myocardial infarction and AV-block, a 42-year-old man with vasospasm culminating in acute inferior myocardial infarction, and an 85-year-old woman with ST segment elevation on the anterior precordial leads after intravenous ceftriaxone administration, have been reported [5-8]. These patients survived with treatment for ACS alone. Accordingly, this is the fourth reported case and the first fatal case of Kounis syndrome induced by ceftriaxone.

The most common symptoms of Kounis syndrome are chest pain and breathing difficulty; however, these symptoms are similar to the symptoms of anaphylaxis and may be missed. Accordingly, it is important to perform ECG. It has been reported that 93.2% of Kounis syndrome patients shows ECG abnormalities [9]. Furthermore, 9.2% patients develop Kounis syndrome after more than 6 hours. Accordingly, if ECG is first performed in the emergency department, then the electrocardiograms can be compared [9]. The therapeutic management of Kounis syndrome is challenging as it aims for myocardial revascularization as well as treatment of the concomitant allergic reaction. The guidelines for the treatment of ACS lack managements for Kounis syndrome, and most of the evidence on the efficacy of treatments are based on individual case reports or case series [9]. This case, in which the patient developed anaphylactic and cardiogenic shock with laryngeal edema, was the most severe case reported to date. However, the patient in the present case should have received adrenaline immediately [8]. Further studies are warranted in order to determine the optimal treatment strategy for patients with such severe reactions.

CONCLUSION

This was the first case in which a patient developed brain death due to anaphylactic shock, laryngeal edema and Kounis syndrome, induced by ceftriaxone. The therapeutic management of Kounis syndrome is challenging as it aims for myocardial revascularization as well as the treatment of the concomitant allergic reaction.

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