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A Case of Kounis Syndrome Caused by Anaphylaxis During Surgery

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Abstract: Kounis syndrome is a hypersensitivity coronary disorder associated with several triggers, such as drugs, foods, environmental, coronary stents and other factors. It was originally proposed by the Greek cardiologist Nicholas Kounis in 1991. Kounis syndrome is a life-threatening and challenging emergency disease, which is constantly being recognized and studied. It is a disease that is constantly being recognized and Kounis syndrome can be classified into three types, involving coronary artery spasm, plaque rupture or stent thrombosis respectively. Most patients with coronary artery spasm caused by allergies can recover completely after active treatment, and the prognosis is good. If not, it may cause severe myocardial damage and even myocardial infarction, which threatens the patient's life. In our case, a 56-year-old female patient was scheduled to undergo right pelvic resection. A few minutes after the start of intravenous succinylated gelatin infusion, she was experienced a decrease in heart rate, blood pressure, oxygen saturation and ST elevation on 2-lead. An anaphylactic reaction was suspected after rapid differential diagnosis and gradually recovered with treatment. In this context, a rapid differential diagnosis and a highly suspicious become essential, because the management of Kounis syndrome is different from the traditional acute coronary syndrome. Kounis syndrome requires simultaneous diagnosis and treatment of both allergic reaction and acute coronary syndrome based on their manifestations and risk factors. This case describes the onset, development, and recovery of Kounis syndrome in this patient in detail, and illustrates the classification, pathophysiology, and treatment of Kounis syndrome. It is hoped that through the management of this case, the occurrence of Kounis syndrome can be rapidly identified and treated accordingly so that avoiding disaster for patients.

Keywords: Kounis Syndrome, Anaphylaxis, Gelofusine

1. Introduction

Kounis syndrome is a form of coronary artery spasm angina caused by an allergic reaction that can lead to serious consequences such as myocardial infarction and arrhythmias. In the United States, the overall incidence of Kounis syndrome in patients hospitalized for allergic/hypersensitivity/hypersensitivity reactions was 1.1%, with a subsequent all-cause in-hospital mortality rate of 7.0% [1]. Since the diagnosis is easily overlooked or missed, the actual prevalence may be higher [2]. The clinical signs and symptoms of Kounis syndrome are diverse, so the diagnosis of Kounis syndrome is difficult, especially during general anesthesia because many other diseases with similar signs and symptoms may occur, thus confusing the diagnosis. We report a case of Kounis syndrome under general anesthesia with anaphylactic shock and ST elevation on 2-lead ECG.

2. Case Presentation

A 56-year-old female was admitted to the hospital because of increasing pain in the right hip that she had experienced for 4 months and was planned to undergo right pelvic resection. She had no history of heart disease, and her preoperative electrocardiogram and transthoracic echocardiography showed normal findings. She was allergic to sulfonamides. The patient was generally in good condition in the period prior to the elective operation.

On the day of surgery, the patient was routinely monitored

with electrocardiogram, pulse oxygen saturation and blood pressure upon admission to the operating room. Anesthesia was administered using midazolam, sufentanil, cisatracurium and propofol. An endotracheal tube was inserted with the assisted of visual laryngoscope and then mechanical controlled ventilation. The tidal volume was set at 8 mL/kg, and the airway pressure was 14 cmH2O (1cmH2O=0.098 kPa). Right internal jugular venous catheter and a radial artery catheter were placed. Remifentanil and sevoflurane were used to maintain anesthesia. The surgical position was left lateral decubitus. Ten minutes after the surgery began, succinylated gelatin (4%) (GEL) (Gelofusine™, B. Braun Australia Pty Ltd) was infused to expand the volume. Hypotension, bradycardia, desaturation and difficult lung inflation developed within minutes of starting the infusion. ST elevation was observed on 2-lead electrocardiogram monitoring. (figure 1) Despite initial management with bolus doses of ephedrine and metaraminol intravenously, hypotension continued to worsen. Considering that the symptoms appeared immediately after a few minutes of Gelofusine infusion and 1 hour after anesthesia induction, Anaphylaxis was the primary suspected diagnosis, and Gelofusine was identified as the likely allergen. The intravenous infusion Gelofusine was immediately discontinued, and management was started with rapid intravenous replacement of circulating blood volume, corticosteroids and epinephrine, and calcium gluconate simultaneously to improve her condition. During this period, 2.5 mg epinephrine was administered intravenously. ECG revealed frequent premature ventricular contractions and ventricular tachycardia. The patient recovered gradually when she prepared to be rolled over for cardiopulmonary resuscitation but still required a continuous infusion of epinephrine and norepinephrine to stabilize. At this time, it was found that the skin was flushed all over the body, and the conjunctiva of both eyes was edematous. Bedside echocardiography showed normal systolic function with no ventricular wall motion abnormalities. Only tumor biopsy was performed. After the operation, the patient was awake and extubated and sent back to the ward for continued monitoring.

Blood tests performed 12 hours after shock revealed elevated cardiac enzymes, e.g., creatine kinase-MB and troponin. The postoperative electrocardiogram shows sinus rhythm with tachycardia.

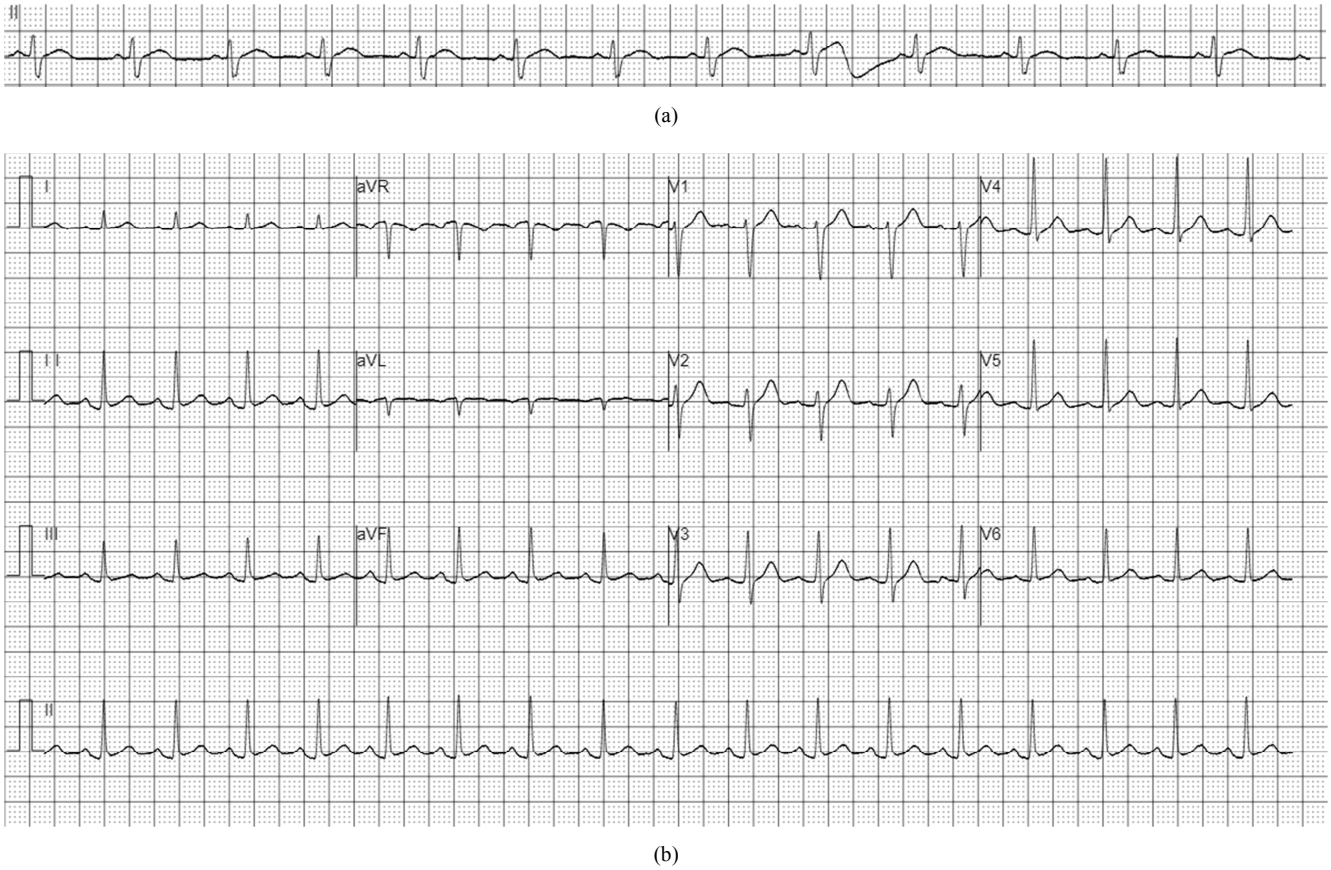

Figure 1. *Intraoperative and postoperative electrocardiogram (ECG). (a) Intraoperative 2-lead ECG showed sinus rhythm, ST elevation. (b) postoperative ECG showed sinus tachycardia.*

The postoperative echocardiographic showed normal dimensions of atriums and ventricles, overall normal systolic function without segmental motility abnormalities or valvular disease. Postoperative coronary computed tomography examination was performed, and the result showed no significant abnormalities in the coronary arteries and the absence of thrombotic

occlusions. (figure 2).

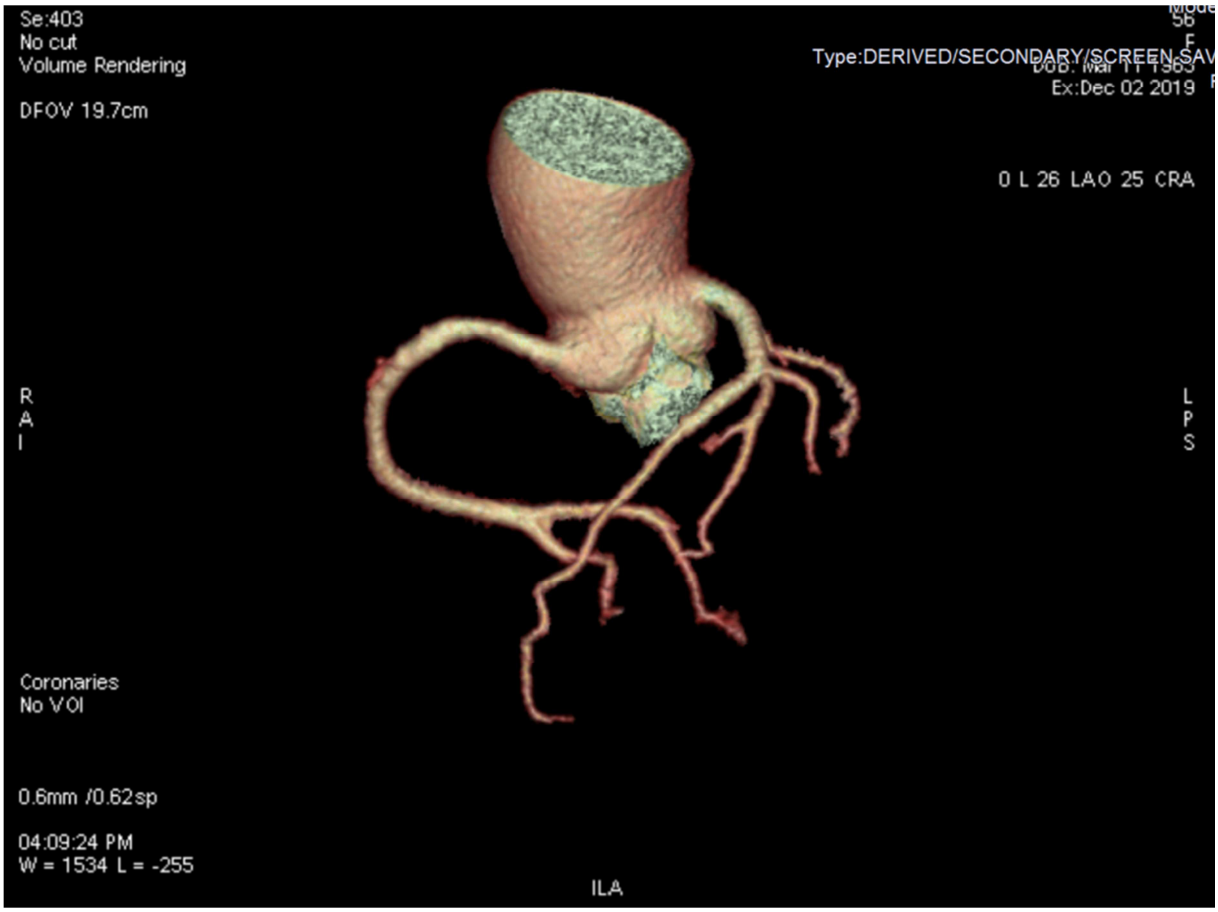

Figure 2. *Coronary computed tomography after operative showed the absence of thrombotic occlusions in left or right coronary artery.*

3. Discussion

An acute coronary event associated with hypersensitivity is known as Kounis syndrome, which is also known as allergic angina or allergic myocardial infarction. It's a life-threatening emergency. Kounis syndrome is considered not a rare but a ubiquitous disease; however, the diagnosis might be missed and unrecognized. An increasing number of cases of Kounis syndrome have been reported around the world, mainly due to the growing awareness of Kounis syndrome among physicians.

Current studies have confirmed that Kounis syndrome caused by many factors, including food, drugs, environmental factors, physical conditions and coronary stents. Any substance, disease or environmental exposure that might induce IgE antibody production, could act as possible causes of Kounis syndrome [3]. Medication is the most common trigger, multiple drugs such as antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), narcotics, antiplatelets, anticoagulants, etc. A review reported that intravenous antibiotics and neuromuscular blocking agents were the most common triggers of Kounis syndrome [4]. Coronary artery stenting, a common procedure for patients with coronary artery disease, has also been found to be a trigger [5].

The clinical symptoms and signs of Kounis syndrome are varied, which include immune-mediated hypersensitivity, allergy and anaphylactic or anaphylactoid reactions (manifestations with angioedema, urticaria and anaphylactic shock, etc.), combined with the cardiac signs and symptoms of acute coronary syndrome (ACS), such as chest pain, hypotension, arrhythmia, acute myocardial infarction, respiratory distress, acute heart failure. Chest pain and ischemic changes on the ECG are the most common clinical symptoms [4], but patients cannot complain about their symptoms under general anesthesia. Cutaneous manifestations, such as urticaria and angioedema, are the most common symptoms of anaphylaxis and often present in the initial stages of anaphylaxis [6]. But cutaneous signs may be absent in rapidly progressive systemic allergic reactions because the subcutaneous vascular bed is susceptible to vasoconstriction during anaphylaxis [7]. Cutaneous signs may therefore appear after the normalization of blood pressure [7]. Due to the absence of skin symptoms early, diagnosis of anaphylaxis may be delayed. Therefore ECG monitoring is particularly important. In our case, the rapid onset of anaphylaxis, initial lack of cutaneous signs and paradoxical bradycardia may be associated with severe anaphylactoid reactions.

The development of Kounis syndrome is a complex process involving the release of mediators such as histamine, neutral proteases, arachidonic acid derivatives, platelet-activating factors, and a variety of cytokines and chemokines from mast cells caused by an allergic reaction, which interact and ultimately leads to coronary artery spasm or thrombosis [8]. Anaphylaxis can also cause abnormal activation of the autonomic nervous system, resulting in excitation of the sympathetic nervous system and depression of the parasympathetic nervous system, which may lead to the development of myocardial ischemia and cardiac arrhythmias.

Kounis syndrome is subdivided into three types: the type 1 results from coronary spasms in normal or nearly normal coronary arteries with or without an increase in cardiac enzymes and troponins, represents a manifestation of endothelial dysfunction or microvascular angina; the type 2 results from spasms or plaque erosion or plaque rupture in coronary arteries with previous atherosclerosis, manifesting as acute myocardial infarction; and the type 3 results from a allergic inflammation that leads to coronary stent thrombosis or stent restenosis [9-10]. Considering clinical symptoms and signs as well as laboratory, electrocardiographic, echocardiographic and angiographic evidence and the context of being administered Gelofusine, the patient was diagnosed with Kounis syndrome type 1.

Kounis syndrome is a medical emergency requiring rapid diagnosis and treatment. The management of these patients is a real challenge for anesthesiologists since no guidelines have yet been established [7]. Anaphylaxis and cardiovascular events in a patient under general anesthesia should be suspected of Kounis syndrome, which requires simultaneous management of anaphylactic shock and acute coronary syndrome. Treatment of Kounis syndrome is difficult, and the difficulty is that the treatment of anaphylactic react might worsen the myocardial injury. Corticosteroids and H1 and H2 antihistamines are commonly used to reduce anaphylaxis [11], but antihistamines can cause hypotension. Epinephrine is the foundation of anaphylaxis treatment, however, its use in Kounis syndrome may exacerbate ischemia and induce coronary vasospasm and tachyarrhythmia [12]. Opioids such as morphine, used for chest pain relief, may induce massive mast cell degranulation, which may worsen anaphylaxis [13]. In our case, frequent premature ventricular contractions and ventricular tachycardia may have been due to the intravenous epinephrine. Corticosteroids (such as hydrocortisone) have a very important role in the treatment of anaphylaxis and allergic acute coronary syndrome, although it has been reported that it may cause myocardial wall thinning and cardiac aneurysms when used in ACS, its use in Kounis syndrome is probably safe and appropriate [13]. Antihistamines and corticosteroids can relieve symptoms in most of the type 1 patients. Coronary spasm is the primary mechanism, so vasodilators (such as nitrate and calcium channel blockers) can be used, but they could induce or worsen hypotension [7]. Patients presenting with distributive shock secondary to severe anaphylactic reaction require appropriate fluid resuscitation. In the Kounis syndrome type 2 (allergic myocardial infarction), an acute coronary syndrome protocol should be followed based on the current guidelines [14]. Type 2 patients must be treated for acute coronary events together with corticosteroids. Type 3 patients need urgent aspiration of intrastent thrombus, and the use of mast cell stabilizers in association with steroids and antihistamines is recommended [15].

4. Conclusion

Generally, Kounis syndrome is not a rare disease, its management requires rapid diagnosis and appropriate treatment. ECG monitoring, cardiovascular and allergic clinical symptoms and signs are mandatory to confirm Kounis syndrome in a patient with clinical, acute reactions. A high index of suspicion is of paramount importance to early diagnosis and initiation of appropriate treatment.

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