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CASE REPORT

Acute Coronary Syndrome in Cisatracurium-induced Anaphylactic Shock: Kounis Syndrome

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In this case report, we describe a 70-year-old male patient who sustained Kounis syndrome induced by cisatracurium administration immediately following induction of general anesthesia. Acute coronary syndrome combined with anaphylactic shock, termed Kounis syndrome, should be investigated in percutaneous coronary intervention to solve this complex and life-threatening condition. A team effort by cardiologist and anesthesiologist is essential for successful resuscitation. In general, the incidence of an anaphylactic reaction to cisatracurium is low, but a high serum IgE level in combination with a positive skin prick test in our patient was strongly suggestive of cisatracurium-induced Kounis syndrome. In addition, a cross-reaction between cisatracurium and rocuronium is reported.

1. Introduction

Kounis syndrome, which comprises allergic angina and allergic myocardial infarction can present as acute coronary syndrome (ACS) but with concurrent anaphylactic/anaphylactoid reactions.^{1,2} Here, we describe a patient who suffered from both an anaphylactic reaction and ACS following cisatracurium administration after induction of general anesthesia.

2. Case Report

A 70-year-old man (78 kg, 165 cm, ASA status II) was scheduled for routine left partial nephrectomy. The patient's medical history included oral drug-controlled diabetes mellitus, hypertension and gout arthritis.

An appendectomy was done some years previously under regional anesthesia without recourse to neuromuscular blocking drugs. No history of systemic drug allergy had ever existed except skin pruritus following administration of anti-gout drugs. Preoperative physical examination, laboratory examination and chest radiography yielded unremarkable findings.

Standard monitors, including a continuous electrocardiograph (ECG), pulse oximeter, noninvasive blood pressure device and thermometer were well set in use prior to the induction of general anesthesia. Baseline arterial pressure was 189/88 mmHg and a sinus cardiac rhythm of 79 beats per minute was recorded. No premedication was administered. General anesthesia was induced with intravenous propofol 120 mg, lidocaine 60 mg, and fentanyl 100 µg.

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Cisatracurium 16 mg was given to facilitate orotracheal intubation and the trachea was accordingly smoothly intubated. Anesthesia was maintained with 2% sevoflurane in O₂ at a flow rate of 6 L per minute. High airway pressure was immediately noted and decreased breath sounds with wheezing were audible. Lidocaine 80 mg and hydrocortisone 100 mg were administered intravenously to manage bronchospasm. Approximately 1 minute later, acute onset of sinus bradycardia (heart rate decreased from 78 to 40 beats per minute) with a decrease in arterial pressure to 65/35 mmHg was noted. The patient's condition continued to decline rapidly and his pulse was no longer detectable. Sevoflurane administration was immediately terminated and cardiopulmonary resuscitation (CPR) with 100% oxygen was initiated. Three intravenous boluses of epinephrine (1 mg each) were administered during CPR. Arterial pulsation was finally detected after 10 minutes of CPR, but hypotension persisted despite dopamine (10 µg/kg per minute) and epinephrine (4 µg per minute) infusion. A 12-lead ECG showed diffuse ST-T changes, suggestive of acute inferior and posterior wall myocardial infarction. A cardiologist was urgently consulted.

Upon evaluation, the attending cardiologist identified a pulseless polymorphic ventricular tachycardia (VT), and defibrillation with a biphasic defibrillator (150 J) was performed four times. Magnesium sulfate 2 g and amiodarone 300 mg were administered intravenously for refractory VT pursuant to the cardiologist's instructions. After the patient's hemodynamic status stabilized, he was taken to the cardiac catheterization room for emergency catheterization. Although angiography revealed a 95% eccentric stenosis at the first obtuse marginal branch (OM1) of the left circumflex artery, the left ventricular performance was adequate. After placement of a Swan-Ganz catheter and its attachment to the monitor, the patient was sent to the cardiac care unit where he was monitored overnight and the tracheal tube was removed the next morning. Recovery was uneventful and neurological sequelae were absent.

Blood sampled for laboratory study immediately after anaphylactic shock was first suspected revealed an abnormally high serum IgE of 762 IU/mL (normal <100 IU/mL) and normal troponin I levels of 0.8 ng/mL (normal <2 ng/mL). After discussing these results with the patient and his family, the attending physicians advised an allergy test via the skin prick technique, and it was done 2 weeks following the incident. A strongly positive result to cisatracurium (at a 1:1000 dilution) and a weakly positive result to rocuronium (at a 1:4 dilution) were noted. No further adverse events were reported and the patient's recovery was uneventful.

Three months later, left total nephrectomy was successfully performed under thoracic epidural anesthesia in combination with general anesthesia via a laryngeal mask without the use of any neuromuscular blocking agent.

3. Discussion

The patient described in this report developed signs of an allergy immediately following the administration of numerous drugs to induce general anesthesia. The signs included bronchospasm, increased airway pressure, cardiovascular collapse and cardiac arrest. In addition, ECG revealed a diffuse ST-T change and acute inferoposterior wall myocardial infarction while arterial cardiac catheterization done at a later time confirmed a 95% eccentric stenosis at OM1 of the left circumflex artery. Anaphylaxis can induce severe vasodilatation resulting in acute decreases in afterload and preload, but in general, heart function is less affected. A stable hemodynamic status requires a sufficient preload, normal cardiac function (in terms of contractility and normal rhythm) and an adequate afterload. Once anaphylaxis has combined with ACS, not only is maintaining adequate afterload and cardiac contractility and/or heart rhythm important, but early percutaneous coronary intervention should also be considered. A team effort by a cardiologist and anesthesiologist is often essential for successful resuscitation.

Patients presenting with systemic allergic reactions in combination with clinical, laboratory or ECG evidence of acute myocardial ischemia were first described by Nicholas G. Kounis, MD, and the entity was therefore termed the Kounis syndrome in 1991.^{1,2}

Two variations of Kounis syndrome have been defined and the one in our patient was classified as variant II.³ Variant II Kounis syndrome is a dormant, preexisting, quiescent atheromatous disease which an acute allergic episode presents as acute myocardial infarction. On the contrary, the type I variant of Kounis syndrome may reflect endothelial dysfunction or microvascular angina. It may progress to acute myocardial infarction (e.g. ST elevated or non-ST elevated myocardial infarction). Type I occurs in patients with normal coronary arteries in whom the acute allergic insult induces coronary artery spasm with normal or raised cardiac enzymes and troponins.

Increasing cases of ACS occurring with an allergic reaction have been reported, but the actual number could be greater than supposed. The drugs reported to account for allergic reactions are used widely in daily clinical application, of which antibiotics,

analgesics, antineoplastics, contrast media, corticosteroids, intravenous anesthetics, nonsteroidal anti-inflammatory drugs, skin disinfectants, thrombolytics, and others, stand out.⁴⁻⁸

Identification of the drugs that could result in an anaphylactic reaction is difficult during anesthesia because many drugs are administered in a relatively short time, especially during induction of anesthesia. In this case, a skin prick test was used to identify the responsible allergen, and cisatracurium was proved to be the cause.

Cisatracurium is reportedly less allergenic than atracurium. It does not induce release of histamine and has no clinically significant cardiovascular effects at doses eight times its ED₉₅ (0.4 mg/kg).⁹ Therefore, cisatracurium is largely replacing atracurium for procurement of muscle relaxation. Nevertheless, several cases of severe anaphylactic reaction following cisatracurium have been reported.^{10,11}

The case presented here not only confirms that cisatracurium can induce severe anaphylaxis,^{10,11} but also reveals that cisatracurium administration can also cause Kounis syndrome. To our knowledge, the patient described herein had no previous exposure to any neuromuscular blocking drug prior to the incident. The high serum IgE level indicated that his reaction to cisatracurium was anaphylactic. IgE-mediated reactions have been reported in patients without previous exposure to neuromuscular blocking drugs due to the cross-reactivity between muscle relaxants and substances with quaternary ammonium ions.¹² Since a positive skin prick test to rocuronium was also identified, a cross-reaction between cisatracurium and rocuronium might have occurred.

In this case, we found that Kounis syndrome can occur following intravenous administration of cisatracurium. This case was clearly suggestive of Kounis syndrome because of the high serum IgE level and positive skin prick test to cisatracurium. This case

also highlights the fact that a cross-reaction can occur between muscle relaxants.

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