



Case report

Case report: Ioversol induced Kounis syndrome and cardiogenic shock

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ABSTRACT

A 50-year-old male patient was admitted to the Cardiology Department of our hospital for intermittent chest pain for 9 days. Coronary angiography showed approximately 70% stenosis in the middle part of the left anterior descending branch. When the procedure was about to end, the patient experienced dyspnea, facial flushing and fall of blood pressure suddenly. At this time, the angiography showed severe spasm and stenosis of the left coronary artery. With antianaphylaxis, pressor therapy, fluid resuscitation and intracoronary administration of nitroglycerin, the left coronary spasm was relieved. A diagnosis of type II kounis syndrome induced by ioversol with cardiogenic shock was made.

1. Introduction

Kounis syndrome is a rare clinical entity that is characterized anaphylactic reaction-induced acute coronary syndromes [1], which is caused by drugs, food or environmental factors [2] and can lead to serious complications. Kounis syndrome consists of three types [3]: type I—coronary spasm; type II—coronary erosion-induced acute myocardial infarction; and type III—stent thrombosis (subtype IIIa) and/or stent restenosis (subtype IIIb) [4]. The diagnosis of Kounis syndrome is mainly based on the clinical manifestations and medical history of patients, and coronary angiography can make an accurate diagnosis. Mast cells are the main cells in the development of Kounis syndrome. Treatment of Kounis syndrome is challenging due to simultaneously occurring cardiac and allergic symptoms. Here, we report a case of type II Kounis syndrome induced by ioversol.

2. Case introduction

A 50-year-old male patient was admitted with intermittent chest pain for 9 days. It was located in the anterior chest and lasted about 5 minutes. He has no hypertension, diabetes and history of food or drug allergies. Admission for physical examination: body temperature 36.6 °C, pulse 65 times/min, blood pressure 130/80 mmHg (1 mmHg = 0.133kPa). Electrocardiogram showed sinus bradycardia (Fig. 1). Echocardiography showed ejection fraction of 66% and mild regurgitation of tricuspid valve. Blood routine, liver function, kidney function, blood lipid and myocardial injury markers were normal. On the 5th day after admission, coronary angiography was performed with ioversol as contrast agent. The angiography showed no obvious stenosis in the left main trunk, but the tubular stenosis in the middle part of the left anterior descending branch (LAD) was approximately 70% with forward blood flow TIMI grade 3 (Fig. 2B). No obvious stenosis was found in the left circumflex branch (LCX) (Fig. 2A) and the right coronary artery (RCA)

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(Fig. 2C). Optical coherence tomography (OCT) was performed on the LAD. Operation procedure: The 6F EBU3.5 guiding catheter was seated well in the left main coronary artery, then SION guide wire was sent to the distal end of the LAD, and OCT probe was sent to the distal end of the LAD along the guide wire after nitroglycerin 200 μ g was given in the left coronary artery. The OCT showed that the minimum lumen diameter was 1.58mm, the minimum lumen area 2.50mm², the fibrous plaque thickness 0.65mm, and the stenosis rate was 72.7% (Fig. 3), and there was no vulnerable plaque in the LAD. Therefore, we did not implant coronary stents. When the guiding catheter was withdrawn and the procedure was about to end, the patient experienced dyspnea and facial flushing suddenly. Invasive arterial pressure measured by radial artery sheath was 71/52 mmHg, heart rate 103 beats/min, sinus rhythm, fingertip oxygen saturation 79%. We considered anaphylaxis or aortic dissection. Intravenous fluids, norepinephrine and epinephrine were administered to maintain blood pressure. Dexamethasone(10 mg) and promethazine (50 mg) were administered to treat allergic reaction. Laryngeal mask was implanted with ventilator assisted ventilation. Observation for 5 minutes, the invasive arterial pressure was 69/50 mmHg. The guiding catheter was sent again to the left coronary sinus orifice and the angiography showed severe spasm of the left main trunk with stenosis of about 80%, both LAD and LCX had severe spasm throughout the whole process with stenosis of 95–99% at the worst with the forward blood flow TIMI grade 2 (Fig. 4). Nitroglycerin 200 μ g was given over and over again(the total amount is 800 μ g) in the left coronary artery. Finally, the angiography showed relief of left coronary spasm with TIMI grade 3 (Fig. 5). At this time, the invasive arterial pressure was 60/45 mmHg. Because the patient had sustained low blood pressure, the intra-aortic balloon pump counterpulsation (IABP) was implanted. After observation for 50 minutes, the patient's invasive arterial pressure increased to 105/71 mmHg, heart rate 95 beats/min and fingertip oxygen saturation 96%. He was admitted to CCU when vital signs was stable. Laboratory evaluation revealed a troponin I was 1.68ng/ml (0–0.034ng/ml) and immunoglobulin quantitative IgE was 531 IU/ml (reference interval <100IU/ml). A diagnosis of typeII kounis syndrome induced by Ioversol with cardiogenic shock was made. The patient's symptoms improved significantly on the 6th postoperative day and he was discharged. Medication after discharge: aspirin 100mg once daily orally and atorvastatin 20mg daily orally.

3. Discussion

Kounis syndrome(KS) was first proposed by Kounis and Zavras in 1991 [1]and it is an acute coronary syndrome caused by allergic reaction, which can lead to severe coronary artery spasm, acute myocardial infarction or acute stent thrombosis. Allergens include drugs, food or environmental factors [2]. Some studies showed that the incidence of KS in allergy patients at the emergency department was 3.4%, and the catheterization laboratory prevalence of KS is 0.002% [3]. Three variants of KS have been described [3]: The type I variant refers to coronary artery spasm induced by inflammatory mediators, but patients are with normal or nearly normal coronary arteries; type II variant refers to anaphylactic reaction induced coronary artery spasm or plaque rupture and pateints are with coronary artery atherosclerosis; and type III variant refers to stent thrombosis (subtype IIIa)and/or stent restenosis (subtype IIIb) induced by stent polymers, stent metals, eluted drugs, dual antiplatelets or environmental exposures [4]. Ioversol is a new type of triiodine-hypotonic nonionic contrast agent, which can cause fever, skin reactions, convulsions, dyspnea and hypersensitivity reactions including KS [5]. Direct imaging evidence of KS caused by Ioversol is rare. Contrast-induced KS is more common in type I and type II in elderly men [6]. This patient was a middle-aged man with coronary atherosclerosis confirmed by coronary angiography and

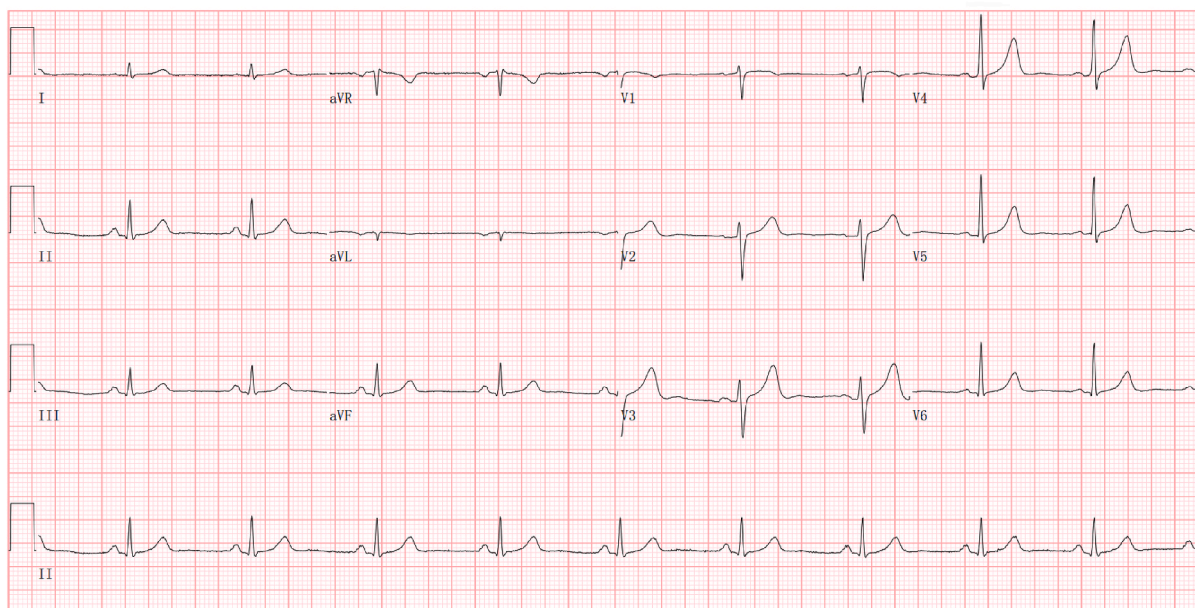


Fig. 1. ECG showed that the heart rate of sinus bradycardia was 58 beats/min.

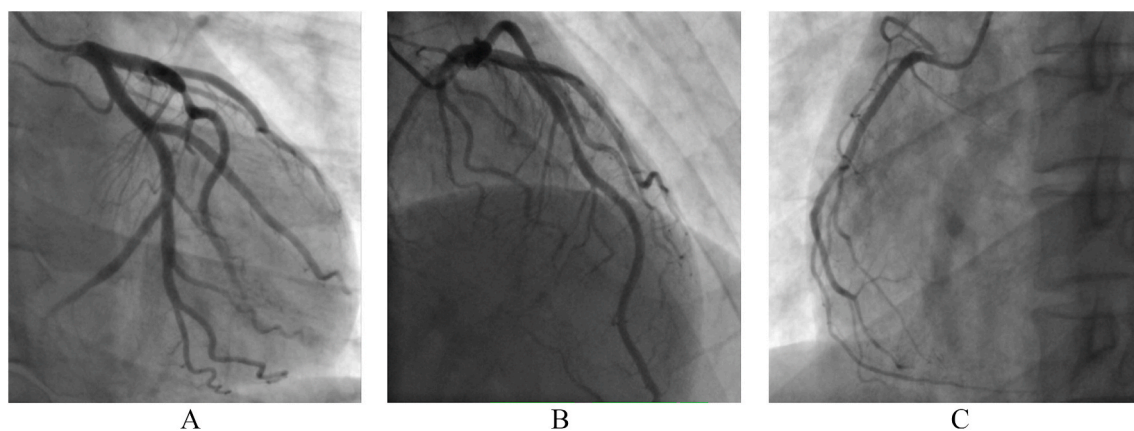


Fig. 2. A. The coronary angiography at foot position showed no significant stenosis in LCX with forward flow TIMI grade 3. B. The coronary angiography in the right shoulder view showed a tubular stenosis of approximately 70% in the middle segment of the LAD with forward flow TIMI grade 3. C. The coronary angiography in the left anterior oblique view showed RCA was no significant stenosis with forward flow TIMI grade 3.

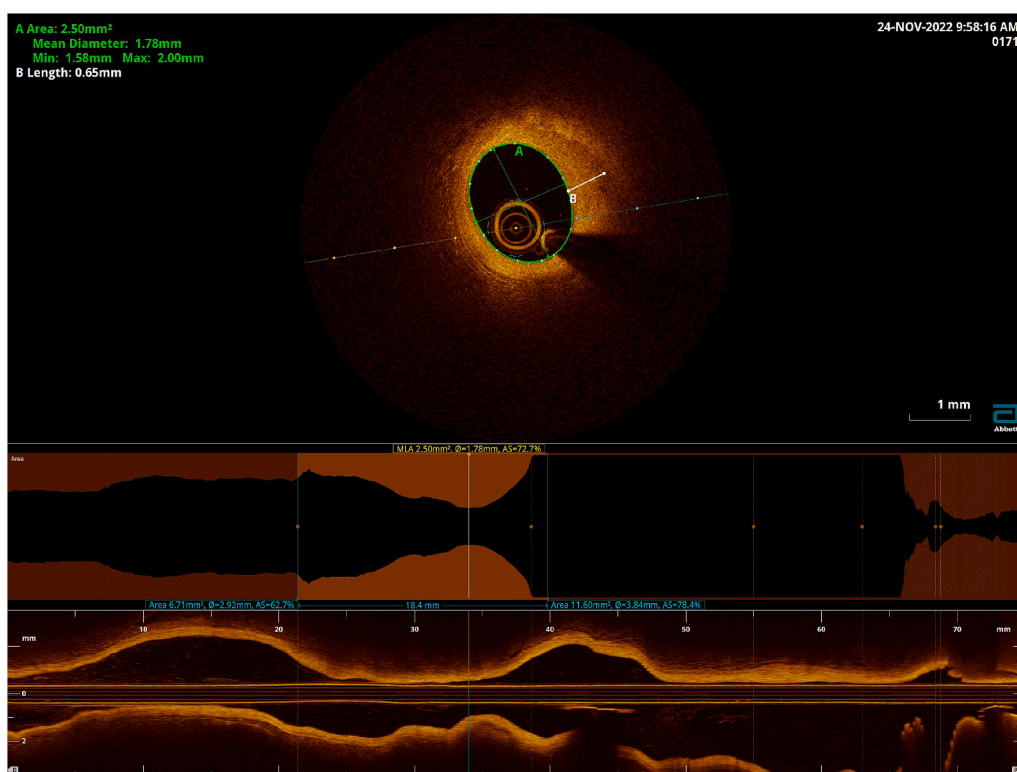


Fig. 3. The OCT showed that the minimum lumen diameter was 1.58 mm, the minimum lumen area 2.50 mm^2 , the fibrous plaque thickness 0.65 mm, and the stenosis rate was 72.7%.

OCT. Severe coronary artery spasm was induced by Ioversol, and the spasm was relieved after intracoronary injection of nitroglycerin, which was diagnosed with type II kounis syndrome.

The pathogenesis of KS is not fully understood [7]. Mast cells are the main cells in the development of KS. When stimulated by allergens, specific IgE is produced, which binds to IgE receptors on the surface of mast cells, thereby releasing histamine, arachidonic acid and other inflammatory mediators, which dilates peripheral blood vessels and cause coronary artery spasm [8]. In heart tissue, mast cells are abundant in coronary plaques [2]. KS needs to be differentiated from coronary air embolism or ascending aortic dissection. There were no bubbles in the angiography and no ascending aortic dissection shadow during the operation in this patient, so related diseases can be basically ruled out. Until now, there is no relevant consensus and guideline for the treatment of KS. The treatment of KS is challenging. Epinephrine and norepinephrine can increase blood pressure but aggravate coronary spasm and

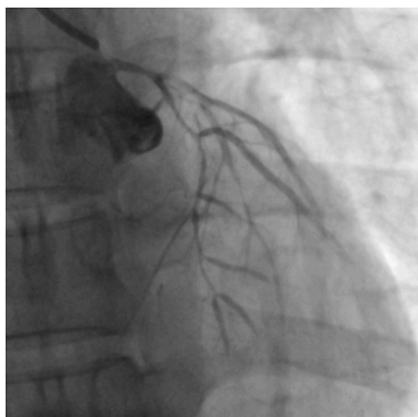


Fig. 4. The coronary angiography showed severe spasm of the left main trunk with stenosis of about 80%, both LAD and LCX had severe spasm throughout the whole process with stenosis of 95–99% at the worst with forward blood flow TIMI grade 2.



Fig. 5. The coronary angiography at foot position showed relief of spasm after intracoronary administration of nitroglycerin and forward flow TIMI grade 3.

myocardial ischemia [9], while nitroglycerin can alleviate coronary spasm but aggravate hypotension. In patients with type I variant, it can be eliminated by treating the allergy alone, such as glucocorticoids and H1 or H2 receptor blockers. For patients with type II variant, an acute myocardial infarction protocol need to be used initially, along with glucocorticoids and antihistamines. For patients with type III variant, an acute myocardial infarction protocol as well as urgent thrombus aspiration of the coronary artery are needed, followed by histologic examination of the aspirate. This patient was type II variant and intracoronary nitroglycerin was given in an emergency, and coronary artery spasm was finally relieved. At the same time, intravenous fluids and vasoactive agents could not maintain blood pressure, so IABP was implanted. Ultimately, the patient's vital signs were stable. Factors affecting the prognosis of KS mainly include the type of it, complications, allergens and so on. In general, type I variants are associated with the best prognosis and type III variants with the worst. Studies have found that the rate of cardiac arrest caused by contrast-induced KS is 23.1% and the mortality rate is 7.7% [6].

Kounis syndrome has both allergic reactions and cardiac symptoms, and the two are overlap. Therefore, it is easy to be missed diagnosed and misdiagnosed in clinical practice. Clinicians should strengthen the understanding of this disease and improve the ability of diagnosis and treatment of it.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data

included in this article.

Author contributions

Baoguo Wang drafted the manuscript as first author. Weihua Zhang and YuFu provided clinical specimens and information. YinWang provided the figures. Shouyan Hao revised the manuscript. All authors read and approved the final manuscript.

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Additional information

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Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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