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CASE REPORT

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Amiodarone triggered Kounis syndrome complicated by refractory cardiac arrest rescued with VA-ECMO

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Key Clinical Message

An interesting case that shows an infrequent cause of cardiorespiratory arrest such as coronary vasospasm due to intravenous amiodarone induced Kounis syndrome. It highlights the usefulness of circulatory support with ECMO in the scenario of CPR.

Abstract

A patient with atrial fibrillation was admitted for an elective electrical cardioversion. He was given an amiodarone bolus that triggered Kounis syndrome with cardiac arrest due to vasospasm requiring emergency coronary angiography with infusion of nitroglycerin. Due to following refractory shock and severe refractory hypoxemia required mechanical circulatory support with ECMO and inhaled nitric oxide with favorable evolution. Allergy to amiodarone was later confirmed.

KEYWORDS

amiodarone, case report, ECMO support, Kounis syndrome, nitric oxide, refractory shock

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common supraventricular arrhythmia. Several studies have shown that sinus rhythm maintenance can improve AF-related symptoms and quality of life.[1] Direct current cardioversion (DCCV) is the preferred choice to restore sinus rhythm in patients with AF and hemodynamic instability. DCCV has been shown to be more effective than pharmacological cardioversion. In stable patients, either pharmacological or electrical cardioversion can be performed. Additionally, pre-treatment with antiarrhythmic drugs can improve the outcomes of electrical cardioversion.[2]

Kounis syndrome is a rare disease that consists of an acute allergic coronary syndrome. It usually presents as an ST-segment elevation acute coronary syndrome.[3] It requires emergency coronary angiography with intracoronary vasodilators infusion and occasionally percutaneous coronary intervention. We present an unusual case of Kounis syndrome triggered by intravenous amiodarone leading to cardiorespiratory arrest and refractory shock due to the vasospasm.

2 | HISTORY OF PRESENTATION

A 60-years-old man with a previous history of persistent AF treated with oral amiodarone was admitted for elective DCCV. He was being treated with amiodarone 200 mg/d (5 days per week) and apixaban 5 mg/12 h. After ensuring

that the patient didn't miss any dose of anticoagulation, a first synchronized 200 J shock under sedation with propofol and midazolam was not effective. It was decided to deliver a second shock with previous administration of a 300 mg bolus of amiodarone. Immediately after amiodarone administration, the patient presented an extensive skin rash associated with pruritus that was shortly followed by cardiac arrest (CA) secondary to pulseless electrical activity. Advanced cardiopulmonary resuscitation (CPR) was started but the patient persisted in CA. A ST-segment elevation was observed on the monitor seconds before the CA so the patient was transferred to the cathlab while performing manual chest compressions. Coronary angiography showed left main coronary artery spasm which completely resolved after 5 boluses of 100 μg of intracoronary nitroglycerin (Figure 1). After 19 min of advanced CPR with administration of 8 mg of adrenaline, 200 mg of hydrocortisone and 5 mg of dexchlorpheniramine recovery of spontaneous circulation was achieved. Echocardiography revealed severe biventricular dysfunction (Video 1). The patient remained in refractory shock despite high doses of vasoactive drugs and the decision was made to provide mechanical circulatory support with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and intra-aortic balloon pump (IABP) implantation.

3 | PAST MEDICAL HISTORY

The patient had a medical history of arterial hypertension, dyslipidemia and sleep apnea-hypoapnea syndrome (SAHS) treated with continuous positive airway pressure machine (CPAP). Persistent AF was diagnosed 5 years ago undergoing electrical cardioversion with premature recurrence. Dronedarone was initially used as an antiarrhythmic drug, but after the recurrence of AF was changed to amiodarone. Echocardiography showed left atrial enlargement with preserved left ventricular function without any valve dysfunction.

Despite the treatment with amiodarone the patient persisted in AF so, a new DCCV was scheduled followed by pulmonary vein isolation.

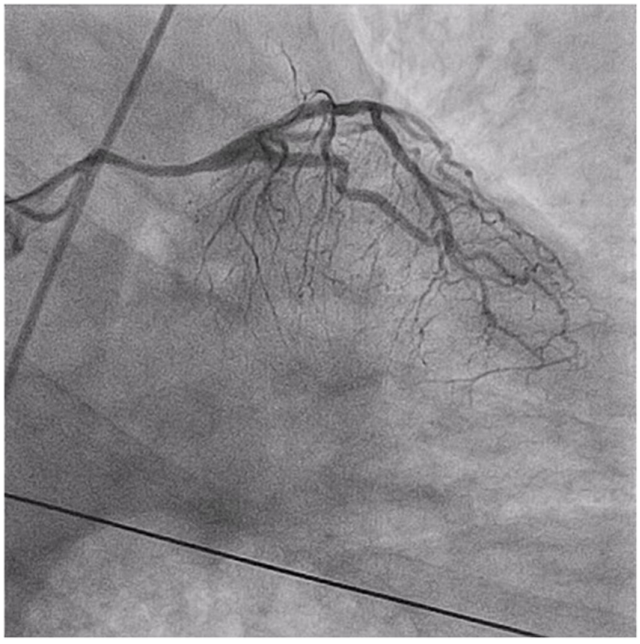

FIGURE 1 Left main coronary spasm. Emergent coronary angiography that shows left main coronary severe spasm.

4 | DIFFERENTIAL DIAGNOSIS

Anaphylactic shock, CA due to acute myocardial infarction, coronary artery embolism, Kounis syndrome or respiratory arrest due to hypoxemia.

5 | INVESTIGATIONS

Non-significant coronary lesions on the coronary angiography and absence of regional wall motion abnormalities rule out the ischemic cardiogenic shock and coronary embolism.

No evidence of hypoxemia on initial blood gases and normal oxygen saturation at the beginning of the case exclude hypoxemic cause.

The sudden presentation after drug administration accompanied by erythema and pruritus led to the diagnosis of anaphylaxis. Coronary angiography showed coronary vasospasm and a tentative diagnosis of Kounis syndrome probably due to amiodarone was made.

6 | MANAGEMENT

The patient was admitted to the intensive cardiac care unit due to refractory shock requiring mechanical circulatory support with VA-ECMO and IABP.

High flow ECMO (3.7–4 L) and aggressive fluid resuscitation were necessary in the first 48 h to keep the patient well perfused. Stress steroids were also employed to counter vasoplegia.

Of note, severe respiratory failure was also observed at admission. Deep sedation, muscular relaxation, high fraction of oxygen in inspired air (FiO_2) and high requirement of positive end-expiratory pressure was needed to achieve normoxemia. There was no response to empiric antibiotic therapy and aggressive negative fluid balance. Suspecting diffuse pulmonary vasoconstriction with ventilation-perfusion mismatch, inhaled nitric oxide

(NO) was started. An excellent response was achieved with a rapid improvement of oxygenation allowing to reduce the FiO_2 requirements. A bronchoscopy was performed, isolating a methicillin-resistant staphylococcus aureus in the cultures with no evidence of complicated pneumonia in the CT scan. After 7 days of target antibiotics the patient remained apyrexial without other signs of infection so treatment was suspended with good evolution.

Subsequently, the patient presented a progressive hemodynamic improvement until VA-ECMO support could be weaned after 5 days. Biventricular function was completely recovered.

Neurologically, the patient evolved without sequelae.

To confirm the diagnosis of allergic reaction, tryptase levels were determined at the beginning and after 24 h. Allergy skin tests were performed resulting positive for amiodarone and confirming the diagnosis (Figure 2).

One year after the event the patient remains asymptomatic (functional class-I of NYHA), with persistent AF and controlled heart rate under treatment with beta-blocker and oral anticoagulation. Finally, due to presence of numerous signs of high arrhythmogenicity substrate in the left atrium (severe atrium dilation, low voltage p waves...) it was decided not to perform the PVI because of low probability of success in restoring durable sinus rhythm.

7 | DISCUSSION

Kounis syndrome was first described in 1991 due to vasospasm from allergic reaction. In our case, the most probable trigger of the Kounis syndrome was the intravenous administration of amiodarone. To diagnose anaphylaxis, in addition to pruritus and skin lesions after the drug administration, determination of serum tryptase during the acute phase with subsequent normalization is useful. Mast cells are the main inflammatory cells in the allergic reaction. Its degranulation produces the release of inflammatory and vasoactive molecules. Tryptase determination is the main marker of mast cell activity with a 73% sensitivity and 98% specificity.[4]

Several drugs have been associated with Kounis syndrome including amiodarone. There are published cases of anaphylactic shock and Kounis syndrome with intravenous amiodarone in patients who already take it orally, especially in cases of allergy to iodine, which is in suspension in some presentations of intravenous amiodarone.[5,6] In addition, it exists one case in the literature about Kounis syndrome related to iodine containing fluids specifically.[7]

Treatment with adrenaline in this pathology is controversial because it could potentially lead to vasospasm recurrence and worsening myocardial ischemia as well as QT interval prolongation. However, in our case it was necessary considering the situation of refractory cardiorespiratory arrest. Vasodilator agents should be contemplated

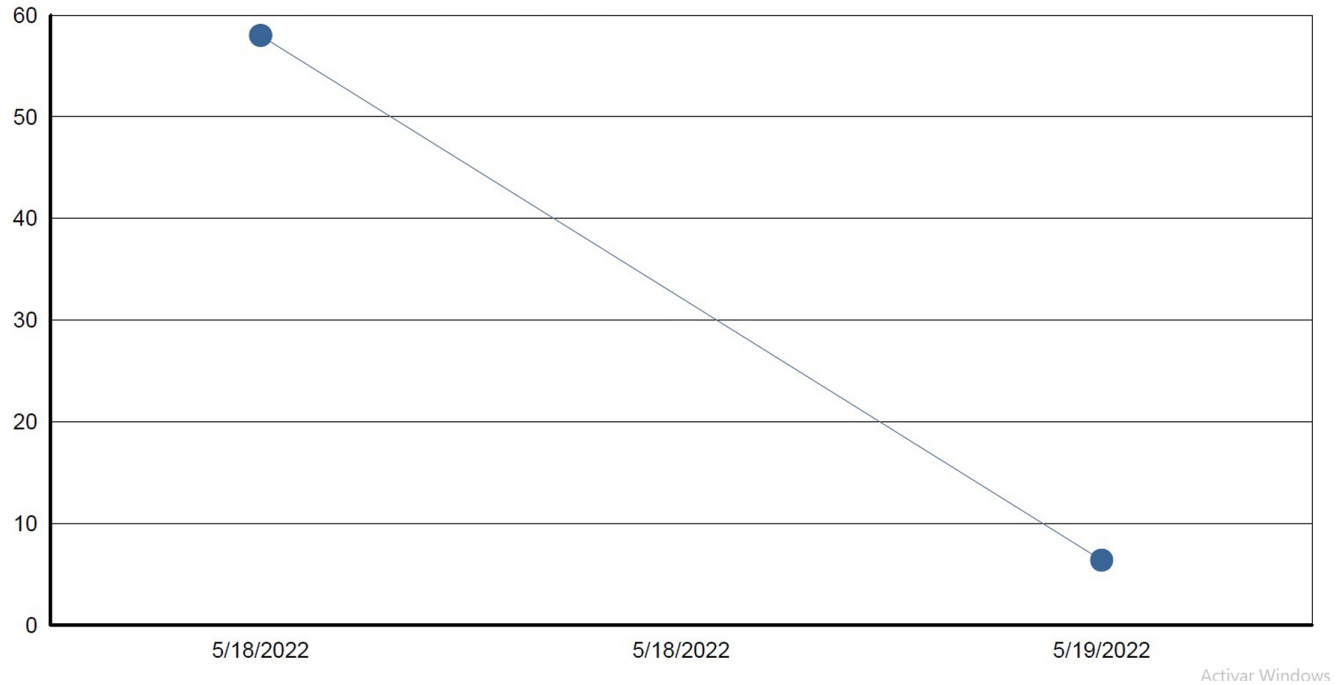

FIGURE 2 Serum-tryptase levels fall. The determination of the serum-tryptase shows elevation in the acute event and its posterior normalization.

as specific treatment for reverting the vasospasm. In our case, intracoronary nitroglycerin was administered.[8]

The use of VA-ECMO is classically used as circulatory support in the cardiogenic shock scenario. Nevertheless, there are other types of shock where it can be useful like the septic or the anaphylactic shock to assure the perfusion until the primary cause is controlled.[9] This case supports the usefulness of ECMO in refractory shock requiring circulatory support and, as far as we know from published evidence, this is the first case of Kounis syndrome triggered by amiodarone which requires support with ECMO.

Another remarkable point to highlight in this case is the usefulness of NO in refractory hypoxemia in a patient with VA-ECMO once the initial treatment has failed (deep sedation, pharmacological relaxation and optimized ventilation). In our case it was effective and prevented further aggressive treatments such as pronation or conversion to veno-arterial–venous extracorporeal membrane oxygenation (VAV-ECMO). NO act as a pulmonary vasodilator, reducing the reflex vasoconstriction that occurs due to hypoxia, improving the pulmonary ventilation/perfusion ratio. And although studies have not shown a reduction in mortality, they have shown a significant improvement of refractory hypoxemia.[10]

8 | CONCLUSIONS

We present a rare form of presentation of Kounis syndrome due to intravenous amiodarone administration. It presents with vasospasm, refractory shock and CA requiring mechanical support with ECMO. It also presents with severe respiratory failure improving with inhaled NO. In this situation mechanical circulatory support with ECMO may be necessary to ensure tissue perfusion. Specifically, in the in-hospital CA, ECMO implantation is an expanding therapy and is showing promising results.

AUTHOR CONTRIBUTIONS

Marc Soriano: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft. **Alessandro Sionis:** Conceptualization; formal analysis; methodology; supervision; writing – review and editing. **Enrique Rodríguez Font:** Conceptualization; methodology. **Ana Bonet:** Conceptualization; methodology. **Lorena Soto:** Conceptualization; methodology. **Manel Tauron:** Conceptualization; methodology. **David Belmar:** Conceptualization; methodology. **Sabiñe Arakama:** Conceptualization; methodology. **Josep Mayol:** Conceptualization; methodology. **Laura Rodríguez:** Conceptualization; data curation; methodology; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

No relationship with industry.

DATA AVAILABILITY STATEMENT

Author elects to not share data.

ETHICS STATEMENT

This report has the approval of the Ethics Committee of our center.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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