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CASE REPORT

BEGINNER

CLINICAL CASE

Acute Coronary Syndrome After Ondansetron Administration in a Pregnant Woman

Kounis Syndrome?

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ABSTRACT

We report on a pregnant woman with acute coronary syndrome probably caused by an allergic reaction to ondansetron. It also discusses the pathophysiology, main allergic triggers, clinical presentation, and management of Kounis syndrome. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:6–8) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 36-year-old woman in the 12th week of pregnancy visited the emergency room presenting with intense nausea. She was treated with 8 mg of intravenous ondansetron. Immediately after drug infusion, she had severe opressive chest pain, headache, and sudden blood pressure elevation. On examination, heart and lung auscultation were normal. She did not present cutaneous or respiratory alterations.

LEARNING OBJECTIVES

- To recognize Kounis syndrome as a possible cause for acute coronary syndrome, especially in patients without cardiovascular risk factors.
- To understand the pathophysiology of Kounis syndrome.
- To act quickly by removing the possible allergic trigger.
- To understand the importance of treating the symptoms of allergy and initiating strategies for acute coronary syndromes simultaneously.

MEDICAL HISTORY

The patient did not have any relevant previous medical history.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included pre-eclampsia, vasospastic angina, and spontaneous coronary dissection.

INVESTIGATIONS

Electrocardiogram (ECG) showed ST-segment elevation in aVR and V_1 and ST-segment depression in the other derivations (**Figure 1**). Serial troponin values at approximately 6-h intervals were 1.18 ng/ml, 1.67 ng/ml, and 0.40 ng/ml (reference value: <0.01 ng/ml).

MANAGEMENT

The patient received dual antiplatelet therapy with 200 mg of aspirin and 300 mg of clopidogrel. She was also treated with sublingual nitrate and 2 mg of

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Informed consent was obtained for this case.

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morphine, and the chest pain ceased. The following ECG showed T-wave inversion in the precordial leads. Echocardiography showed basal segment hypocinesia in the septum. Treatment with 30 mg of diltiazem twice daily was initiated.

FOLLOW-UP

The patient did not have recurrent chest pain and was discharged with dual antiplatelet therapy and diltiazem. A coronary angiography was scheduled for 4 weeks later, when she would be 16 weeks pregnant, to avoid the teratogenic effects of radiation exposure in the early pregnancy. The examination did not show any significant coronary obstructions or vasospasm. The patient did not have any other symptoms and was followed up in the regular clinic until she gave birth to her child.

DISCUSSION

Kounis syndrome (KS) was first described in 1991 by Kounis and Zavras (1). It is defined as an acute coronary syndrome associated with an allergic reaction. There are 3 disease variants. Type I is the most common, and it occurs when there is coronary spasm in patients with normal coronary arteries. Type II is found in patients with prior coronary artery disease who present with atherosclerotic plaque rupture. In type III, stent thrombosis occurs (2). The pathophysiology of KS includes mastocyte and platelet activation with subsequent release of inflammatory mediators, such as histamine, tryptase, platelet activation factor, and cytokines (3). These products promote coronary vasoconstriction and may cause plaque instability in those with previous atherosclerosis.

Taking into consideration it is a rare disease, most information on KS is derived from case reports and case series. Although there has been an increasing number of reports of KS, it is still probably underdiagnosed because clinical suspection depends on physician awareness of its existence. A recent epidemiologic study in the United States showed that the estimated prevalence of KS was 1.1% among patients hospitalized because of allergies, and in-hospital mortality was 7.7% (4). That study was performed using diagnosis codes linked to hospitalizations; therefore, it was not possible to confirm the association between the acute coronary syndrome and the allergic manifestations, define triggers of KS, or differentiate its types.

There are limited data in published reports on the occurrence of KS in women of childbearing age. It is more prevalent in patients ages 40 to 70 years, but cases of KS in children have been reported (5). To our knowledge, this is the first report of a possible case of KS caused by an allergic reaction to ondansetron in a pregnant woman. The patient presented with oppressive chest pain, ST-segment elevation in an ECG performed soon after drug administration, and troponin elevation. Patients with KS can present with acute angina without an increase in cardiac markers or myocardial infarction. Cases of anaphylactic or cardiogenic shock as the primary manifestation of this condition have also been reported (6,7).

ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

KS = Kounis syndrome

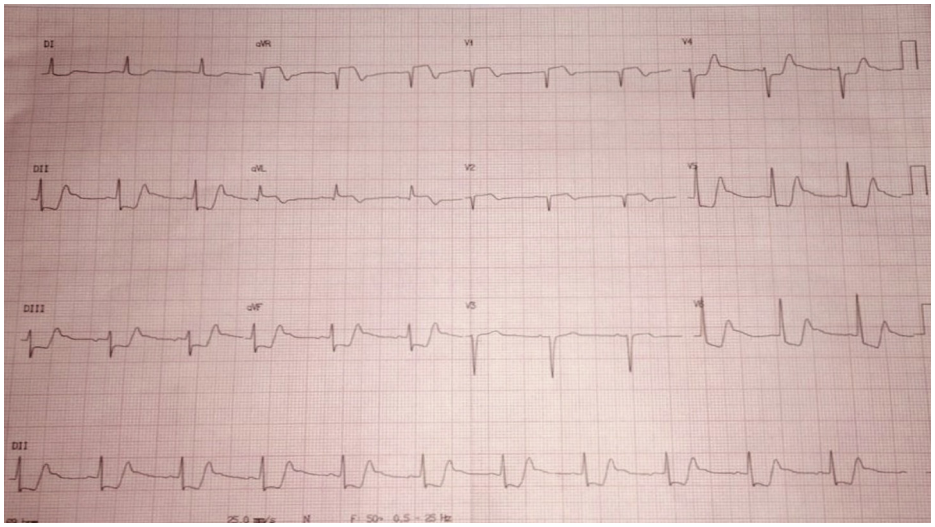
Risk factors for this disease include hypertension, diabetes, dyslipidemia, smoking, and history of allergy. KS should be suspected in patients with acute coronary syndrome without traditional cardiovascular risk factors. The most common triggers of KS are antibiotics, anesthetic drugs, food, and insect bites (8,9).

Ondansetron selectively antagonizes the serotonin receptor 5-HT_3, and it is used as an antiemetic drug, especially for the prevention and treatment of nausea in patients with cancer. Anaphylactic reactions to ondansetron have been previously reported, but they are uncommon (10). A case report described a woman with ovarian cancer who presented with flushing, dyspnea, tongue swelling, and severe hypotension after ondansetron administration for prophylaxis of nausea before chemotherapy. She was treated with intravenous fluids and epinephrine. After this episode, the patient received other antiemetic drugs before chemotherapy without any symptoms of allergy. Cutaneous or respiratory manifestations of allergy may be present in patients with KS, but these are not needed for the diagnosis. In the case reported here, the patient did not present any symptoms of allergy.

In KS, laboratory and imaging results, such as troponin measures, ECG, and echocardiogram, may show acute myocardial ischemia. Vasospasm or coronary stenosis can be found in coronary angiography, and these findings will define the KS type. In the case reported here, a coronary angiography performed 1 month after the index event did not show significant coronary stenosis, which supports the vasospasm hypothesis and the possibility of type I KS. The patient probably did not have pre-existing coronary artery disease because she underwent coronary angiography weeks after the event, and no coronary lesions were observed. An embolic event due to pregnancy could have occurred. However, the symptoms started right after administration of ondansetron, which makes the hypothesis of KS stronger.

The treatment of KS is challenging and should include 2 fronts simultaneously: strategies for acute coronary syndrome based on guideline

FIGURE 1 Electrocardiogram After Symptoms of Chest Pain



Electrocardiogram after clinical symptoms of chest pain showing ST-segment elevation in aVR and V1 and ST-segment depression in the other derivations.

recommendations and therapies focused on the allergic reaction (3). The possible allergic trigger should be immediately removed, when possible. Antihistamines and glucocorticoids may be used in these cases. Intravenous fluids and epinephrine can be prescribed with caution in cases of anaphylactic shock, because there is increased risk for pulmonary congestion and worsening of vasospasm, respectively. Our patient was initially treated with dual antiplatelet therapy, as recommended for acute coronary syndromes in general. In the acute setting, she received nitrate and morphine for chest pain relief. She was discharged with aspirin, clopidogrel, and diltiazem. This calcium-channel blocker was given because there was a strong suspection for vasospasm. She was treated with these medications until coronary angiography was performed, and no coronary stenosis was seen.

CONCLUSIONS

We report a rare case of a pregnant woman with acute coronary syndrome probably related to an allergic reaction to ondansetron. This case illustrates the importance of investigating possible triggers of allergy in patients with acute coronary syndromes, especially in those without cardiovascular risk factors.

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