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Clinical case

Kounis syndrome as an anaphylactic reaction to omeprazole. Case presentation

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SUMMARY

Omeprazole does not usually cause serious adverse reactions in most cases, especially during short-term use. Anaphylactoid reactions can be secondary to medications. We present the case of a 39-year-old male patient who presented with acute coronary syndrome minutes after the administration of intravenous omeprazole. The diagnosis of Kounis syndrome was made considering the association of anaphylactic shock and cardiovascular involvement. We decided to present this case because, despite being a known syndrome, its incidence is very low, hence the difficulties in its diagnosis; its occurrence as an adverse drug reaction is a possibility that should always be considered by the attending physician.

Keywords: Kounis syndrome; Acute coronary syndrome; Anaphylaxis; Omeprazole.

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ABSTRACT

Omeprazole does not usually cause severe adverse reactions in most cases, especially during short-term use. Anaphylactoid reactions may be secondary to medications. We present the case of a 39-year-old male patient who developed an acute coronary syndrome a few minutes after the intravenous administration of omeprazole. The diagnosis of Kounis syndrome was made considering the association between anaphylactic shock and cardiovascular involvement. This case is presented because, despite being a known syndrome, its incidence is very low, which makes diagnosis difficult; its occurrence as an adverse drug reaction should always be considered by the attending physician.

Keywords: Kounis syndrome; Acute coronary syndrome; Anaphylaxis; Omeprazole.

SUMMARY

Omeprazole generally does not cause serious adverse reactions in most cases, especially during short-term use. Anaphylactoid reactions may be secondary to medications. We present the case of a 39-year-old male patient who developed acute coronary syndrome a few minutes after intravenous administration of omeprazole. The diagnosis of Kounis syndrome was made considering the association between anaphylatic shock and cardiovascular compromise. This case is presented because, despite being a known syndrome, its incidence is very low, making diagnosis difficult; If it appears as an adverse reaction to medications, it should always be considered by the attending physician.

Key words: Kounis syndrome; Acute coronary syndrome; Anaphylaxis; Omeprazole.

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Introduction

The association between anaphylactic reaction and cardiovascular disease was suggested when Eugene Clark, in 1938, reported a case of reactive arteritis and carditis in a patient who received large doses of pneumococcal antiserum. (1,2) In 1991, Kounis NG and Zavras GM, in a study entitled: Histamine-induced coronary artery spasm: the concept of allergic angina, defined the concept of allergic angina, which could progress to acute myocardial infarction secondary to an allergic reaction. (3)

Descriptions of the cardiovascular signs and symptoms associated with allergic, anaphylactic, and anaphylactoid reactions began to appear in Australian, English, and German medical literature more than 70 years ago. These reactions were described as morphological cardiac reactions, acute carditis, or lesions with basic features of rheumatic carditis. (2,4)

Omeprazole is the first in a series of active ingredients that act by inhibiting the H+/K+ ATPase pump (proton pump inhibitors). Its introduction revolutionized the treatment of peptic ulcers, gastroesophageal reflux disease (GERD), and gastropathy caused by nonsteroidal anti-inflammatory drugs (NSAIDs), so much so that it is currently the most prescribed active ingredient. It is generally a well-tolerated medication, with mild and usually reversible adverse reactions. The most common are gastrointestinal symptoms. Other reported adverse reactions, listed in the product information, include inhibition of vitamin B12 absorption and urticarial rash. (1,5)

It has been shown thatKounis syndrome (KS) can occur in any race, age group, or geographic location. The number of known causes associated with KS has increased, and it is believed that others remain to be identified.[4,6]

SK is poorly understood, can be fatal, and its true incidence is undetermined. Available information is limited to reviews and a few published case reports, leading to its classification as an uncommon condition, although some researchers believe it is not rare but rather underdiagnosed and underreported.[1,3,5,7]

Despite its specificities, this topic is rarely referred to in the literature and there are no clinical practice guidelines for its proper management. (2,6)The following case is

presented because, despite being a known syndrome, its incidence is very low, which makes diagnosis difficult.

Case presentation

A 39-year-old Black male patient with a history of mixed hemorrhoids, persistent mild bronchial asthma, and previous surgery for intestinal obstruction due to small bowel volvulus presented to the emergency department of the Central Military Hospital in Bissau with severe abdominal pain, nausea but not vomiting, and loose stools. He was questioned and examined by the general surgeon, who found no evidence of an urgent surgical condition and was therefore transferred to the internal medicine clinic.

On physical examination, the patient presented with a soft, non-tender abdomen, epigastrically tender, without rigidity or peritoneal retraction. Examination of the other systems was unremarkable. At that time, a diagnosis of acute gastritis in crisis was made, and hydration and 40 mg of intravenous omeprazole were prescribed. Subsequently, the patient began experiencing a sensation of emptiness, hypotension (60/30 mmHg), severe retrosternal pain, altered mental status, dizziness, nausea, and intense itching in the back.

Positive findings on physical examination: The physical examination did not identify any clinical changes compared to the initial evaluation, except for an increased heart rate of 128 beats per minute and the appearance of wheezing on auscultation. Urgent further tests are indicated.

Additional urgent examinations:

Hemoglobin: 134 g/L

Leukogram: 9.1 x109/L

Eosinophilia: 939 cells/mcL

C-reactive protein: 2.28 mg/dL

Ionogram and blood gas analysis: no alterations.

Blood glucose: 5.9 mmol/L.

Electrocardiogram: sinus rhythm, ST segment elevation > 3.5mV in leads II, III, aVF, V3, V4 and V5. ST segment elevation > 2.5 mV in V1. ST segment depression in leads I and aVL.

Based on these findings, an acute coronary syndrome (ACS) was diagnosed and treatment was started with clopidogrel, fraxiheparin and hydration with 0.9% sodium chloride.

After one hour of supportive treatment, hypotension was observed with no hemodynamic response to volume resuscitation. Dobutamine support was initiated at a dose of 4 µg/kg/min, resulting in an increase in blood pressure to acceptable levels. The patient was transferred to the intensive care unit, and an increase in myocardial injury markers was observed 16 hours after the onset of symptoms, with normalization within the first 48 hours.

In the intensive care unit, the patient experienced anaphylactoid shock and was started on hydrocortisone-type corticosteroid therapy. Blood, stool, and urine cultures were negative. Omeprazole treatment was immediately discontinued due to its association with the onset of the clinical presentation.

At the end of 96 hours, the patient was found to be hemodynamically stable with electrocardiographic parameters within normal limits, and was therefore discharged to the open ward of internal medicine with a diagnosis of SK type I, anaphylaxis to omeprazole and acute gastritis.

Discussion

SK is a disease with unknown epidemiology. In the case presented, the diagnosis was reached based on clinical suspicion, as acute allergic symptoms were observed coinciding with coronary events.[2,8]

The etiology of this syndrome is postulated to involve mast cell mediators (histamine, serotonin, tryptase, chymase and leukotrienes) capable of generating coronary

vasospasm or microvascular angina in SK type I and eroding a pre-existing atheromatous plaque in SK type II. (1)

Brancaccio, et al, (5) state that any drug is a potential causative agent of SK. In practice, the drugs most frequently described as being involved in this syndrome are beta-lactams, NSAIDs, general anesthetics, and iodinated contrast media.

The incidence of hypersensitivity reactions to proton pump inhibitors (PPIs) is increasing due to the growing use of these drugs because of their effectiveness and their frequent use without a prescription. (4)

Authors such as Alves Pinto, et al, (6) conclude that the mechanism of omeprazole anaphylaxis is IgE-mediated (still to be clarified), with a class effect and the possibility of cross-reactivity with other PPIs and even with ranitidine; they describe eight cases of delayed hypersensitivity to all PPIs. The known frequency of anaphylactic reaction to PPIs is between 0.2% and 0.7%.

According to a literature review, nine cases of anaphylactic shock to PPIs were described, four of which involved omeprazole. However, after further study with skin tests, the causative agent was found to be, for the most part, the compound present in the capsule. Regarding KS associated with anaphylactic reaction to omeprazole, there is one reported case in 2010 and another in 2020. (5,9)

Bohórquez Riveroet al. (2) conclude that the pathophysiological mechanisms of KS are diverse, complex, intricate, and under investigation. Hypersensitivity, anaphylaxis, the presence of mast cells in cardiac tissue, and their degranulation with the release of inflammatory mediators are primary elements. Mast cell activation and degranulation can occur through various mechanisms, including the immunoglobulin E (IgE) pathway, histamine-releasing factors derived from macrophages and T lymphocytes, or anaphylatoxins via the complement activation system.

Castrillón-Martínez C(4) has proposed that there is a threshold level of mast cell activation and mediator release above which coronary spasm or atherosclerotic plaque rupture develops. This threshold would be associated with the location of the antigen-

antibody reaction, the area of exposure, the release of mediators, and the severity of the reaction.

The consulted authors agree that there is still no pathognomonic test for Kaposi's sarcoma (KS) and that a high index of suspicion should be maintained in the context of a patient with anaphylaxis and acute coronary syndrome (ACS). This suspicion should be based on a thorough clinical evaluation and specific complementary tests. Elevated serum tryptase and histamine levels, elevated biomarkers of myocardial damage (troponin I or T and CK-MB enzyme), and electrocardiographic abnormalities characteristic of ACS should be observed. (1,3,4,8)

Currently, treatment is controversial due to a lack of clinical practice guidelines. Therapeutic management is based on individual experiences reported in the literature, and expert recommendations for ACS and anaphylaxis are often extrapolated. (5,6)

Authors such asCastrillón-Martínez C(4), Reyes Echeverría, et al (7) and Alves Pinto, et al, (6) report cases similar to the one described in the present study.

The limitation of the study presented in this research is given in lthe lack of allergy tests and coronary angiography prevented the case from being properly concluded.

Conclusions

The authors consider it important to draw attention toheKounis syndromeAlthough infrequent, this condition can occur, and if the attending physician is unfamiliar with it, they will be unable to make the diagnosis. This case of KS secondary to an anaphylactic reaction to intravenous omeprazole is the first described in Guinea-Bissau.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authorship contribution

Conceptualization, supervision and validation:Yuneysis Veliz Guevara.

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Research, methodology and writing:Admir Gonçalves Monteiro, Pedro Rafael Casado Méndez.

Writing – review and editing:Pedro Rafael Casado Méndez, Yuneysis Veliz Guevara.