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CASE REPORT

Type I Kounis syndrome variant: A case report and literature review

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ABSTRACT

Kounis syndrome defined as the occurrence of acute coronary syndrome in the setting of allergic reaction due to mast cells activation and inflammatory mediators release that induces coronary vasospasm, plaque erosion, or even stent thrombosis. A 25-year-old postpartum female with asthma and recurrent episodes of chest pain was admitted with ST-segment elevation myocardial infarction in the setting of coronary artery spasms. The patient was started on calcium channel blockers and nitrite-based medication with no improvement. She was noted to have eosinophilia and initiation of corticosteroid-based regimen lead to resolution of chest pain episodes and normalization of eosinophilia. Kounis syndrome should be considered in young patients with chest pain. Coronary vasodilators are considered as the first-line of treatment. The use of corticosteroids has been described in the literature in severe or refractory cases.

Key words: Allergic coronary artery syndrome, coronary artery vasospasm, Kounis syndrome

INTRODUCTION

Kounis syndrome is defined as the concurrence of acute coronary syndromes (ACSs) such as coronary spasm, acute myocardial infarction, and stent thrombosis, with conditions associated with mast-cell and platelet activation involving interrelated and interacting inflammatory cells in the setting of allergic or hypersensitivity and anaphylactic or anaphylactoid insults.[1]

Although many questions about the exact pathophysiologic mechanism of Kounis syndrome remain unanswered, the increasing number of cases published shows that this condition should be considered in the differential diagnosis of ischemic heart disease.

CASE REPORT

A 25-year-old female patient with a history of asthma, allergic rhinitis, and migraine headaches presented to the emergency department with recurrent episodes of chest pain. She had no cardiovascular risk factors. The patient had an uncomplicated vaginal delivery 6 months prior. She began complaining of intermittent substernal chest pain, described as a pressure sensation, lasting a few seconds to an hour, with radiation to the back. Symptoms were associated with diaphoresis and dyspnea but had no apparent triggers such as exertion, emotional stress, food consumption, or environmental exposure.

On the day of admission, the patient was first seen at an outside facility with similar complaints. A 12 lead electrocardiogram was performed showing 2 mm ST-elevation in leads V3 and V4 with reciprocal inferior lead changes [Figure 1]. A diagnostic left heart cardiac catheterization (LHC) revealed significant mid left anterior descending (LAD) and right coronary artery (RCA) stenosis consistent with coronary vasospasm that resolved with administration of intracoronary nitroglycerin and nicardipine [Figure 2a-d]. However, the patient's chest pain did not resolve and was transferred to our facility for further evaluation.

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A repeat LHC showed mild to moderate residual stenosis involving the mid-RCA and mild stenosis involving the proximal LAD. No coronary intervention was required. During her hospitalization, the patient's troponin T, creatine kinase and creatine kinase-MB peaked at 6.2 ng/ml, 2897 U/L and 285.4 ng/ml, respectively. Her urine drugs screen was negative. Transthoracic echocardiogram revealed a depressed left ventricular ejection fraction (LVEF) of 35% with severe hypokinesis of the anterior and anterolateral walls consistent with an infarct of the LAD distribution. Cardiac magnetic resonance imaging revealed a LVEF of 29% and late gadolinium enhancement showing transmural infarction in the distal LAD territory and evidence of microvascular obstruction [Figure 3a and b].

On admission, the patient was noted to have eosinophilia of 10% (1.54 absolute eosinophils count), which peaked at 25% (2.52 absolute eosinophils count) on day 6 with leukocytosis of 15.7 on admission only. Laboratory workup vasculitis including cytoplasmic-anti-neutrophil cytoplasmic antibodie (C-ANCA), perinuclear-ANCA (P-ANCA), and atypical P-ANCA were all negative. IgE and tryptase levels were within the reference range. The patient suffered recurrent daily episodes of chest pain with ST-segment elevation on the cardiac monitor. These episodes were resolved with sublingual nitroglycerin in 5–10 min interval [Figure 4a and b].

Due to the extensive LAD infarction in the setting of severe coronary vasospasms, and the significant eosinophilia; Type 1 Kounis syndrome was suspected. She was started on prednisone 40 mg daily with a resolution of the eosinophilia and chest pain within 2 days. The patient was started on amlodipine, isosorbide mononitrate, loratidine, ranitidine, and montelukast before discharge. She was discharged on a prednisone taper (started with 30 mg with 10 mg dose reduction every day then 5 mg maintenance dose). On 4 weeks follow-up, the patient denied any symptoms recurrence.

DISCUSSION

Kounis syndrome or "allergic myocardial infraction" is defined as the concurrence of ACSs (coronary spasm, acute myocardial infarction, and stent thrombosis) in the setting of mast-cell and platelet activation from allergic or anaphylactic insults.[1]

Three variants have been described.[2] Type I, which our patient most likely had, includes normal coronary arteries without risk factors for CAD, and with the acute release of inflammatory mediators that may induce coronary artery

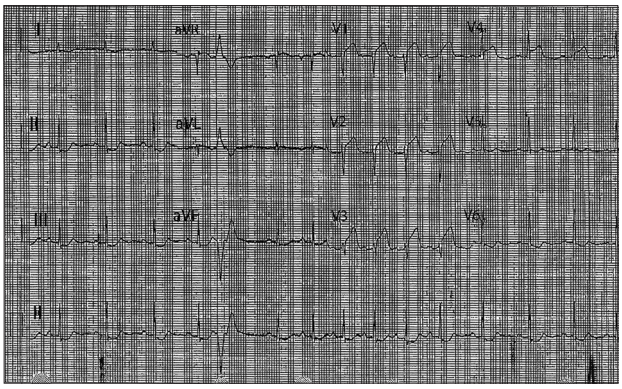

Figure 1: 12 lead electrocardiogram showing ST-segment elevation at V3–V4 with reciprocal changes at lead II and III

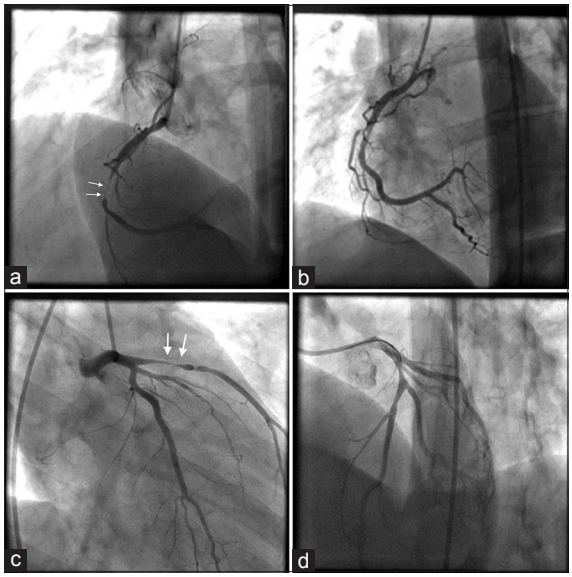

Figure 2: Coronary angiography at the time of her presentation at the outline hospital. (a) Severe stenosis at mid right coronary artery. (b) Repeat angiography after nitroglycerin infusion with near complete resolution of the right coronary artery stenosis. (c) Moderate-severe stenosis at proximal left anterior descending artery. (d) Repeat angiography after nitroglycerin infusion with near complete resolution of the left anterior descending coronary stenosis

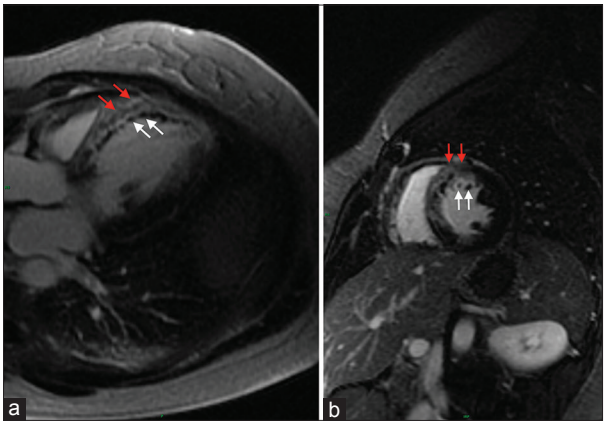

Figure 3: Cardiac magnetic resonance imaging, (a) Mid ventricular short axis slice demonstrating transmural infarct (red arrows) of the anterior septum with evidence of microvascular obstruction (white arrows) on delayed gadolinium. (b) Two-chambers view showing transmural infarction (red arrows) of the anterior septum with evidence of microvascular obstruction (white arrows) delayed gadolinium

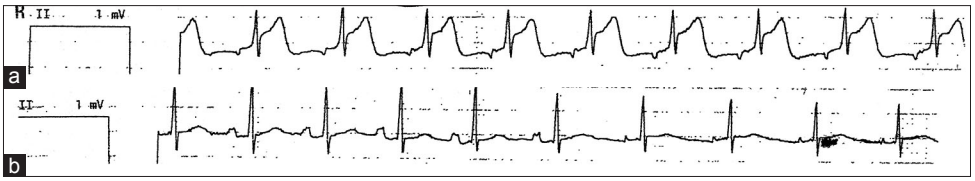

Figure 4: Cardiac monitor rhythm strips. (a) ST-segment elevation associated with chest pain when the patient woke up in the morning. (b) Resolution of ST-segment elevation and chest pain after two sublingual nitroglycerin 0.4 mg tablets

spasm with or without cardiac enzymes elevation and subsequent myocardial infarction. Type II includes culprit but quiescent preexisting atheromatous disease in which the acute release of inflammatory mediators may induce coronary artery spasm with or without associated plaque erosion or rupture manifesting as acute myocardial infarction. Type III includes coronary artery stent thrombosis in which aspirated thrombus specimens stained with hematoxylin and eosin and Giemsa stain demonstrate the presence of eosinophils and mast cells, respectively.

Inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet-activating factor, eosinophils and a variety of cytokines and chemokines have been implicated in its pathophysiology.[3] Eosinophils synthesize leukotriene C4, a potent stimulant of vasoactivity smooth muscle contraction. Eosinophils also activates mast cells and basophils to produce vasoactive substances.[4] Patients with eosinophilia and coronary vasospasm were found to have a high risk of recurrent coronary events despite treatment.[4]

Treatment is aimed at coronary artery vasodilators and allergic reaction amelioration. Calcium channel blockers and nitrates are considered the first-line in the management.[5]

Histamine induces tissue factor expression, through H1 receptors, which mediates thrombus formation in inflammation and vasospasm and hence, H1 receptor blockers may be useful in the management of Kounis syndrome, variant angina and ACS.[5-7] H2 receptors blockers use have been suggested in Kounis syndrome.[5] The use of mast cells stabilizers such as sodium cromoglycate and ketotifen has been suggested; although, their efficacy is not clear.[5]

The use of corticosteroids reported to be effective in cases with refractory vasospastic angina (VSA).[8] Corticosteroids use found to be effective in treating anginal symptoms and normalizing the eosinophil count too.[9] Variable corticosteroids doses and regimens have been used. However the optimal regimen is yet to be determined. In some cases, patients' symptoms relapsed after dropping the dose below a certain point, while others tolerated being tapered off completely with no reported symptomatic recurrence.[8]

CONCLUSION

Kounis syndrome needs to be considered in patients presenting with chest pain, especially at young age. Coronary vessels vasodilators are considered to be the first line of treatment. The use of corticosteroids has been described in the literature, especially in severe or refractory cases with symptomatic relief, but optimal regimen yet to be determined. Further studies are necessary to determine the long-term efficacy of each treatment option and thereby establishing the definitive treatment strategy for refractory VSA.

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Conflicts of interest

There are no conflicts of interest.

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