Peer Review File

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Reviewer A

This is an interesting case report of allergic acute coronary syndrome.

We thank the Reviewer for the constructive comments and suggestions. This is our point-to-point reply.

Comments:

1) Consider replacing "Allergic angina" in the title with "Allergic myocardial infarction" or "Allergic acute coronary syndrome" as the patient presented had non ST elevation myocardial infarction and not angina.

   We acknowledge these criticisms rightly made. We have modified the title accordingly.

2) Page 2, line 82: What is meant by "cornage"?

   We thank the reviewer for this comment. We changed the word “cornage” to “wheezing” (page 4 line 75).

3) Did the patient smoke cigarettes? This may increase the likelihood of Kounis syndrome

   We greatly appreciate the constructive comment, we have specified the fact the patient never smoked on page 4, line 80 *“52-year-old never-smoker woman”*.

4) Page 3, line 96: replace ST "tract" with ST "segment".

   We welcome the reviewer’s advice; we have made the substitution accordingly (page 4 line 87-88).

5) Page 3, line 102: replace FEVS with LV ejection fraction (LVEF).

   We completely agree with this observation; we have replaced FEVS with LVEF, as suggested (page 4 line 93).

6) What was the time interval between ECG and coronary angiography? It is possible that transient ST elevation from coronary artery spasm was not documented on ECGs.

   We thank the reviewer for his comment. Transient ST elevation from coronary artery spasm was not documented on ECG or during coronary angiogram. The first ECG documented a diffuse depression of the ST segment and prolonged QT interval. It was performed at 1.57 pm, while the coronary angiogram at 6.00 pm. This information was added in the manuscript, page 4 lines 88-89.

7) This was a type 2 myocardial infarct, or myocardial infarct without obstructive coronary artery disease. The presumed mechanism is likely coronary artery spasm secondary to allergic drug reaction (IgE mediated mast cell degranulation). Although typically epicardial coronary artery spasm results in ST segment elevation, this may be transient and result in subsequent ST depression/T wave inversion on ECG. The coronary angiogram did not show any obstructive CAD or evidence of thrombus on ulcerated plaque to support type 2 Kounis syndrome although this may have been missed without optical coherence tomography or intracoronary ultrasound.

   We thank the reviewer for the comment. We have now modified the manuscript stating Type I Kounis Syndrome throughout.

8) I would recommend stating in the Discussion: The patient described had an anterolateral NSTEMI in the setting of an allergic response--unclear whether this was type 1 or 2 Kounis syndrome.

We thank the reviewer for this advise. The patient had an anterolateral NSTEMI in the setting of an allergic response, with no evidence of obstructive CAD at the coronary angiogram. As the reviewer says, this was a type II myocardial infarction, and the mechanism is the coronary artery spasm secondary to allergic drug reaction. This is consistent with a type I Kounis syndrome. These details were added in the manuscript on pages 5 and 6 lines 124-129.

9) Page 3, line 132: Replace "paradigmatic" which means typical example with "unusual".

We have rephrased the paragraph as mentioned in reply n.8

10) Could you add information on the patient's outcome? Was she continued on ASA? Was a calcium channel blocker added? I assume that oxaliplatin was not administered again.

The patient was discharged with indication to continue dual antiplatelet therapy with ASA 100 mg and clopidogrel 75 mg for one month, and then single antiplatelet therapy with ASA. Treatment with calcium blockers has not been prescribed. Oxaliplatin was not administered again. These details were added in the manuscript as requested (page 5 lines 109-112).

Reviewer B

This is a unique and interesting case report in Kounis syndrome after administration of oxaliplatin. The authors concluded that a final diagnosis of Kounis syndrome type II variant induced by oxaliplatinum has been made, based on the clinical history together with the exclusion of any other possible cause of acute coronary syndrome.

However, there are some concerns with this case repot.

We thank the Reviewer for the constructive comments and suggestions. This is our point-to-point reply.

1) I don’t think the diagnosis of Kounis syndrome is correctly enough because the author did not rule out possibility of drug induced eosinophilic myocarditis. The authors have to rule out eosinophilic myocarditis.

We thank the reviewer for his comment. However, the absence of eosinophilia on peripheral blood and the positive B-cell proliferation assay in response to oxaliplation rouled out a possible diagnosis of eosinophilic myocarditis. (Page 5 lines 107-109).

2) The authors described Kounis syndrome type II (coronary plaque rupture) in the manuscript. It should be described type I if coronary spasm might be thought.

We thank the reviewer for the comments. We have modified the manuscript accordingly.