Author's response to reviews

Title: TNK for ST-elevation myocardial infarction in a patient treated with Drotrecogin Alfa Activated (DrotAA) for severe sepsis: A Case Report

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Author's response to reviews: see over
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Dear JMC Editorial:

Thank you very much for your interest and for reviewing our submission. We appreciate the reviewers’ comments as they improve and strengthen our paper.

Please find below listed our rebuttal to the reviewer’s comment on a point per point basis. All changes are marked in red font on the manuscript for ease of tracking:

Reviewer 1:
General Comments:
1. We clarified the timeline of events to strengthen septic shock diagnosis: Day 0: initial ED visit with pneumonia on CXR. Day 2, 0 hour: respiratory distress with fever, no hemodynamic changes, no ischemic ECG changes and troponin elevation, but at level that may have been consistent with sepsis-induced cardiac dysfunction. 4th hour: hemodynamic instability, continued fever, no ECG changes, met criteria for SIRS with multi-organ failure.
2. The manuscript stated the patient had 4 hours of heparin. Other than ASA, no other “antiagregant therapy” was used.

Abstract
1. Introduction: The effect of DrotAA on mortality is further qualified in the introduction. Statement modified “DrotAA, an activated protein C, promotes fibrinolysis in patients with severe sepsis.”
2. Conclusion modified to: “In patients with severe sepsis or septic shock complicated by myocardial infarction, it is difficult to elicit if the myocardial infarction is an isolated event or caused by the sepsis process.”

Case presentation:
1. Unnecessary acronyms deleted
2. Accupril changed to quinapril, lipitor to atorvastatin, levophed to norepinephrine.
3. APACHE II score was 26
4. Regarding septic shock issue, see above for timeline. Also, we have included other labs except CRP which was not performed. Echocardiogram was only done post-TNK treatment.
5. The pneumococcus was sensitive to azithromycin

Discussion:
1. Differential diagnosis for ST-elevation and elevated troponins added, including a discussion on Takotsubo.
2. MI treatment used on this patient was described (ASA + TNK + heparin; primary PCI was unavailable at our centre during the time of presentation (weekend), GPIIIa/b is not used routinely in our centre for patients not undergoing PCI, plavix was not considered b/c increased risk of bleeding with
patient on APC). Evidence for standard treatment of STEMI is beyond the scope of this paper.

3. We can only speculate on the cause of a possible MI in this patient – he had mild non-occlusive coronary artery disease on cardiac catheterization and a pre-existing thrombus is possible. Also, there is no good evidence to suggest that APC can prevent or treat CAD (see text).

4. Discussion re: vasopressin increasing cardiac arrests briefly touched upon.

Reviewer 2

1. “Was this a real STEMI as assessed by the authors or a septic myocardial infarction?” This is the thrust of the paper in which we do not know exactly. Other differentials, such as stress cardiomyopathy were also discussed in the revised paper. As we did not have access to primary PCI, we choose a path in which to treat it as a true STEMI secondary to coronary thrombotic event. However, the angiogram post-TNK did not show definitive evidence of thrombosis. Lastly this patient still developed MI while on activated protein C, which would presumably decrease the likelihood of thrombosis (although there are no good human trials to support this).

2. We feel this should be reported because of the difficulties in differentiating sepsis-induced/ stress-induced cardiac dysfunction from thrombotic disease in intensive care patients.

Sincerely your,

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Authenticated Electronically