Author's response to reviews

Title: Heat Stroke Presenting with Encephalopathy and MRI Findings of Diffuse Cerebral Injury and Hemorrhage

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Author's response to reviews: see over
Dear Executive Editor,

Thank you for your kind response and reviews of our manuscript. We were pleased to hear that our manuscript was rated as potentially acceptable for publication in *BMC Neurology*, subject to adequate revision and response to the comments raised by the reviewers. We have revised the manuscript based on the comments made by the reviewers for your consideration.

As you note, in general the reviewers found our submission interesting, but we have been asked for major revisions. Below you will find responses to the comments by the reviewers.

In regard to Reviewer Misra:

1. The patient’s highest temperature was not 100 degrees. Unfortunately, we don’t have the temperature from the outside hospital where patient first presented. However, we do know that during those days patient was cattle ranching the temperatures outside were well above 100 degrees Fahrenheit.

2. The patient was not tested specifically for Hashimoto’s thyroiditis. However, thyroid studies were normal as reflected in manuscript. In addition, Hashimoto’s thyroiditis does not present with the imaging findings discussed in our manuscript.

3. The patient was evaluated for infection via blood cultures, urine culture, chest xray, and csf analysis. All of which were negative. This is discussed in brief in the manuscript.

4. We have deleted table 1 per reviewer’s request.
5. The issue of ESR being elevated is discussed in manuscript in detail. We propose that heat stroke results in an exaggerated systemic inflammatory response that leads to surrogate markers such as ESR and CRP being elevated.

6. B12, folate, and homocysteine were normal. These details have been added to manuscript.

7. We respectfully disagree with reviewer regarding this manuscript being of interest to radiology journal only. The diagnosis of heat stroke is a clinical diagnosis not radiographic.

8. We respectfully disagree with reviewer on this point. Our manuscript details the process including labs, imaging, and history/physical to sufficiently rule out other diagnoses.

9. This patient had an MRA brain, CTA head, and lumbar puncture which all were without evidence suggestive of CNS vasculitis.

In regard to Reviewer Yamashita:

1. The patient’s highest temperature was not 100 degrees. Unfortunately, we don’t have the temperature from the outside hospital where patient first presented. However, we do know that during those days patient was cattle ranching the temperatures outside were above 100 degrees Fahrenheit.

2. We respectfully disagree with this point. Our patient had other laboratories suggestive of multiorgan dysfunction including an elevated lactate, elevated creatinine, and elevated tranaminases.

3. Patient’s CK was 31 normal. In addition, this patient did not have the classical symptoms of muscle rigidity and/or autonomic instability to suggest neuroleptic malignant syndrome. A comment regarding normal CK was added to our manuscript. Furthermore, CSF analysis was done on the patient, which did not reveal any evidence of CNS infectious process. This patient did not meet criteria for hypercoaguable evaluation. He had no evidence of prior thrombophilia. He had no familial evidence of thrombophilia. And per history and exam and workup, a definitive diagnosis was made.

4. We disagree that this patient has a hypercoagulable state due to hemoconcentration, dehydration, and hyperhomocysteinemia. In fact, this patient’s homocysteine level was normal. Our patient did not have atrial fibrillation while on telemetry. His transthoracic echocardiogram was normal.
including normal EF, normal atria size, and no evidence of hypokinesis. Given these findings, we did not feel this patient warranted a TEE. We agree with the reviewer that the intraventricular hemorrhage could have been a secondary hemorrhage related to ischemic event.

5. Unfortunately, the patient did not have a repeat MRI brain. We did not think this was justifiable clinically. We believe the reviewer is incorrectly assuming that the lesions in heat stroke should be perfectly symmetrical. We extensively discuss the MRI findings in our patient and compare it to previous reports. In fact, similar to previous case reports, our patient showed hyperintense lesions in the cerebellum, frontal and parietal lobes as well as medial thalami.

Again, we appreciate all the comments raised by the reviewers and believe the changes enhance our manuscript. We would like to thank you for allowing us to resubmit a revised copy of the manuscript to the *BMC Neurology* for consideration of publication.

Sincerely Yours,

Dr. Waldo Guerrero