Author’s response to reviews

Title: Hypoglycemic Encephalopathy Mimicking Acute Ischemic Stroke in Clinical Presentation and Magnetic Resonance Imaging: A Case Report

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Author’s response to reviews:

Dear Dr. Krüger

Thank you for allowing us to revise our paper. The constructive advice of the peer reviewers has substantially improved our paper. The following statement is the point-to-point response to the comments.

Brian Buck (Reviewer 1)
Q1: In order to interpret the DWI sequences the ADC maps should be provided. It would be important if the suggestion is that there is cytotoxic edema and restricted diffusion to show that these areas of increased signal on DWI are associated with low ADC. Ideally given the neuroimaging focus of the journal a FLAIR sequence should be included. The b-value of the DWI image should be included in the figure legend.
A1: Thank you for your kind remind. The b-value of the DWI was b=1000. We’ve added the corresponding ADC map and T2-Flair images at the same level of the original DWI in our revised manuscript (page 5,6,10, case presentation and figure legend sections). The high signal on DWI, low signal on ADC map, and isointensity on T2-Flair images is suggestive of cytotoxic edema.

Q2: The follow up MRI scan is performed at 1 month. In patients with ischemic stroke DWI imaging changes would usually disappear by this time point. (American Journal of Neuroradiology April 2001, 22 (4) 637-644). Without an earlier MRI scan is it difficult to claim that the evolution of DWI changes is different between hypoglycemia and stroke. This should be discussed as a limitation.
A2: Thank you for your comment. We totally agreed that the DWI abnormality in ischemic stroke would also disappears after 1 months of disease onset. Therefore, it is difficult to claim that the evolution of DWI abnormality is different between hypoglycemia and ischemia with no earlier MR study. We’ve already added this concept in our limitation (page 7,8, discussion and conclusions.
Q3: I am concerned this comment "This "excitotoxic edema" protects axons from intracellular edema and irreversible damage [2, 8, 9], and explains the reversible DWI findings of hypoglycemic encephalopathy" is speculative, not supported by the references, and possibly incorrect. To my knowledge there is no evidence directly linking the reversibility of DWI changes in hypoglycemia to a protective effect of excitotoxic edema. This statement should be presented as a hypothesis rather than fact.
A3: Thank you for your comment. It is true that the link between “the excitotoxic edema phenomenon“ and “the reversible DWI findings of hypoglycemic encephalopathy” is still unclear and should be a hypothesis only. Further prospective studies with larger sample should be performed to validate the hypothesis. Therefore, we’ve revised the description as following, “In this phenomenon of excitotoxic edema, axons could be protected from intracellular edema and irreversible damage [2, 8, 9], which may explain the reversible clinical symptoms and imaging abnormality after controlling for blood glucose.” (page 7, discussion and conclusions section).

Q4: Time from symptom onset to initial MRI should be reported if available
A4: The initial MRI was performed 24 hours after the initial event. We’ve added this information in our manuscript (page 5, case presentation section).

Marie Luby (Reviewer 2)
There was no comment from Marie Luby. Thank you very much.

Salvador Pedraza (Reviewer 3)
Q1: The authors can explain that the ADC was decreased.
A1: We’ve added the corresponding ADC map and T2-Flair images at the same level of the original DWI in our revised manuscript (page 5,6,10, case presentation and figure legend sections).

Q2: The authors can add that there are two patters of lesion distribution (reference 3). The lesion locates on white mater tract has better outcome that lesions affecting cortical gray matter. The authors can add the reversibility of brain lesions is also a predictor of good clinical outcome
A2: Thank you for your recommendations. Several prognostic factors correlated to the patients’ outcome have been added to the manuscript, including severity and duration of the hypoglycemia, the distribution of water diffusion restriction seen on DWI, and recovery or not at following up MR images. We also emphasize the good prognostic factors in our manuscript (page 7, discussion and conclusions section).

Q3: The authors can declare as limitation, the presentation of a unique case. Further prospective studies with larger sample can validate the predictive value of DWI on hypoglycemic encephalopathy
A3: Thank you for your reminder. We’ve revised our manuscript and added this limitation (page 8, discussion and conclusions section).

Q4: The authors cannot make statement about favorable outcome of hypoglycemic encephalopathy based on water diffusion restriction involving only the motor tract on DWI
A4: Thank you for your comment. We’ve revised our descriptions and added some discussions about the correlation between lesion distribution and clinical outcome in our manuscript (page 7, discussion and conclusions section).
Q5: The 9 references are correct, but the authors can consider adding this reference

A5: Thank you for your recommendation. We’ve reviewed this article and revised our manuscript as well as the references according to your recommendation (page 11, reference section).

Q6: The authors can add an image to figure 1 showing the ADC decrease
A6: We’ve added both ADC map and T2-Flair images in figure 1 and figure 2,

We have revised our manuscript according to all your concerns, and the revised sentences were all marked in red color.

Sincerely,

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