

## Response to the Reviewer's Comments

### Reviewer #1

We appreciate your comments. Your decision gave us great confidence and we was able to revise the manuscript with confidence. Thank you for using your precious time for us.

Specific Comments to Authors:

A good case.

Respond

- We appreciate your decision.

### Reviewer #2

We appreciate your comments. Based on your comments, we checked our overall manuscript. As a result, our manuscript is improved the scientific quality and enriched. Thank you for using your precious time for us.

Below is the response to your comments.

Specific Comments to Authors:

1. You need to explain more about the mechanism of MSC transplantation in the regeneration of the neurons and brain tissue.

Response

- We included the mechanisms of the transplantation of MSCs and the regeneration of brain damages in the 'Discussion' part.

2. Did you recommend the MSCs transplantation during the acute phase of stroke or as a part of rehabilitation? I asked because the aforementioned management was done several weeks after the primary symptoms and also about 2 weeks after initial hospital discharge.

Response

- We recommended MM-UC-MSC transplantation for the treatment of a patient. He needed another treatment option because the acute ischemic stroke had worsened during the primary treatment. When the patient and caregiver visited our clinic, we suggested MM-UC-MSC transplantation as an alternative based on the patient's information (history of the disease, MRI images, and doctor's opinion at the time of primary treatment., etc.). After sufficient consultation with them, the patient decided on treatment.

3. Did you recommend the MSCs transplantation in all types of stroke (hemorrhagic or thrombotic)? with any severity regardless of the affected area?

Response

- We recommended MM-UC-MSC transplantation in patients with hemorrhagic stroke regardless of the area affected. The reason is that it is well-known that MSCs promote the regeneration of damaged blood vessels. However, we do not recommend the transplantation of MM-UC-MSCs to thrombotic stroke patients because studies are more needed about the relation between transplantation of MSCs and thrombotic stroke.

4. You used twice MSCs transplantation in the reported case. Did you follow any guidelines? Or you use did it according to the clinical symptoms or CT scan findings?

Response

- We transplanted MSCs twice according to the guideline. However, as our purpose was to treat patients, we were informed that additional transplantation may be necessary depending on the symptoms with the patient's consent. The patient was cured with two transplants determined according to the guideline.

5. The following paper is suggested to use in general considerations: • Cell Transplant. 2018 Dec; 27(12):1723-1730. DOI: 10.1177/0963689718806846. Epub 2018 Oct 22. Mesenchymal Stem Cell Therapy in Stroke: A Systematic Review of Literature in Pre-Clinical and Clinical Research. Haiqing Zheng, Bin Zhang, Pratik Y Chhatbar, Yi Dong, Ali Alawieh, Forrest Lowe, Xiquan Hu, Wuwei Feng.

Response

- Thanks for letting me know about a good paper. We read the paper you

recommended. I was able to confirm that it was a paper that could be a standard in the design of our manuscript. However, it has been confirmed that large and small corrections are inevitable when citing this paper at this stage. Therefore, we are sorry for not being able to cite this paper.

6. You claimed that the reported case is contrary to other studies and didn't develop any presentation such as chills, fever, and nausea. Did you have any suggestions for other physicians around the world to avoid such adverse effects following MSCs transplantation?

Response

- Various clinical trials and case reports have reported symptoms such as chills, fever, and nausea after MSC transplantation, and the cause is still unknown. In our case, less than 5% of patients had these symptoms.

If this value is low level, the use of minimally manipulated MSCs is estimated to be one of the candidates about causes.

## **Reviewer #2**

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Specific Comments to Authors:

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Respond

- We appreciate your decision.