Response To Reviewer and Editor's Comments

To science editor:

The author misspelled SERPINCI in the abstract and spelled SERPINC1 elsewhere.

Response: Revised.

To company editor-in-chief:

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: All figures has been arranged in a PowerPoint file. The grant application form has also been uploaded.

To reviewer:

1. However, as a case report, this manuscript lacks a clinical perspective. The patient had been suffering from headache for 10 years. Headache is one of the most common chief complaint in outpatient clinics or emergency departments. But most of the cases are not critical. Diagnosis of CVST is challenging also because they do not present typical or classical symptoms or laboratory data. In addition to the gene mutation, it would reinforce the impact of this report if they mentioned more detail of clinical courses such as "what was specifically suspicious and how they decided to perform MRI."

Response: In this case, the patient had a headache for only 10 days (not 10 years as the reviewer mentioned), which was an acute course of disease. When middle-aged men with family history of venous thrombosis showed symptoms of acute

unexplained headache, nausea, vomit and severe cranial hypertension with fundus optic papilledema, they should be highly vigilant against CVST and need further cranial MRI + MRV check. We have added the description of clinical perspective before cranial MRI + MRV, and highlighted in yellow background in the revised manuscript.

2. Moreover, description of particular differences in clinical signs would be of great help to broaden our knowledge. If this gene mutation does not only cause CVST but also lead to specific symptoms, we can focus on those signs when we see patients with headache next time.

Response: We checked the clinical symptoms of this patient repeatedly. However, the clinical symptoms of this patient are relatively simple, which only exhibited intracranial hypertension of headache with nausea, vomiting and fundus optic papilledema. The above is one of the common clinical manifestations of CVST. Due to the rarity of the case, no other special clinical characteristics have been found. In General, patients with CVST caused by serpinc1 gene mutation generally have a significant decrease in AT level. However, the mutation of rs2227589 special site only leads to a slight decrease in AT level in this patient, suggesting that serious CVST can still occur even AT level in the normal range. This case illustrates that serpinc1 gene detection is important for the severe CVST patient, even the AT level is slightly lower but still in the normal range. The corresponding description was added in the conclusion section of the revised manuscript highlighted by yellow background.