

Dear Editors,

Thank you for sending me your comments on our manuscript entitled, "Sunitinib-Induced Hyperammonemic Encephalopathy in Metastatic GIST: A Case Report" . We also appreciate the time and effort you and each of the reviewers have dedicated to providing insightful feedback on ways to strengthen our paper. Thus, it is with great pleasure that we resubmit our article for further consideration. We have incorporated changes that reflect the detailed suggestions you have graciously provided. We also hope that our edits and the responses we provide below satisfactorily address all the issues and concerns you and the reviewers have noted.

To facilitate your review of our revisions, the following is a point-by-point response to the questions and comments delivered in your letter.

☆Although the hyperammonemic encephalopathy caused by Sunitinib is rare, a few cases have been reported at least since 2011. The author's case report did not find new ideas or possibly reasons. Although the author mentioned that a longer period from the start of treatment to the onset of hyperammonemic encephalopathy than those of cases reported in the past. However, the case of this manuscript is not definitively different from the previous ones.

→As you point out, ammonia encephalopathy caused by sunitinib has been reported in the past, but is extremely rare. However, there are no papers that summarize past reports. It is also possible that the patient had increased tumor mass in the liver, which may have impaired the the ability to metabolize ammonia through the urea cycle, and that the patient also had mild renal impairment and decreased urinary excretion of ammonia, which may have contributed to the hyperammonemia. Therefore, we believe it is worth reporting on this rare side effect, as it differs in some respects from previous reports.

Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries. We have worked hard to incorporate your feedback and hope that these revisions persuade you to accept our submission.

Sincerely,

Takaoki Hayakawa