Response to reviewer's comments

Dear Editors and Reviewers,

Thank you all for your great comments and suggestions! We have revised the manuscript accordingly and please find our response below for every point. We are happy to answer any further questions you may have for this case report and do further revision if required.

Yours sincerely,
Qiaofeng Ye

Reviewer #1:
Scientific Quality: Grade C (Good)
Language Quality: Grade A (Priority publishing)
Conclusion: Major revision
Specific Comments to Authors: .

Major criticism: -Vancomycin induced seizure was first described by Caglayan et al. in a 10-year-old girl in 1992. (Caglayan, S., Ozdogru, E., Aksit, S., Kansoy, S., & Senturk, H. (1992). Vancomycin-Induced Hypertension with Transient Blindness and Generalized Seizure. Pediatrics International, 34(1), 90–91.doi:10.1111/j.1442-200x.1992.tb00932.x)
Response:
Thanks for sharing this report that we were not aware of. Accordingly, we deleted the statement "This is the first case" in the CONCLUSION section, and made adjustment to other statement in the abstract and the INTRODUCTION section.

Although Caglayan et al. reported the vancomycin-induced seizure, they did not measure the plasma concentration of vancomycin and it was not sure if the vancomycin concentration was within the normal range. In our case, therapeutic drug monitoring was conducted within few days after the convulsion onset, which showed abnormally high plasma concentrations of vancomycin (both trough and peak concentrations). We also calculated the area under the concentration-time curve within 24 hours ($AUC_{0\text{-}24h}$), which is a recommended index for evaluating its exposure, with Bayesian approach. The convulsion onset in our case was related to the abnormal pharmacokinetics of vancomycin which was possible related to the chemotherapy applied to the patients or the disease state of neuroblastoma. Therefore, our case is quite different from the case reported by Caglayan et al., and it is still worth noting this potential risk of using vancomycin in the clinical settings.

Minor criticisms:
-Case report section is unnecessarily long and should be shortened.
Response:
Thanks for the comment. The CASE PRESENTATION section has been shortened.

-I would like to see information of the staging, especially to rule out brain metastasis.

Response:

Thanks for the suggestion. This patient was classified as Stage IV. We added the information of the staging to CASE PRESENTATION *History of present illness* section and the FINAL DIAGNOSIS section.

-CSF results (especially cytology and biochemistry), brain imaging results and EEG report are missing in case report section.

Response:

Thanks for this comment. We added the CSF results, brain imaging results and EEG report to the CASE PRESENTATION section, the detail of which are stated as follows:

On day 23, 0.8 mL of CSF sample was collected and tested, the report of which showed clear colorless appearance, a negative Pandy's reaction for detecting protein levels, 1×10^6 /L cell count, and no growth of bacteria or fungi.

On day 27, electroencephalogram (EEG) showed slower than normal blood flow in middle cerebral artery, and mildly insufficient blood supply. Other parameters of EEG were within normal range.

CT scan of the brain on day 22 revealed widened sulcus fissure and full supratentorial ventricle. There was no abnormal density shadow in the cerebral parenchyma. Thickening of the mucosa of nasal sinuses could be seen. Magnetic resonance imaging (MRI) was conducted on day 23 to further evaluate the brain. The results showed the splenium of corpus callosum had abnormal patchy signal shadow on T1WI, T2 tirm and T2WI images. No other abnormal signal from the rest of the brain was observed.

-Normal ranges of CRP, vancomycin... should be indicated.

Response:

Normal ranges of CRP, HGB, PLT, RBC, WBC, and vancomycin plasma peak and trough concentrations were added into the text with parenthesis, and also provided in the legend of Figure 1.

Normal ranges: CRP < 8 mg/L; HGB 110-160 g/L; PLT 100-400 $\times 10^9$/L; RBC 4.0-5.5 $\times 10^{12}$/L; WBC 4.0-10.0 $\times 10^9$/L; vancomycin peak concentration 20-40 mg/L, vancomycin trough concentration 5-10 mg/L.

-The dose and infusion time of vancomycin should be mentioned.

Response:

Thanks for this reminder! The dose and infusion duration of vancomycin were mentioned in the TREATMENT section. "On day 15 in hospital, vancomycin 200 mg q8h with an infusion duration of 40 minutes and fluconazole 48 mg daily (qd) were prescribed as anti-infective treatment considering the continuous fever". We did not consider the infusion duration in the first simulation with MwPharm software (which was used to get the concentration-time curve and calculate the $AUC_{0\text{-}24h}$). We found that the infusion duration of vancomycin was about 40 minutes for this patient, so we replace the Figure 2 with a new simulated concentration-time curve and recalculated the $AUC_{0\text{-}24h}$ which was 1086.57

mg·h /L

Comments from science editor

5 Issues raised:

(1) I found no "Author contribution" section. Please provide the author contributions;

Response: We have provided the author contributions in the title page.

(2) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: Grant application approval documents have been uploaded.

(3) I found the authors did not provide the original figures. 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;

Response: The original figure documents have been uploaded.

(4) I found the "Case Presentation" did not meet our requirements. Please re-write the "Case Presentation" section, and add "FINAL DIAGNOSIS", "TREATMENT", and "OUTCOME AND FOLLOW-UP" section to the main text, according to the Guidelines and Requirements for Manuscript Revision;

Response: The "CASE PRESENTATION" section has been re-written according to the Guidelines and Requirements for Manuscript Revision. We have also added the "FINAL DIAGNOSIS", "TREATMENT", and "OUTCOME AND FOLLOW-UP" sections to the main text.

(5) please write the "Core Tip" section, and provide an audio core tip file where the core tip content is recorded;

Response: "Core Tip" section has been added to the part below the key words. The core tip content has been recorded into an audio file.

(6) please provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.

Response: The signed Conflict-of-Interest Disclosure Form and Copyright license Agreement have been uploaded.