Author’s response to reviews

Title: The therapeutic value of cerebrospinal fluid ctDNA detection by Next-Generation Sequencing for meningeal carcinomatosis: a case report

Authors:
Xiaosu Guo (guoxiaosu1@163.com)
Junzhao Cui (1097709288@qq.com)
Yue Zhao (1727945768@qq.com)
Weixin Han (862624896@qq.com)
Yueli Zou (sunnygirlzy@126.com)
Ruiping Gao (310691385@qq.com)
Qing Li (2362797612@qq.com)
Xiaoqing Li (337681974@qq.com)
Junying He (hjy_zn@126.com)
Hui Bu (buhui881@163.com)

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Author’s response to reviews:

Dear Valentina Pinzi,

We are submitting the revised manuscript with the ID NURL-D-18-00509, entitled "The therapeutic value of cerebrospinal fluid ctDNA detection by Next-Generation Sequencing for meningeal carcinomatosis: a case report" for publication in BMC Neurology. According to the comments, we have already revised the manuscript. All revisions have been marked in red in the revised manuscript. The following are our reply to the comments, item by item.

Once again, thank you for your kind reconsideration.

Yours sincerely,

Hui Bu
Technical Comments:

1. Figures:
Please upload figures as figure files.
Answer: As suggested, we will upload figures as figure files. Thanks!

2. Figure legends:
Figure legends must be included in the main manuscript text file at the end of the document, rather than being a part of the figure file. For each figure or table, the following information should be provided: Figure or table number (in sequence, using Arabic numerals - i.e. Figure 1, 2, 3 etc); short title of figure or table (maximum 15 words); detailed legend, up to 300 words.
Answer: As suggested, we have put the figure legends in the main manuscript text file at the end of the document and marked in red in the “Figure legends” section of the revised manuscript. In addition, we have provided the figure number as suggested. And the word count of the short title of figure and detailed legend was within the specified range. Thanks!

Editor Comments:

Dear authors,

I would ask you to please revise your paper in depth based on both Reviewer 1 and Reviewer #2's comments, and to re-submit it. We would also refer you to the journal's Guide for Authors and request that you ensure that your revised manuscript contains all the requested characteristics.
Answer: We thank the Reviewer for his/her kind evaluation of our work. As suggested, we have revised our paper in depth based on both Reviewer 1 and Reviewer #2's comments. The related changes have been marked in red in the revised manuscript. Additionally, we ensure that our revised manuscript contains all the requested characteristics. Thanks!

Reviewer reports:

(Reviewer 1)
The case report is well described and the procedure seems to be useful and innovative. However English is unacceptable and should be carefully revise
Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have revised the text and marked in red in the revised manuscript. Thanks again!
1. Abstract; this needs to be re-written as the patient was already gefitinib for a known EGFR exon 19 Del mutation, so the chronology is incorrect.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for presenting the incorrect chronology. In fact, a 53-year man with lung cancer was included in this study. The gene detection of pleural effusion showed that the 19-Del mutation in exon of the EGFR gene in 11th March, 2015. He began to orally take gefitinib 250mg once a day for 11 months from December, 2015. In 3th November, 2016, he presented to the hospital with dizziness, headache and a transient blurred vision. In addition, he discontinued gefitinib and orally taken AZD9291 90-100mg once a day in November, 2016. We have rewritten and marked in red in the “Abstract” section of the revised manuscript. Thanks again!

2. Background; guidance for LMD management are available from EANO-ESMO; https://www.esmo.org/Guidelines/Neuro-Oncology/EANO-ESMO-Leptomeningeal-Metastasis-Clinical-Practice-Guidelines

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are appreciated that you can provide the valuable suggestion of background. After reading the clinical guidance, we found that although EANO-ESMO clinical practice guidelines of leptomeninges metastasis have been presented the evidences from the recommendations based more on expert opinion and consensus are on the low level. Given the limitations in the diagnosis and treatment of MC, missed diagnosis and delayed treatment are inevitable. We have added the related contented and cited the reference and marked in red in the “Background” section of the revised manuscript. Thanks again!

3. Background; please reference the final statement on page 3.

Answer: We thank the Reviewer for his/her kind evaluation of our work. Thanks again!

4. Results; case presentation; again this needs to be re-written to make the chronology clear

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for presenting the incorrect chronology. In fact, a 53-year man with lung cancer was included in this study. The gene detection of pleural effusion showed that the 19-Del mutation in exon of EGFR gene in 11th March, 2015. He began to orally take gefitinib 250mg once a day for 11 months from December, 2015. In 3th November, 2016, he presented to the hospital with dizziness, headache and a transient blurred vision. We have rewritten and marked in red in the “Case presentation” section of the revised manuscript. Thanks again!

5. Results; case presentation; its unclear regarding whether the patient clinically responded to the IT methotrexate or not, please add this.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for omitting the information. In this process, the patient was in stable condition and appeared no significant disease progression and no side effects of medicine. We have added the information and marked in red in the “Case presentation” section of the revised manuscript. Thanks again!

6. Conclusion; ctDNA has already been demonstrated to be a useful technology in this setting.

Answer: We thank the Reviewer for his/her kind evaluation of our work. Indeed, ctDNA has already been demonstrated to be a useful technology in this setting. We have rewritten and marked in red in the “Conclusion” section of the revised manuscript. Thanks again!