

Dear Editors and Reviewers:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled **“Non-alcoholic Wernicke encephalopathy in an esophageal cancer patient receiving radiotherapy: A case report and literature review”**. (ID: 73666). We have studied reviewer's comments carefully and have made revision which marked in red in the paper. Attached please find the revised version, which we would like to submit for your kind consideration. We would like to express our great appreciation to you and reviewers for comments on our paper. Looking forward to hearing from you.

Thank you and best regards.

Yours sincerely,

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Round 1

List of Responses

Dear Editors and Reviewers:

Thank you for your letter and the reviewer comments concerning our manuscript entitled **“Non-alcoholic Wernicke encephalopathy in an esophageal cancer patient receiving radiotherapy: A case report and literature review”**. (ID: 73666). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have tried our best to revise our manuscript according to the comments. Revised portion are marked in red in the paper, and these changes will not influence the content and framework of the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1 and Science editor:

1. Response to comment: On physical examination- assessment of nutritional status should be reported as it is relevant to this case report.

Response: We have described the patient's nutritional status in the physical examination section.

2. Response to comment: When the patient started receiving radiotherapy was repeated vomiting a consequence of radiotherapy-induced malabsorption, was there associated abdominal pain or diarrhea? Is the duration and dosage of radiotherapy for the first 8 days sufficient to cause radiotherapy-induced malabsorption in reference to existing literature? if this was not due to possible radiotherapy- I presume the esophageal carcinoma would rather present with regurgitation.

Response: In addition to vomiting, the patient had symptoms of dorsalgia and no diarrhea. We have added this information and highlighted it in red. According to your comments, we searched relevant literature again carefully. Unfortunately, there was no literature report on whether radiotherapy can induce thiamine malabsorption. It needs to be confirmed by more studies in

the future. We concluded that chronic malnutrition caused by repeated eating obstruction and vomiting was the main reason of Wernicke encephalopathy in our patient. In addition, the glucose within parenteral nutrition supplement accelerated the consumption of thiamine and the onset of Wernicke encephalopathy. We have revised the content of the article.

3. Response to comment: On the description of the nutritional supplementation- insufficient vitamins is reported- was thiamine given or not- if it was, how much, was it adequate dosage or inadequate; the statement provided is too vague to draw firm conclusions pertaining to thiamine deficiency.

Response: Thank you so much for your comment and we have made correction already in the manuscript and marked in red. Thiamine was not added to the peripheral nutritional supplementation.

4. Response to comment: In the published literature, how does radiotherapy induce, or exacerbate thiamine deficiency- is it in a similar manner as the one you hypothesize, through malabsorption?

Response: According to your comments, we searched relevant literature again carefully. Unfortunately, there was no literature report on whether radiotherapy can accelerate thiamine deficiency. It needs to be confirmed by more studies in the future. We concluded that chronic malnutrition caused by repeated eating obstruction and vomiting was the main reason of Wernicke encephalopathy in our patient. In addition, the glucose within parenteral nutrition supplement accelerated the consumption of thiamine and the onset of Wernicke encephalopathy. We have revised the content of the article in red.

5. Response to comment: "It recommends that a diagnosis of.." review this line, I believe there is a grammatical error. "glucosemight.." A minor typographical error.

Response: Thank you for your rigorous advice. We have revised the grammatical and typographical errors according to your advice.

6. Response to comment: It may be worth discussing the biochemical

diagnosis of thiamine deficiency also- that may lead to Wernicke encephalopathy.

Response: Thank you for your rigorous advice. We have added the biochemical diagnosis of thiamine deficiency.

7. Response to comment: Stating generally that the use of glucose should be avoided needs to be reviewed. stating that glucose should be used with caution- as hypoglycemia is also hazardous.

Response: Thanks for your suggestion, we have optimized the presentation.

Reviewer #2:

1.Response to comment: Language usage and grammar need to be improved.

Response: Considering the editor's suggestion. We have sent our manuscript to a native English-speaking expert to polish the language further.

2.Response to comment: Radiotherapy is one of the most common therapeutic modalities in the treatment of locally advanced esophageal cancer. Wernicke encephalopathy associated with radiotherapy is very rare. The current case already had malnutrition before and received TPN during radiotherapy, all these are risk factors for the development Wernicke encephalopathy as the authors discussed in the paper. Therefore, radiation therapy might not be the reason for the development of Wernicke encephalopathy in this case. Please revise the paper accordingly.

Response: According to your comments, we concluded that chronic malnutrition caused by repeated food obstruction and vomiting was the main reason of Wernicke encephalopathy in our patient. In addition, the glucose within parenteral nutrition supplement accelerated the consumption of thiamine and the onset of Wernicke encephalopathy. We have revised the content of the article in red.

Company editor-in-chief:

1.Response to comment: 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: Thank you for your rigorous advice. We have revised and improved the figures according to your advice, and provided the original files.

2.Response to comment: Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: We have uploaded the approved grant application form and funding agency copy of approval document.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Round 2

Comments: The authors made significant improvement and answered my comments. But there are still English language usage errors which need to be improved. For example, this sentence needs to be written in standard English style "It is significant under-recognition and delay in the diagnosis or treatment of Wernicke encephalopathy in departments of oncology.

Response: Dear Editors: Thank you for your letter and the reviewer comments concerning our manuscript entitled "Non-alcoholic Wernicke encephalopathy in an esophageal cancer patient receiving radiotherapy: A case report and literature review" (ID: 73666). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. Considering the editor's suggestion, we have sent our manuscript to a native English-speaking expert to polish the language further. Revised portion are marked in red in the paper, and these changes will not influence the content and framework of the paper. We also provide a new language editing proof documents. In addition, an

audio file describing our final core tip has been submitted according to the comments. We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

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