

Response letter

Dear Editor and Reviewers:

We submitted the manuscript of “Metastatic neuroendocrine carcinoma in bone marrow with unknown primary site, spontaneous regression or unexplored: A case report ” (No. 77949) for your kind consideration to be published in the *World Journal of Clinical Cases*.

We received the detailed remarks and suggestions from the editor and reviewers on Jun. 27th, 2022. We appreciated these kind comments and suggestions, which helped us a great deal in revising this manuscript. We have modified our paper according to these suggestions and all the revisions in the manuscript are highlighted in red.

Now, we have re-submitted our revised manuscript online. We believe the re-prepared manuscript has been improved greatly and hope that you will reconsider its publication in the *World Journal of Clinical Cases*.

Sincerely yours,

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Answering reviewers

Reviewer #1:

Specific Comments to Authors: No

Reviewer #2:

Specific Comments to Authors: Thank you for the excellent case report.

Some minor corrections are required: 1/"Physical examination revealed anemia." I think it is better to mention the anemia in the paragraph of laboratory tests. 2/immunohistological reaction: Chromogranin A was negative. Is it possible to define NET only on CD56 AND Synaptophysin?

Re: Thanks for your kind comments and good suggestions . We have presented the peripheral blood count including hemoglobin in *Table 1* in the paragraph of laboratory examinations. The diagnosis of neuroendocrine carcinoma (NEC) is based on both morphology and immunohistochemistry (IHC). For IHC, at least two of the three proteins CD56, chromogranin A and synaptophysin should be positive.

Reviewer #3:

Specific Comments to Authors: The authors reported one NEC bone marrow (BM) metastasis without identifying the primary site. Comments:

1. The case was confirmed by BM biopsy. Where was the location/site the BM was biopsied? Why chose the location/site? Any imaging study

showed abnormality in the biopsy site before the biopsy? Since the PET scan did not show any primary sites, how about the bone marrow? Anything to suggest BM abnormality? Do the authors think the BM was diffusely involved or only the biopsy site was involved? 2. Since no primary site was identified, the authors asked the question was the primary tumor spontaneously regressed or was unexplored? This was not mentioned in both the abstract and core tip. The authors should focus on why they thought the primary tumor was spontaneously regressed or was unexplored? How to confirm this assumption in the discussion instead of talking about how to treat this tumor. Many of the discussions regarding treatment can be deleted.

Re: Thanks for the reviewer's detailed review and kind comments. Our bone marrow (BM) biopsy site was right posterior superior iliac spine and we have added the BM biopsy site in the paragraph of laboratory examinations in our revised paper. For our reported case, ^{18}F -FDG PET/CT demonstrated intense and diffuse ^{18}F -FDG uptake in the BM of bilateral iliac bones and no abnormal uptake in other sites of the whole body. Based on the above, we chose the posterior superior iliac spine as the BM biopsy site. In the revised manuscript, we have mentioned that the primary tumor spontaneously regressed or was unexplored in both the abstract and core tip. Furthermore, we have deleted some content about treatment in the discussion part.