Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-21-473

Reviewer A

General Comment

The current case report showed the complete remission of gastric and intracranial lesion after chemotherapy with R-CHOP and intrathecal chemotherapy. It is interesting for this rare presentation of CNS involvement of gastric MALT lymphoma. There are few issues should be addressed before publications.

Response:

We are thankful to the reviewer for appreciating our work. We have considered all the reviewers' comments revised the manuscript accordingly.

In the introduction section:

Comment 1: The CNS should provide the full name.

Response 1: We provided full name of CNS upon its first appearance in Introduction Part of the revised manuscript (see Page 3, lines51, 52).

Comment 2: The brief description of the incidences of disseminated stage of gastric MALT lymphoma.

Response 2: We have added brief description of the incidences of disseminated stage of gastric MALT lymphoma in the Introduction Part of our revised manuscript (see Page 2, line 44 and Page3, line 45).

In the case report section:

Comment 1: Considering that most MALT lymphomas are not detected by routinely PET scan examination, how to explain why this patient was positive for PET scan, and provide the brief description.Response 1: In the current study, we used PET-CT scan to detect the increased uptake of fludeoxyglucose in the stomach, the thoracic and abdominal lymph nodes, and the right basal ganglia mass. Previous study showed that PET is effective tool for detecting those parameter in MALT lymphoma (1-3).

Comment 2: If the high-grade components existed in the low-grade MALT lymphoma of this patient, because gastric MALT lymphoma patients had rarely ulcerative lesions in the stomach?

Response 2: This patient showed ulcerative lesions and gastric MALT Lymphoma patients have ulcerative lesions in some cases as reported (4, 5).

In the discussion section:

Comment 1: Although CNS involvement has been rarely reported in gastric MALT lymphoma, there are few cases reports showing the CNS involvements of MALT

lymphoma (for example, Hematology Reports 2010; volume 2:e10; Ann Hematol. 2013 Jul;92(7):989-92.). This information would be helpful for readers.
Response 1: We are thankful to the reviewer for suggesting these studies. We have thoroughly checked them and cited (9) & (10) in our revised manuscript (see Page 5, line101).
Comment 2: In addition to Helicobacter pylori eradication therapy is essential in all gastric MALT lymphoma regardless of disease stage (7), Helicobacter pylori eradication therapy is also indicated for Helicobacter pylori-negative gastric MALT lymphoma (for example, Sci Rep. 2017 Oct 30;7(1):14333; Cancer Manag Res. 2019 Sep 20;11:8577-8587.) 0. This information would be helpful for readers.
Response 2: We are thankful to the reviewer for suggesting these studies. We have thoroughly checked them and cited (12) & (13) in our revised manuscript as "A significant number of patients with HP-negative gastric MALT responded to first-line Helicobacter pylori therapy (12, 13)" (see Page 5, lines105,106).
Comment 3: In the page 4, "When antibiotic therapy is insufficient to achieve disease regression, irradiation …….), this information should be cited references.
Response 3: We have added proper citations (14, 15) in the above mention sentence of the revised manuscript (see Page 5, line108).

Reviewer B

Comment 1: Although initial presentation was with disseminated disease and therefore presumed CNS metastasis of MALT, there is a long latency period (May 2012 to Feb 2019). Can you clarify the role of biopsy at recurrence and the possibility of primary CNS lymphoma (independent of MALT lymphoma)? Any additional information from CSF cytology?
Response 1: At the beginning of 2012 and recurrence in 2019, tumor cells were found in CSF. After the treatment in early 2012, the patient was reviewed, and no tumor cells were found in CSF. After the recurrence treatment in 2019, the tumor cells were not found in CSF.

Comment 2: There are other reports in the literature (at least 2) of MALT with CNS manifestation- would be useful to reference/include in discussion.
Response 2: We have cited other studies documented (9, 10) on MALT with CNS in the discussion section of revised manuscript (see Page 5, line101).

Comment 3: Discuss the decision to pursue R-CHOP vs other therapies. For example, this case report mentioned achieving CR with use of high dose methotrexate (Arai A, Taomoto K, Yokoyama M, et al. [A case of CNS metastasis from gastric MALT lymphoma]. No Shinkei geka. Neurological Surgery. 2009 Dec;37(12):1235-1240)
Response 3: We have discussed the R-CHOP regimen selection for this patient in the revised manuscript (see Page 6, lines113-121).

Comment 4: I would suggest avoiding strong statements like recommending this treatment approach based on 1 case.

Response 4: We have low down the tone of strong statements in the revised draft of our manuscript (see Page 2, lines 30-33 and Page6, lines 122-124) as "Based on this successful case, chemoimmunotherapy combined with intrathecal chemotherapy could possibly be used for the treatment of gastric MALT lymphoma with central nervous system involvement.".

Comment 5: As we continue to move towards precision medicine in oncology- I would recommend mentioning briefly newer therapies such as targeted therapies (novel agents targeting BTK and Pi3K) or the use of immunomodulatory agents which may be especially pertinent in the relapse setting. See below 2 references:
Kiesewetter B, Raderer M. Immunomodulatory treatment for mucosa-associated lymphoid tissue lymphoma (MALT lymphoma). Hematol Oncol. 2020 Oct;38(4):417-424. doi: 10.1002/hon.2754. Epub 2020 Jun 23. PMID: 32469432)
Raderer M, Kiesewetter B. How I treat MALT lymphoma: 'a subjective interpretation of the gospel according to Isaacson….'. ESMO Open. 2020 Jul;5(4):e000812. doi: 10.1136/esmoopen-2020-000812. PMID: 32723771; PMCID: PMC7388885.

Response 5: In our revised manuscript, we briefly mentioned the novel treatment approaches such as targeted therapies or the use of immunomodulatory agents which may be especially pertinent in the relapse setting (see Page 6, lines 125-132 and Page7, lines 133,134).

References

1. Perry C, Herishanu Y, Metzer U, et al. Diagnostic accuracy of PET/CT in patients with extranodal marginal zone MALT lymphoma. Eur J Haematol 2007;79:205-9.
2. Theodossy T, Prvulovich E, Hyde NC. FDG-PET and MALT lymphoma in the parotid gland. Oral Oncology Extra 2005;41:230-233.
3. Tsai HK, Li S, Ng AK, et al. Role of radiation therapy in the treatment of stage I/II mucosa-associated lymphoid tissue lymphoma. Ann Oncol 2007;18:672-8.
4. Violeta Filip P, Cuciureanu D, Sorina Diaconu L, et al. MALT lymphoma: epidemiology, clinical diagnosis and treatment. J Med Life 2018;11:187-193.
5. Zullo A, Hassan C, Ridola L, et al. Gastric MALT lymphoma: old and new insights. Ann Gastroenterol 2014;27:27-33.