

## Peer Review File

Article Information: <https://dx.doi.org/10.21037/jgo-22-469>

### Reviewer A

The authors submit a case presentation of multiple metachronous presentation of gastric cancer in the setting of EBV. This case is of interest given that EBV associated gastric cancer is more common in younger patients and has a better prognosis than non EBV-associated gastric cancer thus metachronous cancers could be a clinical problem. There is little data at all in regards to the risk of metachronous gastric cancer in the setting of EBV. Unfortunately, a single case report does not provide enough data to guide endoscopic surveillance guidelines for EBV-associated gastric cancer. EBV is not routinely tested and thus identifying these individuals early is difficult. Typically, these individuals are identified as in this case report in retrospect after they have multiply recurrent cancer and thus the true denominator is not know. The case report is reasonable for publication but not in this journal. There are journals that accept exclusively case reports and might be a better target for the authors

Low impact case report. recommend different journal

→We thank the reviewer for the valuable comments. We conducted an extensive literature search but could not find a study that followed patients as frequently and for as long as our study. Accordingly, we believe that this is a rare case that is worth publishing. As you pointed out, EBVaGC occurs at a relatively early age and tends to be poorly differentiated. Although characteristic findings such as lymphocyte invasion are observed in advanced cases, they are atypical in patients with early gastric cancer like this case. Hence, diagnosing EBVaGC in routine clinical practice appears to be challenging. Moreover, gastric cancer may re-occur after distal gastrectomy at a higher incidence and at more locations in patients like the one described in our report than in patients with HP infection alone. Therefore, we believe it is necessary to increase awareness among physicians that EBV can cause upper and middle gastric cancer because this knowledge is important for determining treatment strategy. We agree that further cases need to be accumulated in real-world settings, but we believe that this journal is the best place to publish the first case of this kind because of its readership.

### Reviewer B

The authors report a very interesting and rare case. This case was diagnosed with Epstein-Barr virus-associated gastric carcinoma 3 times in 15 years. But does it deserve to be published as a rare case? Epstein-Barr virus-associated gastric carcinoma is a cancer with a good prognosis. However, as it can recur as in the above case, surveillance should be performed after treatment. This paper has several issues to be addressed.

1. This thesis needs English proofreading in its current state.
2. Pathology classification should be accurately described. What does the term highly differentiated mean?
3. What are the clinical implications of PDL-1 immunohistochemistry results? What do the

authors want to say?

4. You are using too many abbreviations. pT1b, Ly0, V0, pLM0, pVM0

5. Is there any clinical significance other than that this case is rare?

Comment 1: This thesis needs English proofreading in its current state.

Reply 1: We thank you for your comments. Per your suggestions, please find below our responses and the revisions and additions to the manuscript.

Comment 2: Pathology classification should be accurately described. What does the term highly differentiated mean?

Reply 2: Thank you for pointing this out, we have modified our text as " well differentiated ".

Changes in the text: Page 5, Line 112; Page 8, Line 135.

Comment 3: What are the clinical implications of PDL-1 immunohistochemistry results? What do the authors want to say?

Reply 3: We conducted PDL-1 immunohistochemical staining to verify recent reports and to investigate the possible usefulness of exploring anti-PD-1 antibody therapy in patients with metastases or relapse.

Changes in the text: Page 13, Line 220-223.

Comment 4: You are using too many abbreviations. pT1b, Ly0, V0, pLM0, pVM0

Reply 4: Thank you very much for reviewing our manuscript and offering valuable advice.

We have modified our text as advised.

Changes in the text: Page 6, Line 107-108; Page 7, Line 112-113; Page 7, Line 125-126; Page 8, Line 133; Page 8, Line 135-136.

Comment 5: Is there any clinical significance other than that this case is rare?

Reply 5: It aims to increase awareness among clinicians and pathologists of the necessity of considering EBVaGC when deciding on the treatment strategy after reoccurrence of gastric cancer.

Changes in the text: Page 4, Line 64 -66; Page 13, Line 230-232.

As for others, "remaining]" was changed to "remnant".

Changes in the text: Page 3, Line 52; Page 5, Line 86; Page 7, Line 113,117,122,124; Page 12, Line 207; Page 3, Line 52; Page 19, Line 327,329,335; Page20 ,Line 353.

---