

Jan 14, 2017

Dear Editors;

Thank you for the thoughtful review of the manuscript.

All authors have agreed to accept all the revisions which have been revised by your editorial staff. We have carefully reviewed and revised the manuscript. All authors have read and approved the revised manuscript.

We thank you again for the careful review of our paper for publication in *World Journal of Gastroenterology*. We look forward hearing from the editorial staff.

Sincerely yours,

Jieun Lee

Reviewer #1

1. ABSTRACT: The authors should emphasize that the initial suspicion was primary gastric cancer. The importance of immunohistochemical stain should be mentioned, since the histopathological exam on hematoxylin and eosin was not conclusive. Thus, the correct diagnosis prevented gastric surgical resection. This would benefit the readers.

→ First of all, thank you for the thoughtful, comprehensive review of the manuscript. The points that reviewer mentioned was revised in the abstract as follows;

Breast cancer with stomach metastasis rare with an incidence of 1% or less among metastatic breast cancer patients. We experienced a case of breast cancer metastasizing to the stomach in 65-year-old female patient. She experienced dyspepsia and poor oral intake before visiting the clinic. Diffuse infiltration with nodular mucosal thickening of the stomach wall was observed, suggesting advanced gastric cancer based on gross endoscopic finding. Spread of poorly cohesive tumor cells in the gastric mucosa observed upon hematoxylin and eosin (H&E) stain resembled signet ring cell carcinoma, but diffuse positive staining for GATA3 in immunohistochemical stain allowed for a conclusive diagnosis of breast cancer metastasizing to the stomach. Based on the final diagnosis, systemic chemotherapy was administered instead of primary surgical resection. After 2 cycles of docetaxel administration, she showed a partial response based on abdominal CT scan. This case is an unusual presentation of breast cancer metastasizing to the gastrointestinal tract.

2. In the “Discussion” section, a review of the previous cases from the literature could be added (as a Table).

→ Thank you for the considerate review. The characteristics of previous cited cases are summarized as a Table 1 in the manuscript.

3. Figures (endoscopy, endoscopic ultrasound, abdominal CT scan, and microscopy) are of very good quality, perfectly illustrative; however, their legend with explanations should be reviewed (especially for Figure nr. 3)

→ Thank you for the review. The legends are revised as follows;

Figure 1. Upper endoscopy shows diffuse infiltrative mucosal lesion with extensive nodular thickening of the stomach wall, involving lower two-thirds of body.

Figure 2. Endoscopic ultrasound shows subserosal invasion of the gastric lesion with lymph node involvement (A). Abdomen CT scan shows infiltrative gastric lesion involving cardia and angle of stomach (arrowhead) with enlarged perigastric lymph node (arrow).

Figure 3. Pathologic features of endoscopic biopsy specimen (A, B). Discohesive tumor cells are infiltrated in the stroma of the stomach mucosal tissue (H&E $\times 40$, A). Tumor cells show enlarged centrally located nucleus without intracytoplasmic clear mucin. The tumor cells had no connection to the remained normal gastric mucosal tissue (H&E $\times 400$, B). Previous breast cancer pathology was reviewed (C). Discohesive tumor cells were arranged in indian file. The tumor cells had enlarged centrally located nucleus without intracytoplasmic mucin (H&E $\times 400$, C). Immunohistochemical stains and molecular test of tumor was done (D~J). Diffuse strong nucleus expression of GATA3 was observed (GATA3 $\times 400$, D). Focal, less than one percentage cytoplasmic expression of GCDFP was detected (GCDFP $\times 400$, E). Negative stain for E-cadherin (E-cadherin $\times 400$, F). Negative stains for ER and

PR (ER × 400, PR × 400, G,H). Immunohistochemical stain for HER-2 was equivocal (HER-2 × 400, I). Silver in situ hybridization (SISH) for determination of HER2 gene status.

Reviewer #2

1. What is the time interval between the breast cancer and gastric mets?

→ Thank you for the considerate review. The gastric metastasis developed 4 years after the surgery. This is added in the manuscript as follows;

The stomach metastasis developed 4 years after surgery and 2 years after the initiation of an aromatase inhibitor use.

2) A literature review of not only cases in Korea but also other case reports from the world would be useful 3) Details of prior cases such as type of breast cancer associated with gastric mets, age/ sex of pt, interval between breast and gastric mets presentation, endoscopic appearance, distinct histological findings, modality of treatments used will be useful for gastroenterologists. This can be presented in a tabular format.

→ The characteristics of previous cited cases are summarized as a Table 1 in the manuscript. In the table, detailed information of the case is described comprising the pathologic, clinical characteristics and treatment outcomes.