

**Dear Editor:**

Thank you for considering our manuscript entitled “Isolated vaginal metastasis from stage I colon cancer: A case report” and for your kind response and advice.

We have read the peer-review report and have revised our manuscript accordingly. In addition, we have re-edited the manuscript for better language and clarity.

**Response to Reviewer 1 (reviewer code: 03551817):**

This manuscript is the first case report of vaginal metastasis from stage I colorectal cancer written in English. Detection and exploration through the collection of clinical samples is a good solution.

However, there is also some places need to supplement to make the quality of the manuscript better. 1. Is the sample size studied in this manuscript reasonable and representative? Whether surgical removal of the vagina can be used as the main treatment for the simple vaginal metastasis of colorectal cancer? 2. Some references in this manuscript are outdated (references in the last five years account for only one third). It is recommended that references be replaced with recent ones.

Comment:

1. Is the sample size studied in this manuscript reasonable and representative? Whether surgical removal of the vagina can be used as the main treatment for the simple vaginal metastasis of colorectal cancer?

Answer:

1. Thus far, only 57 cases of vaginal metastasis have been published worldwide. Among them, only 22 cases have been reported in English. Because of the rarity, the appropriate treatment would be hard to determine. Over the past years, radiotherapy is the most commonly used treatment, followed by surgery. Surgical excision seems to be a feasible option for the treatment of vaginal metastasis. However, it is uncertain whether surgery is appropriate as the main treatment because of the paucity of reported cases. Moreover, because vaginal metastasis appears to spread hematogenously, adjuvant chemotherapy seems to be helpful. However, the patient was reluctant to receive adjuvant chemotherapy, and the multidisciplinary team decided not to perform it following discussions. Only four cases of adjuvant chemotherapy have been reported to date, so the role of chemotherapy as well has not been elucidated.

Meanwhile, the 'core tip' and 3<sup>rd</sup> paragraph of the discussion, which describes the treatment of vaginal metastasis, have been revised to clarify that the appropriate treatment has not yet been determined.

Comment:

2. Some references in this manuscript are outdated (references in the last five years account for only one third). It is recommended that references be replaced with recent ones.

Answer:

2. Thank you for indicating this issue. We have searched the literature for reported cases of vaginal metastasis. Among the 27 references cited in our manuscript, 22 are previous case reports. Thus, these could not be changed or replaced. However, reference number 10 (Stock RG et al. Gynecol Oncol 1995;56:45-52) has been replaced with recent literature (Hacker NF et al. Int J Gynaecol Obstet 2015;131(Suppl 2): S84-S87) according to the reviewers' comments.

**Reply to the reviewer 4 (reviewer's code: 00038617):**

In this paper, the authors reported a rare case of vaginal metastasis (VM) derived from stage I (T2N0) sigmoid colon cancer. They also reviewed the reported 22 cases of VM from colorectal cancer (CRC). VM could occur even in patients with stage I CRC and most VM occurs within 2 years after the diagnosis of colorectal cancer. This case suggested that the prognosis would be favorable if the VM occurred solely. This manuscript was well written and had a certain value to publication.

Answer: Thank you for your kind response.

We hope that the revised manuscript can be acceptable and look forward to hearing from you soon.

Sincerely,

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