Author's response to reviews

Title: Small invasive colon cancer with systemic metastasis: A case report

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Author's response to reviews: see over
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BMC gastroenterology
Executive Editor Tim Shipley
Professor Robin Cassady-Cain,

Thank you very much for your and the three reviewers' encouraging and constructive comments.

We addressed the other comments, and the details are listed in the attached sheet. We hope that you will find the revision satisfactory for publication in the "BMC Gastroenterology".

Thank you again for your kind attention to our manuscript.

Sincerely,

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Reponse to Reviewer #1

Thank you very much for carefully reading our manuscript.

1. The authors should comment, whether they had before performed examinations to detect MSI.

The patient described in this study is very young. We agree that she could have hereditary nonpolyposis colorectal cancer. She did not have a medical or family history of HNPCC-associated cancers such as colorectal cancer, endometrial cancer, and gastric cancer. Therefore, she did not fulfill Amsterdam criteria II. Her age, i.e. 35 years, is in accordance with the Bethesda guidelines, which are used as recommendation criteria for MSI testing. However, this time she did not agree to undergo MSI testing (page 5, line 13-16 in the revised manuscript).
**Reponses to Reviewer #2**

Thank you very much for carefully reading our manuscript.

1. ‘The authors did not explain how the molecular pathway for “de novo” colon cancers is different from traditional adenoma-carcinoma sequence.
If this has not been addressed in the literature, the authors should acknowledge this and emphasize that their assumption to classify this lesion as “de novo” colon cancer is just based on the morphology and clinical behaviour.’

   Thank you for your kind suggestion. In accordance with your suggestion, in the revised manuscript, we have mentioned that the diagnosis of ‘de novo’ colon cancer was based on only its morphology and clinical behaviour (page 6-7, line 25-1 in the revised manuscript).

2. ‘The authors should also include the data from microsatellite instability testing (at least by Immunohistochemistry) to rule out MSI-H type cancer.’

   The patient’s age is 35 years, which is in accordance with the Bethesda guidelines; these guidelines are used as recommendation criteria for MSI testing. However, until the end of February 2011, she did not agree to undergo MSI testing (page 5, line 13-16 in the revised manuscript).
Reponses to Reviewer #3

Thank you very much for carefully reading our manuscript.

1. ‘I recommend the authors to change the title of this manuscript.’

We agree that ‘severe metastasis’ is not an appropriate term in this context. We have changed the title to ‘Systemic metastasis’ and have replicated this change in the rest of the manuscript.

2. ‘Please clarify whether the patient had aspiration cytology or biopsy of the cervical lymph node.’

The patient underwent We performed both aspiration cytology and biopsy of the cervical lymph node; we have added this information in the revised manuscript (page 3, line 18 in the revised manuscript).

3. ‘The authors need to verify why they performed endoscopic submucosal resection rather than a biopsy.’

To confirm whether the lesion is primary colorectal cancer or is the metastasis site of some other cancer, it is very important to prove the existence of mucosal cancer components in the lesion. Diagnostic EMR is more suitable than biopsy in this regard because we could obtain the entire specimen and evaluate it better in the case of EMR.

4. ‘I believe that the patient had upper endoscope. Even though the result was negative, it should be described.’

The results of upper endoscopy were negative for malignancy; we have provided these data in the revised manuscript (page 3, line 22-23 in the revised manuscript).