Point-by-point responses to Reviewer's comments

We would like to thank all reviewers for their positive evaluation and valuable comments. We have revised our manuscript based on these comments and responded to the reviewers' comments point-by-point below. The comments from the reviewers are shown in *blue italic* and our responses are shown in black regular.

Reviewer #1

In this case report, the authors described the metastasis of the left shoulder skin and left neck lymph node in a patient with ascending colon cancer. It is an interesting article. However, there are some concerns about this article.

1. There are no images of left neck lymph nodes and left shoulder skin.

Response: We are sorry for the missing images in the initially submitted manuscript. In the revised manuscript, we have added the image of recovered surgical wounds in the left shoulder and left neck lymph node (Figure 6), as we have not taken images at the first diagnosis.

2. An image of the color doppler ultrasound examination is absent.

Response: We are sorry for the missing image in the initially submitted manuscript, we have added the color Doppler ultrasound image in the revised manuscript (Figure 5).

3. In the introduction, the term "XELOX chemotherapy" is not preferred to use. It should be oxaliplatin and capecitabine chemotherapy.

Response: We have changed the usage of 'XELOX chemotherapy' into 'oxaliplatin and capecitabine chemotherapy'.

4. The authors could present a table of laboratory data.

Response: We have added the table of laboratory examinations in the first diagnosis (Table 1) and the follow-up examinations (Table 2).

5. In the histopathological examination, the authors could present immunochemical staining.

Response: We have added the immunohistochemical staining of resected cutaneous mass, ascending colon tumor mass, and cervical lymph node (Figures 1-3). The results of immunohistochemical staining revealed similar expression patterns across all tissues and suggested a skip metastasis.

6. There is no measure in the resected specimen nor the histopathological picture's microscope magnification value.

Response: We have added the scale bar of the resected specimen (Figure 2A) and the H&E

and immunohistochemical staining images are all in 10X magnification.

7. The author stated that the patient's prognosis is good; however, it is unbelievable. Is the patient still alive? They could present the figure of the clinical course.

Response: The patient is still alive and we have asked for another follow-up evaluation on 03/23/2022, and we have taken the image of recovered surgical wounds (Figure 6). Meanwhile, we have added the evaluation results of both CT examination and laboratory tests of CEA and CA-125 during the follow-up (Table 2).

8. The number of references is small and not updated.

Response: We have added more updated references about tumor metastasis.

9. The description of the case report is too concise.

Response: We have added more clinical evidence to support our conclusion about the skip metastasis of ascending colon tumor into the left shoulder and left neck lymph node. And we have added more laboratory data to support the good prognosis of the patient in this case report. We hope the updated results can better support the conclusion in this case report.

Reviewer #2

corrige cycle of chemotherapy specify the histology and stage of the TNM neoplasm,

Response: We have added the TNM stage to this patient (AJCC, 8th edition), and developed the chemotherapy treatment based on the NCCN guidelines (Version 2016).

also describe how it was ascertained that the lymph node is a mts of colon (FNAC, FNAB?)

Response: We have added the immunohistochemical staining of resected cutaneous mass, ascending colon tumor mass, and cervical lymph node (Figures 1-3). Based on the shared expression pattern (CK20+, CDX2+), we concluded that the skip metastasis of the left shoulder and left neck lymph node.

WERE INVASION OF SMALL LYMPH-VASCULAR SPACES IN THE PRIMITIVE CANCER?

Response: We have found the vascular tumor thrombi in primitive cancer.

Reviewer #3

The authors reported a case with skip nodal metastases of colon cancer to the neck nodes. Although it is interesting, the detail the authors provided is not completed. They should give the readers missing crucial information.

Title and Abstract -There was confusing where the tumor was (cecum vs. ascending colon). The authors stated differently on many parts of this manuscript.

Response: We have unified the tumor site as the ascending colon in the revised manuscript.

Introduction -Too short introduction. Just one sentence mentioned previous knowledge. Please review more previous literature about skip metastasis lymph nodes.

Response: We have added more references and introductions about the tumor metastasis and skip metastasis in the introduction section.

Case presentation -Please show the picture of mass on the left shoulder. It is the key in this case report.

Response: In the revised manuscript, we add the image of recovered surgical wounds of the left shoulder and left neck lymph node (Figure 6), as we have not taken images at the first diagnosis.

-This patient had colon cancer at a very young age. Please mention about family history of colon cancer. He might have hereditary colorectal cancer.

Response: This patient does not have a family history of colon cancer.

-The authors should provide CEA level in the laboratory section.

Response: In the revised manuscript, we have added the CEA value at the first diagnosis (Table 1) and follow-up examinations (Table 2).

-The authors stated that there was no palpable neck node, but many neck nodes were seen on USG. The authors should provide the node characteristics (size, border, echo), and they should state why LN metastases were suspected.

Response: We are sorry for the misleading conclusion about palpable lymph nodes, we have not identified the palpable lymph node at the first diagnosis, which was found after the surgical resection of ascending colon cancer. We have added more detailed characteristics of color Doppler examination of the left neck. We have observed no obvious medullary echoes in the left neck lymph nodes and we suspected a lymph node metastasis.

-Please show the picture of the neck node + doppler USG. They are important.

Response: We are sorry for the missing image in the initially submitted manuscript, we have added the color Doppler ultrasound image in the revised manuscript (Figure 5).

-The authors should provide the sequence of investigations. It wasn't very clear. Why do they perform colonoscopy? Did the authors send IHC staining that made them suspected colorectal cancer metastasis?

Response: We have added the immunohistochemical staining of resected cutaneous mass, ascending colon tumor mass, and cervical lymph node (Figures 1-3). Based on the expression pattern (CK20+, CDX2+) in resected cutaneous mass, we suspected a colon metastasis in the left shoulder and further performed the abdomen CT and colonoscopy examinations.

-The authors stated that they performed resection of the neck node. They should note how many neck nodes and what operation they did (Modified radical neck dissection or excision)?

Response: We have performed left cervical lymphadenectomy for complete removal of the lymph nodes.

-What modalities do the authors use for surveillance for neck nodes and shoulder mass?

Response: We have added the immunohistochemical staining of resected cutaneous mass, ascending colon tumor mass, and cervical lymph node (Figures 1-3). The results of immunohistochemical staining revealed similar expression patterns across all tissues, and suggested a skip metastasis of neck nodes and shoulder mass.

Overall, if the authors could provide the missing crucial information, I believe this manuscript could be quite an interesting case report.

Response: We hope the revised manuscript can better support the conclusion in this case report.