Dear editor,

We submit hereby a revised manuscript entitled “Primary sigmoid squamous cell carcinoma with liver metastasis: A case report”(Manu script NO.: 72507, Case Report), which is co-authored by Xinyang Li, Gen Teng, Xing Zhao and Cuimin Zhu. We have carefully revis ed the manuscript text based on the format requirements of the *Wor ld Journal of Clinical Cases* and the Reviewers’ suggestions. The c hanges we have made are highlighted with yellow background in th e marked revised manuscript. We would be very grateful if the ma nuscript could be published in the *World Journal of Clinical Cases*. Additionally, clean revised manuscript and clean revised supporting information are also uploaded. The following part is the point-by-po int responses to the editor:

Reviewer #1:

Specific Comments to Authors: Thank you for this interesting case report. I believe presenting rate/difficult cases sis essential for the h elp of other colleagues that knight come across similar challenges.

Response: We gratefully thanks for the precious time the reviewer s pent reviewing our manuscript. To our delight, it was the reviewer who gave the manuscript a high evaluation. At the same time, we really hope that the case report can be known to more people. Tha nk you again!

Reviewer #2:

Specific Comments to Authors: I really appreciate reading this case report. I have some comments as follows: Abstract: it is not clear. It seems that the patient was operated for constipation and colon cancer found during the surgery. Itroduction: it seems too long. Most of the first paragraphs can be reported in the discussion and only summarized in the introduction. Treatment: what do the Authors mean for intensive CT? Moreover, in this section the Authors reported data regarding the followup and adjuvant treatment that overlap the section outcomes and followup. Discussion: it seems too long. Moreover, I would suggest a scientific English editing. Words as hemicolectum are not used. Perhaps the Authors mean hemicolectomy.

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:

(1)Abstract: it is not clear. It seems that the patient was operated f or constipation and colon cancer found during the surgery.

Response: After listening to your suggestions, we have revised the abstract in detail and added the necessary content. The content is s hown in the yellow background modification part of the text.

(2)Itroduction: it seems too long. Most of the first paragraphs can be reported in the discussion and only summarized in the introducti on.

Response: We have listened to your suggestions, and we have cut down and summarized the content of the introduction. The revised content is shown in the introduction section of the text.

(3)Treatment: what do the Authors mean for intensive CT? Moreover, in this section the Authors reported data regarding the followup and adjuvant treatment that overlap the section outcomes and followup.

Response: Intensive ct what I mean is CT enhancement scan. This expression has been corrected where it is used in the text. Regarding the overlap between the content of the treatment and the follow-up, corrections and deletion of duplicate content have been made in the text. Please see the original treatment section for details.

(4)Discussion: it seems too long. Moreover, I would suggest a scientific English editing. Words as hemicolectum are not used. Perhaps the Authors mean hemicolectomy.

Response: The word hemicolectum is misapplied, and it should be the right hemicolon. We have made reasonable cuts in the discussion section. Regarding the English editing, we have asked a professional agency to do the language touch-ups.

Thank you again for your valuable suggestions!

Reviewer #3:

Specific Comments to Authors: Interesting case. Detailed description of surgical intervention will be interesting, as well as explanation

of treatment of liver mets. Why you did not performed liver surger y in this case?

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:The patient was free of liver metastases at the time of initial diagnosis. After surgical treatment and 6 cycles of postoperative adjuvant chemotherapy, the disease progressed and multiple liver metastases were found. However, surgery for liver me tastases was not performed because the liver metastases were multip le lesions.Thank you again for your valuable suggestions!

Reviewer #4:

Specific Comments to Authors: SCC of the colon is extremely rare (0.1% of all cases). Diagnosis requires finding no involvement of cloacogenic or squamous lined mucosa, no squamous cell carcinoma elsewhere and thorough sampling to exclude adenosquamous carcinoma. In this case, the authors state that the tumor is 30 cm away from the anal verge somewhat excluding cloacogenic embryologic nests as origins of the SCC (this is the most common mechanism to get SCC in the colon and should be added to the discussion). Issues: The paper should be really reviewed by a pathologist 1) The figure of the H&E stained slides is not very informative. It only shows the tumor but no normal structure of the colon. Also, the figure legend should state if the section came from the resection specimen. In terms of staging, the text says it was a pT4b. This means it grew into a

neighboring organ or structure. Which organ or structure was it? It would be good to show tumor invasion into the organ/structure qualifying for a pT4b stage. At least show some muscularis propria with tumor going through the subserosal tissue into the peritoneum (use 2x objective). 2) The timeline of the case is not complete. When was the biopsy of the liver metastasis performed? What was the clinical stage of the tumor at initial colonoscopy. What was the pathological stage of the tumor after sigmoid colon resection. Was the liver metastasis already known at that time? The clinical stage at the time of diagnosis is important to define treatment strategy. Was up front systemic therapy offered and if not, why? None of these important clinical decision making facts are stated in the case report. 3) The figure legend of Figure 3 are not using normal pathological nomenclature. What is a "colonoscopic bite"? What does "post-operative colonization" mean? Is a "puncture of the liver metastasis" a needle core biopsy? What does "postcolonic" mean? 4) Exclusion of cloacogenic or squamous lined mucosa, no squamous cell carcinoma elsewhere and thorough sampling to exclude adenosquamous carcinoma is not stated in the text.

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:

(1)SCC of the colon is extremely rare (0.1% of all cases). Diagnosis requires finding no involvement of cloacogenic or squamous lined mucosa,

no squamous cell carcinoma elsewhere and thorough sampling to exclude adenosquamous carcinoma. In this case, the authors state that the tumor is 30 cm away from the anal verge somewhat excluding cloacogenic embryologic nests as origins of the SCC (this is the most common mechanism to get SCC in the colon and should be added to the discussion).

Response: We strongly agree with you and we have put this mech anism" the tumor is 30 cm away from the anal verge somewhat ex cluding cloacogenic embryologic nests as origins of the SCC" in th e discussion section.

(2)The figure of the H&E stained slides is not very informative. It only shows the tumor but no normal structure of the colon. Also, the figure legend should state if the section came from the resection specimen. In terms of staging, the text says it was a pT4b. This means it grew into a neighboring organ or structure. Which organ or structure was it? It would be good to show tumor invasion into the organ/structure qualifying for a pT4b stage. At least show some muscularis propria with tumor going through the subserosal tissue into the peritoneum (use 2x objective).

Response: We added H&E stained slides that jointly show cancerou s and normal colonic structures,as Figure 4A, and we have labeled the source of the specimens in the legend. In terms of staging, Intr aoperatively, we saw the mass budgeting the anterior peritoneum. S o we graded T as T4b.But unfortunately, we didn't get a slice of t

hat.We added an H&E stained slide, which showed that the cancero us tissue invaded the entire intestinal wall,as Figure 5.

(3)The timeline of the case is not complete. When was the biopsy of the liver metastasis performed? What was the clinical stage of th e tumor at initial colonoscopy. What was the pathological stage of the tumor after sigmoid colon resection. Was the liver metastasis alr eady known at that time? The clinical stage at the time of diagnosi s is important to define treatment strategy. Was up front systemic t herapy offered and if not, why? None of these important clinical d ecision making facts are stated in the case report.

Response: The patient's liver puncture biopsy was performed in No vember 2019, which is 7 months postoperatively. The patient's initia l colonoscopy determined cT4aN0M0, stage IIB, while the pathologi cal stage determined after surgical resection of the tumor was pT4b N0M0, stage IIC. Because the patient was stage IIB at the time of initial diagnosis, its stage was early and surgical treatment should b e preferred and no prior systemic treatment was required. The answ er to this question we have added in the original article where nec essary。

(4)The figure legend of Figure 3 are not using normal pathological nomenclature. What is a "colonoscopic bite"? What does "post-opera tive colonization" mean? Is a "puncture of the liver metastasis" a n

eedle core biopsy? What does "postcolonic" mean?

Response: We have removed the above phrase. And the legend has been re-labeled correctly. Please refer to the legend in the original text for details.

(5)Exclusion of cloacogenic or squamous lined mucosa, no squamous cell carcinoma elsewhere and thorough sampling to exclude adenosquamous carcinoma is not stated in the text.

Response: We have refined these 3 areas of diagnosis in the third paragraph of the discussion section, as indicated by the yellow coatings.

Thank you again for your valuable suggestions!

Reviewer #5:

Specific Comments to Authors: The case is interesting because it is a rare one. However the presentation is not perfect, it is hard to follow and somehow confusing. I recommend authors have their article revised by someone more professional in scientific writing. Some questions: - had authors tested liver function tests at the time of tumor diagnosis, and if so, were they normal? Had the patient anemia in lab tests. A table of full lab tests results is appropriate.- More detailed data on surgical procedure, for example with what margin the tumor had been resected? If any regional lymph nodes had been resected for pathology? - Have you not performed ablative or i

rradiation therapies for the liver metastases? - If you investigated a ny of the found mutations in the liver metastasis was constitutional/ germ cell (existing in every body cells; e.g. like in WBC)?

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:

(1)The case is interesting because it is a rare one. However the pre sentation is not perfect, it is hard to follow and somehow confusin g. I recommend authors have their article revised by someone more professional in scientific writing.

Response: We have hired a professional to do the language touch-u ps and hope to clear up your doubts.

(2)had authors tested liver function tests at the time of tumor diagn osis, and if so, were they normal? Had the patient anemia in lab te sts. A table of full lab tests results is appropriate.

Response: Liver function tests were performed at the time of tumor diagnosis and the results were generally normal. After laboratory tes ts, the patient was not anemic. Patient-related laboratory results are shown in Table 1.

(3)- More detailed data on surgical procedure, for example with wh at margin the tumor had been resected? If any regional lymph node s had been resected for pathology?

Response: The sigmoid colon was incised at 12 cm from the proxi

mal edge of the tumor and 6 cm from the distal edgeof the tumor. Eight lymph nodes were sent for examination, and no lymph node metastasis was seen on postoperative pathology.

(4)- Have you not performed ablative or irradiation therapies for th e liver metastases?

Response: Because the liver metastases were multiple, the patient di d not have ablation or irradiation treatment for the liver metastases.

(5)- If you investigated any of the found mutations in the liver met astasis was constitutional/germ cell (existing in every body cells; e. g. like in WBC)?

Response: According to the genetic test report of the liver metastas es, the patient has a somatic mutation in this part of the lesion, as shown in Table2.

Thank you again for your valuable suggestions!

Reviewer #6:

Specific Comments to Authors: Although the topic is interesting, t he case is presented in a very disorganized way, making it very dif ficult to follow. The section headers are different from the common ly accepted styles and should be standardized. Introduction part: 1. "squamous carcinoma alone is rare, accounting for approximately 0. 25% of all colorectal cancers." sentence needs citation. 2. "and its prognosis seems to be worse than that of simple adenocarcinoma."

sentence needs citation. Final diagnosis part: 1. The reason for the need of peritoneal resection should be elucidated since peritoneal in volvement dramatically affects prognosis. 2. Although it is noted th at there were no metastatic lymph nodes, the number of harvested l ymph nodes should be disclosed. 3. Preoperative CT images of the liver proving it being metastasis free should also be added in the fi gures. Treatment part: 1. Since the liver metastasis seems to be con fined to right posterior segments of the liver, the authors should elu cidate why liver resection was not considered as a treatment option for the patient since the tumor appears to be insensitive to chemoth erapy? Discussion part: 1. "Therefore, squamous cell carcinoma in t he primary colon is very rare, and the incidence is about 0.025-0.1% of colon cancer." sentence needs citation. Overall evaluation: The t opic is quite interesting and should be reported, however the author s needs to address the specific messages of this particular case and there is a bit of need for language polishing.

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:

(1)Although the topic is interesting, the case is presented in a very disorganized way, making it very difficult to follow. The section he aders are different from the commonly accepted styles and should b e standardized.

Response: We have hired a professional to do the language touch-ups and hope to clear up your doubts.

(2)Introduction part: 1. "squamous carcinoma alone is rare, accounting for approximately 0.25% of all colorectal cancers." sentence needs citation. 2. "and its prognosis seems to be worse than that of simpleadenocarcinoma." sentence needs citation.

Response: "squamous carcinoma alone is rare, accounting for approximately 0.25% of all colorectal cancers." and “its prognosis seems to be worse than that of simple adenocarcinoma." These two sentences have been clearly marked in the text with citations, as shown in yellow markings.

(3)Final diagnosis part: 1. The reason for the need of peritoneal resection should be elucidated since peritoneal involvement dramatically affects prognosis. 2. Although it is noted that there were no metastatic lymph nodes, the number of harvested lymph nodes should be disclosed. 3. Preoperative CT images of the liver proving it being metastasis free should also be added in the figures.

Response: 1: The patient's peritoneum was removed because the tumor had invaded the anterior peritoneum. 2: Eight lymph nodes were sent for examination, and no lymph node metastasis was seen on postoperative pathology. 3: The patient's preoperative liver CT imageshave been supplemented in the text, as shown in Figure 1b.

(4)Treatment part: 1. Since the liver metastasis seems to be confine d to right posterior segments of the liver, the authors should elucid ate why liver resection was not considered as a treatment option fo r the patient since the tumor appears to be insensitive to chemother apy?

Response: The reason why patients do not undergo surgery for liver metastases is that the liver is a multiple metastasis.

(5)Discussion part: 1. "Therefore, squamous cell carcinoma in the p rimary colon is very rare, and the incidence is about 0.025-0.1% of colon cancer." sentence needs citation.

Response: This sentence has been clearly marked in the discussion part with the citation, as shown in yellow markings.

(6)Overall evaluation: The topic is quite interesting and should be r eported, however the authors needs to address the specific messages of this particular case and there is a bit of need for language polis hing.

Response: We strongly agree with you and we have added some sp ecific information about the case as suggested by your reviewers. Most importantly, we have hired professionals to touch up the articl e.

Thank you again for your valuable suggestions!

Science editor:

Squamous cell carcinoma of the colon is extremely rare and I am very interested in it. The manuscript is well written and can be hel pful for the readers to ameliorate the diagnostic and therapeutic app roach for this scenario. Nevertheless, there are a number points that may deserve some revisions. 1. More detailed surgical data. 2. For some sentences with specific numbers, the author should add literat ure citations after the sentences.

Response: We gratefully appreciate for your valuable suggestions. O ur response is as follows:

1. More detailed surgical data.

Response: Thank you very much for your valuable advice, and we have added some details of the surgery in the article, as shown in the final diagnosis section.

2. For some sentences with specific numbers, the author should add literature citations after the sentences.

Response: We have added literature citations to these sentences, as shown in the corresponding part of the article.

Thank you again for your review!

Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manus cript, and the relevant ethics documents, all of which have met the

basic publishing requirements of the World Journal of Clinical Case s, and the manuscript is conditionally accepted. I have sent the ma nuscript to the author(s) for its revision according to the Peer-Revie w Report, Editorial Office's comments and the Criteria for Manuscr ipt Revision by Authors. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following websit e for the professional English language editing companies we recom mend: https://www.wjgnet.com/bpg/gerinfo/240. Before final acceptanc e, uniform presentation should be used for figures showing the sam e or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Ple ase prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the ed itor.

Response: We gratefully appreciate for your valuable letter,and we h ave checked the manuscript throughout and also revised manuscript according to the *World Journal of Clinical Cases* in the revised ma nuscript,and uploaded the necessary documents such as English lang uage certificate.

We sincerely hope that this revised manuscript has addressed all

your comments and suggestions. We appreciated for reviewers' war m work earnestly,and hope that the correction will meet with appro val.Once again,thank you very much for your comments and sugges tions.