

Dear Editor,

We deeply appreciate the work and time made by the editors and the reviewers in reviewing our manuscript. We have revised our manuscript according to the reviewers' comments. We believe that our manuscript has been improved greatly. Please find our response to the special comments below:

Reviewer #1:

Overall, a case report worth publishing. It will need some minor revisions as follows:

1. Abstract (background) Line21-22: Change to The diagnosis of pancreatic metastases is difficult and predominantly relies on CT, pathology and immunohistochemistry.

Response: We have revised the background (line 41-42 now) according to the comments from the reviewer.

2. Case summary: 1. Case summary -Please add chronology of events. 2. Case summary- please add brief information about the staging and therapy (?adjuvant therapy)of the sigmoid cancer. 3. case summary-Please add brief information about the pulmonary metastasis (number of mets, any post-op chemotherapy etc) 4. Case summary- I would suggest modifying the following line: 'The colonic origin of the pancreatic metastasis was further confirmed by highly concordant gene mutation profiles across the three lesions, including most frequently colon cancer oncogenic driver mutations in APC, TP53, KRAS, and FBXW7.' 'Concordant gene mutation profiles were observed across the three lesions that included oncogenic driver mutations most frequently seen in colon cancer (e.g., APC, TP53, KRAS, and FBXW7).'

Response: We have added the chronology of the events, a brief information about the staging and therapy of the sigmoid cancer, a brief information about the pulmonary metastasis, and modified the last sentence according to the reviewer's comments. In addition, because of the 150 words limitation in the case summary part, we cannot add more information about the patient and also revise parts of the sentences in order to meet the requirement of the journal.

3. Core tip Line 51-53: Modify as follows- To our knowledge, this is the first case reported to utilize NGS sequencing to detect tissue of origin in pancreatic metastasis from colon cancer.

Response: We have revised the core tip (line 72-74 now) as the comments from the reviewer.

4. History of present illness Please add detailed information about the staging and therapy (?adjuvant therapy) of the sigmoid cancer. History of present illness Please add detailed information about the pulmonary metastasis (number of mets, any post-op chemotherapy etc)

Response: We have added the the staging and therapy of the sigmoid cancer, and the information about the pulmonary metastasis.

5. Physical examination and laboratory testing carcinoembryonic antigen (CEA) level was at an elevated 23.17 mg/mL- is it ng/ml? Also, provide normal lab value/range of CEA and CA 19-9.

Response: We have corrected the unit of CEA. Normal range of CEA and CA-19-9 are also added.

6. Inconsistent statements: Line 107-109 : A review of pathological specimens indicated moderately to poorly differentiated adenocarcinoma invading duodenal submucosa, muscular layer, and serosa. Line 110-111: There was no involvement of the stomach, duodenum, gallbladder, or periphery of pancreatic islets.

Response: We have corrected Line 110-111 (Line 142-144 now) as follows: There was no tumor involvement of the stomach, gallbladder or the surgical incisional edges of duodenum and pancreas.

7. Line 149-153: Meaning unclear. Also, the conclusion of the PulMiCC study is highly controversial and was discounted by the NICE guideline.

Response: We have deleted Line 149-153 (Line 179 now) which is related to PulMiCC trial according to the comments from the reviewer.