January 28, 2021

Lian-Sheng Ma, Science Editor,

Company Editor-in-Chief, Editorial Office

World Journal of Clinical Cases

Dear Editors:

On behalf of the co-authors, I thank you for giving me the opportunity to revise and re-submit our manuscript titled, "Sarcomatoid carcinoma of the pancreas: multimodality imaging findings with serial imaging follow-up: A case report and literature review" (Manuscript No.: 60659). I also thank the reviewers for their insightful comments, suggestions, and questions about our study, which, we believe, have helped us to significantly strengthen our article. Several valid issues were pointed out in the review and, after careful consideration, we have made requisite revisions to the manuscript. Below, you will find our point-by-point responses to the reviewers' comments, questions, and concerns; the corresponding changes in the manuscript are indicated in italics. Our revised manuscript is attached as a separate document, and the corresponding changes are highlighted in red.

We sincerely hope that our responses and revisions have adequately addressed the reviewers' concerns and that our manuscript is now suitable for publication in the *World Journal of Clinical Cases.*

Thank you once again, we are grateful for the opportunity to be published in the Journal.

Sincerely,

Jeong Eun Lee

M.D, Professor,

Department of Radiology, Chungnam National University Hospital,

Chungnam National University School of Medicine, 282 Munhwa-ro, Jung-gu,

Daejeon 301-721 Korea

Telephone: 82-42-280-7333

Fax: 82-42-253-0061

Email: nasa80@cnuh.co.kr

Editor's Comments to the Author:

We are pleased to inform you that, after preview by the Editorial Office and peer review, as well as CrossCheck and Google plagiarism detection, we believe that the academic quality, language quality, and ethics of your manuscript (Manuscript NO.: 60659, Case Report) basically meet the publishing requirements of the World Journal of Clinical Cases. As such, we have made the preliminary decision that it is acceptable for publication after your appropriate revision. Upon our receipt of your revised manuscript, we will send it for re-review. We will then make a final decision on whether to accept the manuscript or not, based on the reviewers' comments, the quality of the revised manuscript, and the relevant documents. Please follow the steps outlined below to revise your manuscript to meet the requirements for final acceptance and publication.

Science editor:

1 Scientific quality: The manuscript describes a case report of the multimodality imaging for pancreatic sarcomatoid carcinoma. The topic is within the scope of the WJCC. (1) Classification: Grade C, Grade C and Grade E; (2) Summary of the Peer-Review Report: The case information is complete and detailed. This case report includes the dynamic progression of the pancreatic lesion. The authors should add the discussion of "multimodality imaging findings" or management of pancreatic cystic lesions base on this case and present the normal range of CA19-9 and CEA. It is recommended to rearrange the discussion and the article within two new publications on this subject. The authors need to add incidence, aetiology, treatment and outcome in introduction. The questions raised by the reviewers should be answered; and (3) Format: There is 1 table and 6 figures. A total of 29 references are cited, including 5 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A, Grade A and Grade B. A language editing certificate

issued by Editage was provided. 3 Academic norms and rules: The authors provided the CARE Checklist – 2016, and the Signed Informed Consent. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJCC. The corresponding author has not published articles in the BPG. 5 Issues raised: I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Reviewer #1

Comments

Thank you for the opportunity to review the manuscript by Lim et al. The manuscript is interesting and very well-written with only minor spelling errors. Although the topic is rare, it is, however, described in several case-reports which is also being pointed out by the authors. Therefore, added scientific value of this paper is questionable. I have also several other comments on the work: 1) Introduction is too short and offers no background knowledge on the topic, which is placed in the discussion section instead. I suggest mentioning incidence, aetiology (focusing on the difference between PSC and other similar pancreatic malignancies), treatment and outcome. 2) The authors state that this case-report offers "emphasis on chronological changes in multimodality imaging findings". Please specify which specific changes are being referred to? 3) Discussion section should focus on differentiation between PSC and other malignancies. It is even possible to diagnose preoperatively? Genomic evaluation of this tumor would offer an interesting perspective, and possibly answer some of the questions on development of the disease. I suggest writing a systematic review on the topic instead? Focusing on histopathological and molecular characteristics

Response:

First, we thank Reviewer #1 for carefully evaluating our case report and for offering constructive suggestions to improve our manuscript.

Specific comments and response:

1) Introduction is too short and offers no background knowledge on the topic, which is placed in the discussion section instead. I suggest mentioning incidence, aetiology (focusing on the difference between PSC and other similar pancreatic malignancies), treatment and outcome

Response

Thank you for your comment concerning the length of our introduction. We have provided further brief details concerning PSC including etiology, history, and treatment, and outcome. Other detailed features are mentioned in the introduction session, as follows:

'Pancreatic sarcomatoid carcinoma (PSC) is an extremely rare but highly malignant variant of pancreatic carcinoma, classified as sarcomatoid in undifferentiated carcinoma according to the World Health Organization classification[1,2]. PSC is histologically composed of a mixture of carcinomatous and sarcomatous elements; however, the pathogenesis of PSC remains unknown. Following the first reported case of PSC in 1951, approximately 40 cases have been reported, with a mean patient age of 67 years[3,4]. To date, PSC has not been fully described and no current treatment guidelines exist, with most reported patients having undergone surgical resection and adjuvant chemotherapy. However, the prognosis of PSC is dismal, with a reported median survival rate of 6 months[4]. Moreover, characteristic radiological findings for PSC have not been established. Therefore, an early and accurate diagnosis is important in determining the course of treatment given PSC has a poor prognosis and shows rapid progression. Here, we report clinical and imaging findings in relation to PSC in a 64-year-old woman, with an emphasis on chronological changes in multimodality imaging findings using computed tomography (CT) and magnetic resonance imaging (MRI), as well as a corresponding literature review of 24 cases with appropriate images.

'

2) The authors state that this case-report offers "emphasis on chronological changes in multimodality imaging findings". Please specify which specific changes are being referred to?

Response

Thank you for your valuable comments. We have added the importance of chronological changes in multimodality imaging findings in the Discussion session.

Our chronological image follow-up indicated a change in PCS size and morphology from a small cystic lesion with calcification at the tail of pancreas on the initial CT scans to an enlarged mixed solid cystic mass. It also showed a rapid growth pattern, from 2.8 cm to 5.4 cm in diameter within six months, which was similar to a previously reported rapid growth pattern[10]..'

Strategies to improve treatment options and prognosis for PSC remain limited due to its rapid progression and rare occurrence. We found that PSC also initially appears similar to other pancreatic cystic tumors in terms of chronologic changes and multimodality imaging findings. Given that no management guidelines for PSC exist, it may be necessary to refer to worrisome features and/or high-risk stigmata of the lesion, as detailed in the ACR 2017 guideline[12]. Therefore, evaluation of cystic pancreatic lesions using multimodality imaging is crucial, and serial follow-up imaging studies are helpful for treatment planning. CT is the primary imaging modality for evaluating pancreatic solid and cystic lesions but has some limitations. Endoscopic ultrasonography, MRI, especially T2-sequencing, is more useful for evaluating key features due to its superior soft-tissue contrast resolution

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3) Discussion section should focus on differentiation between PSC and other malignancies. It is even possible to diagnose preoperatively?

Response

Given its extremely rare prevalence, a preoperative diagnosis is very challenging. We have presented a differential diagnosis of PCS and malignant MCN and PDAC with cystic change. According to the ACR guidelines, we consider that evaluation of a pancreatic cystic lesion using multimodality images is helpful for the diagnosis of PSC.

'Strategies to improve treatment options and prognosis for PSC remain limited due to its rapid progression and rare occurrence. We found that PSC also initially appears similar to other pancreatic cystic tumors in terms of chronologic changes and multimodality imaging findings. Given that no management guidelines for PSC exist, it may be necessary to refer to worrisome features and/or high-risk stigmata of the lesion, as detailed in the ACR 2017 guideline[12]. Therefore, evaluation of cystic pancreatic lesions using multimodality imaging is crucial, and serial follow-up imaging studies are helpful for treatment planning. CT is the primary imaging modality for evaluating pancreatic solid and cystic lesions but has some limitations. Endoscopic ultrasonography, MRI, especially T2-sequencing, is more useful for evaluating key features due to its superior soft-tissue contrast resolution.'

4) Genomic evaluation of this tumor would offer an interesting perspective, and possibly answer some of the questions on development of the disease. I suggest writing a systematic review on the topic instead. Focusing on histopathological and molecular characteristics

Response

Thank you for your valuable comments, and we agree that your suggestion could be an interesting research topic. However, unfortunately, sarcomatoid carcinoma of the pancreas is very rare; therefore, it is difficult to perform to genomic evaluation. If we have an opportunity to study more cases of sarcomatoid carcinoma of the pancreas, we will include a genomic evaluation in future studies. Once again, I sincerely appreciate your suggestion.

Reviewer #2

I personally like this case report very much. The case information is complete and detailed. This case report includes the dynamic progression of the pancreatic lesion. The article discusses the histological characteristics, clinical features and prognosis of this rare disease, and discusses the differential diagnosis with MCN. There is no discussion about the "multimodality imaging findings", which is shown in the title. Compared with other literature, this is the novel content of this article. In recent years, imaging diagnosis has shifted from focusing on pathological diagnosis to grading diagnosis based on aggression and prognosis. For example, LI-RADS, PI-RADS and BI-RADS. Incidental pancreatic cyst management is a hot topic in pancreatic imaging for many years. The guidelines ACR2017 and Fukuoka2017 are currently applied. My suggest is to add the discussion of management of pancreatic cystic lesions base on this case. I believe this will make the case report unique and of higher academic value. 1.add the discussion of “multimodality imaging findings” or management of pancreatic cystic lesions base on this case. 2.In "Further diagnostic work-up"part. "Radical resection of the pancreas was planned". Do you mean "Radical resection of the pancreatic tumor was planned. " 3. Please present the normal range of CA19-9 and CEA.

Response:

We thank the reviewer #2 for these considered and supportive comments. We are confident that your suggestions will improve the value of our manuscript.

Specific comments and response:

2-1.add the discussion of “multimodality imaging findings” or management of pancreatic cystic lesions base on this case.

Response:

Thank you for your sincere comments. We have added management of multimodality imaging findings and management of pancreatic cystic lesions in the discussion session.

'Strategies to improve treatment options and prognosis for PSC remain limited due to its rapid progression and rare occurrence. We found that PSC also initially appears similar to other pancreatic cystic tumors in terms of chronologic changes and multimodality imaging findings. Given that no management guidelines for PSC exist, it may be necessary to refer to worrisome features and/or high-risk stigmata of the lesion, as detailed in the ACR 2017 guideline[12]. Therefore, evaluation of cystic pancreatic lesions using multimodality imaging is crucial, and serial follow-up imaging studies are helpful for treatment planning. CT is the primary imaging modality for evaluating pancreatic solid and cystic lesions but has some limitations. Endoscopic ultrasonography, MRI, especially T2-sequencing, is more useful for evaluating key features due to its superior soft-tissue contrast resolution.'

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2-2. In "Further diagnostic work-up"part. "Radical resection of the pancreas was planned". Do you mean "Radical resection of the pancreatic tumor was planned. "

Response:

Thank you for your detailed comment. We have revised the wording in the "Further diagnostic work-up" section, as follows:

'Radical resection of the pancreatic tumor was planned.'

2-3. Please present the normal range of CA19-9 and CEA.

Response:

Thank you for your kind comment. We have added these ranges, as follows:

'Laboratory analysis indicated both carbohydrate antigen 19-9 (CA 19-9; 6.39 U/mL) and carcinoembryonic antigen (CEA; 1.98 ng/mL) levels were within the normal range (CA 19-9, <27 U/mL; CEA, <4.7 ng/mL). Liver function tests and complete blood count results, except for a slightly increased WBC (12000/μL) count, were within the normal range.'

Reviewer #3

The case report was well designed and presented. However, there are two new publications on this subject, one is epidemiology research and the other is a case report. It is recommended to rearrange the discussion and the article within these publications. Relevant references are given below. 1. Pancreatic Carcinosarcoma Clinical Outcome Analysis of the National Cancer Institute Database. Alhatem A, Quinn PL, Xia W, Chokshi RJ. J Surg Res. 2020 Dec 3;259:62-70. doi: 10.1016/j.jss.2020.11.033. 2. Treatment of Rare and Aggressive Pancreatic Carcinosarcoma. ACG Case Rep J. 2020 May 6;7(5):e00379. doi: 10.14309/crj.0000000000000379. eCollection 2020 May.

Response:

We thank Reviewer #3 for the thorough review, positive comments, and insightful suggestions to improve our manuscript. Thank you for suggesting these relevant references, which we have included as per your suggestion.

Reference 4: Alhatem A, Quinn PL, Xia W, Chokshi RJ. Pancreatic Carcinosarcoma Clinical Outcome Analysis of the National Cancer Institute Database. Journal of Surgical Research 2020; 259: 62-70

'Following the first reported case of PSC in 1951, approximately 40 cases have been reported, with a mean patient age of 67 years[3,4].'

Reference 33: Quinn PL, Ohioma D, Jones AM, Ahlawat SK, Chokshi RJ. Treatment of Rare and Aggressive Pancreatic Carcinosarcoma. ACG Case Reports Journal 2020; 7: e00379

We have summarized and included this case report in Table 1, as follows:

'Quinn et al., 2020[33]

42/F Epigastric pain NM Body, tail 11.3 x 7.34 x 10.6 Complex cystic, multiloculated.'