

ANSWERING REVIEWERS



June 12, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10640-review.doc).

Title: A huge adenosquamous carcinoma of the pancreas with sarcomatoid change: an unusual case report

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Responses to the comments of Reviewer #1:

1. Interesting to note that CK7 was also positive in the sarcomatoid component, showing that the epithelial phenotype is still maintained, hence not a true sarcoma. Sometimes poorly differentiate squamous cell carcinomas may assume a "sarcomatoid" appearance. It would be interesting to see the immunoexpression of CK5/6 and p63 on the sarcomatoid component. Could this just represent a poorly differentiated squamous cell component?

Response: The sarcomatoid component was not a true sarcoma, in this point, we agree with reviewer. The sarcomatoid component has an appearance of transition from an epithelial morphology towards a sarcomatoid phenotype. In our opinion, EMT is a possible explanation for this phenomenon. We also examined that immunoexpression of p63 on the sarcomatoid component as the reviewer's suggestion, and it also indicated that the sarcomatoid component lost the epithelial phenotype.

Responses to the comments of Reviewer #2:

2. While the clinical presentation is nicely performed, the scientific component is overestimated. The authors checked only the E-cadherin and vimentin expression as possible markers of EMT. This is only descriptive analysis which is not enough to make a conclusion that the EMT is occurred. Thus, the authors should (i) change the title of their manuscript omitting the EMT, (ii) change or delete the last sentence in the first paragraph of the Discussion omitting the "...had undergone EMT", (iii) delete the sentence "In our case, portions of the pancreatic..." from the 3d paragraph as overestimated, and (iv) rewrite the conclusion – the last sentence of the last paragraph omitting the EMT.

Response: The suggestion from the reviewer is helpful and we had mad revisions in our manuscript. The title and the sentence which were mentioned by reviewer has been had mad revisions as the reviewer's suggestion.

Responses to the comments of Reviewer #3:

3. This is an interesting case report. A few comments as below: Title: "Epithelial-mesenchymal transition in huge adenosquamous carcinoma of the pancreas: an unusual case report" is too strong and

not very accurate. There is sarcomatous component in the adenosquamous carcinoma, and immunohistochemical analysis suggests or implies epithelial-mesenchymal transition. Abstract: "This report will provide a reference case for other surgeons." This is not a good sentence to end the Abstract. Introduction, 1st sentence: "Adenosquamous carcinoma always arises in organs that are predilection sites for adenocarcinoma, such as the gastrointestinal tract and uterus,". ... This should include pancreas, for the fact that adenocarcinoma is the most common histopathology of pancreatic cancer. Introduction, 3rd paragraph: "with the aim of providing a reference case for other surgeons." This sentence does not indicate the significance of this case report. Peer review: "This report will provide a reference case for other surgeons." This sentence does not indicate the significance of this case report. Need to mention and cite the following references that report sarcoma/adenosquamous carcinoma in other organs including thymus, esophagus, and stomach: Thymic carcinosarcoma consisting of sarcomatous and adenosquamous carcinomatous component. Liu YG, Sun KK, Sui XZ, Li JF, Wang J. Chin Med J (Engl). 2012 Nov;125(22):4154-5. PMID:23158163 Synchronous primary carcinosarcoma and adenosquamous carcinoma of the esophagus. Zhao S, Xue Q, Ye B, Lu H, He J, Zhao H. Ann Thorac Surg. 2011 Mar;91(3):926-8. PMID:21353036 Gastric carcinosarcoma, coexistence of adenosquamous carcinoma and rhabdomyosarcoma: a case report. Sato Y, Shimozono T, Kawano S, Toyoda K, Onoe K, Asada Y, Hayashi T. Histopathology. 2001 Nov;39(5):543-4. PMID:11737318

Response: The title and the sentence which were mentioned by reviewer has been had mad revisions as the reviewer's suggestion. The references which were mentioned by reviewer have been added in our manuscript.

Responses to the comments of Reviewer #4:

Major comments 1. Most of the readers are unfamiliar with epithelial-mesenchymal transition (EMT). Thus, additional description of EMT such as the relation of tumor invasion or metastasis with immunohistochemical staining may help further understanding of EMT. Please add the summary of case reports, if any. 2. Surgical resection is rarely indicated for pancreatic cancer with a diameter of 15 cm. Please add the status of vascular invasion such as celiac artery or SMA. Was there no vascular involvement due to the characteristics of expanding, not invading, nature of this tumor? Minor comments 1. Given the lack of evidence in Chinese traditional medicine, the description of post-surgical treatment course appeared unnecessary. 2. Please add the value of the other tumor markers such as CEA and SCC. 3. The author stated that surgical margins were negative. Please mention the exact postoperative pathological diagnosis such as vascular or lymphatic invasion.

Response: 1. We have provided additional description of EMT such as the relation of tumor invasion or metastasis as reviewer's suggestion. 2. Celiac artery and superior mesenteric artery were displaced but without involvement, however, splenic artery had been enclosed by the mass. We has explained it in our manuscript. The main point of our manuscript is that a routine radical surgery without aggressive treatment strategies was still appropriate for adenosquamous carcinoma of the pancreas with sarcomatoid change. The original sentences mad misunderstand for it. We had mad revisions to declare our original intent. The value of the other tumor markers such as CEA and SCC has been provided in our manuscript. The postoperative pathological diagnosis including vascular and lymphatic invasion has been declared in our manuscript.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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