Author's response to reviews

Title: Multimodality curative treatment of salivary gland cancer liver metastases with drug-eluting beads chemoembolization, radiofrequency ablation and surgical resection: A case report

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Author's response to reviews: see over
Dear Editor,

We thank you for your interesting comments and constructive criticisms of our manuscript entitled “Multimodality curative treatment of salivary gland cancer liver metastases with drug-eluting beads chemoembolization, radiofrequency ablation and surgical resection: A case report”.

We have revised the manuscript according to the reviewers’ suggestions. Please find below a point-by-point list of all the changes made. Underlined phrases denote amended or newly added text in the revised manuscript. We also attach an annotated text file with numbered lines where you can refer for each change and revision made.

Sincerely,

The authors,

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1st sentence: "A 51 year old female patient had a routine liver ultrasound examination, due to a history of large bowel polypectomies".

This is not evidence-based medicine, since there is no data to support the use of ultrasound examination as a follow-up tool in patients with polypectomy.

We agree with the reviewer that this is not an evidence-based indication for liver ultrasound. Nevertheless the referring physician requested the ultrasound for that reason and it would not be precise to state a different reason. We rephrased the phrase due to a history of large bowel polypectomies to following a history of large bowel polypectomies (line 77) to avoid any misleading statements.

Why MRI was first choice diagnostic tool after ultrasound and not contrast enhanced CT scan?

This was once more a choice of the referring physician. It was based mainly on the relatively young age of the patient. We agree that this is not the usual medical practice, but there is no contraindication in evaluating liver lesions by MRI. The phrase “Due to the relatively young age of the patient, in order to avoid exposure to ionizing radiation, the referring physician decided to further evaluate the lesions with MRI of the abdomen” (lines 80-82), has been added.
3d Paragraph sentence 2: The phrase "the patient was put on chemotherapy" needs to be changed.

This phrase has been replaced by the patient started chemotherapy treatment (line 99).

Why PET was selected as a follow-up examination after one year, especially since there was no earlier PET examination to be used a baseline.

In our effort not to get into too much details on the follow up of the patient we only mentioned the most recent imaging which was the MRI of the abdomen and the PET scan, leading to the reasonable remark of the reviewer. The patient had a CT of the neck, chest and abdomen 8 months after surgery, which was clear of any recurrent or metastatic disease. At the one year follow up, in an effort to reduce the radiation exposure we performed an MRI of the abdomen and a PET scan to screen the rest of the body, with a view to perform another CT at the 18months follow up. In order to make this clear we added the following to the text:

Case presentation (lines 132-133): Eight months after surgery a CT scan of the neck, chest, abdomen and pelvis was clear of disease.

Discussion (lines 187-195): The modality and frequency of follow up for such a metastatic tumor is not well-established. We used CT at 3 months and then at 8 months because a CT of the liver was also performed during the percutaneous radiofrequency ablation. At 1 year, in an effort to reduce the radiation dose we used an MRI of the abdomen and a PET scan, bearing in mind though, that since there was no previous PET the tumor could be PET negative and render a false negative result.
However the effective dose was reduced in this way from 25mSv (CT nech, chest, abdomen and pelvis) to 14mSv (PET scan with low dose CT) approximately.

Finally my major concern is the following:

Considering that metastases of adenoid cystic cancer are usually multiple and that survival with adenoid cystic cancer may be prolonged without treatment, it is unclear that resection of metastases prolongs survival The natural history of Malignant Salivary Gland Tumors is varied, and some patients remain asymptomatic for protracted periods of time. This is especially true for adenoid cystic carcinomas, particularly when metastases are limited to the lung. Although there is a wide spectrum of biologic behavior, median survival following the development of metastatic disease is approximately three years, substantially longer than expected for most other solid tumors. So according to my opinion it is not clear if the whole thrapeutic project will prolong the overall survival of the patient even though there is no metastatic disease at the one year of follow-up.

We agree with the reviewer about the biological diversity of the tumor. The patient presented had quite aggressive disease. Additionally for an otherwise healthy 51 years old patient, a survival of 3 years is not satisfactory and the rapid progression of the disease despite chemotherapy made as seek a more radical treatment modality. We have added a paragraph at the end of the discussion, explaining all that and making clear that there is no proof about the survival benefit, since this is only a case report and there is no long enough follow up.
Discussion (lines 197-207): Surgery is definitely not the treatment of choice for patients with liver metastatic disease from adenoid cystic carcinoma, since survival even without treatment can be prolonged and there is no solid evidence that resection of the metastases prolongs survival. The biologic behavior, though, of the tumor of this particular patient, bearing in mind the rapid increase in size of the lesions, was quite aggressive. Furthermore, the young age of the patient, rendered her a good candidate for surgery and urged us to offer a more aggressive therapeutic approach, in order to offer her a chance of living disease free and possibly prolonging survival. Nevertheless, further follow up is needed, since late recurrence is quite often in adenoid cystic carcinoma, but since the tumor burden has been reduced, any recurrence would be more easily treatable with radiofrequency ablation.