Author's response to reviews

Title: Renal cell carcinoma with intramyocardial metastases

Authors:

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Author's response to reviews: see over
Reviewer: Heinric Williams

Thank you for your case report. It showed what we already know about clear cell renal cell carcinoma: it can metastasize to any part of the body.

Authors response: Yes, the authors agree ccRCC may metastasize to any part of the body, but intramyocardial metastases are more unexpected – rare – finding.

One thing that is lacking from your report is whether all the sites you identified as metastatic renal cell carcinoma were biopsy proven metastatic deposits. I presumed the surgical resected sites were consistent with metastases.

Authors response: Yes, all surgical resection sites were consistent with ccRCC.

Your report also showed the role of metastatectomy in this disease but I am not sure if the later metastatectomies were indicated since it did not result in resection of all visible disease which is the principle of metastatectomy in renal cancer.

Authors response: Lesions were removed in order to confirm ccRCC and exclude secondary cancer. Moreover skin lesions removal also increased QoL of the patient. Femoral bone metastasis removal enabled to keep activity of the patient, who was able to walk without walking aid (cain, crutches or walker) until final deterioration. After bi-lobectomy of the right lung and total right hip replacement the patient was disease free.

Another benefit of this manuscript is the role of sequencing of systemic therapies, their duration of action, response rate and efficacy following previous systemic treatments.

Authors response: Data on importance of treatment sequencing has been cited in Discussion. The work of the authors has been presented and cited in this paragraph:


I must say that your case report discussing only the cardiac metastatic site is over-reaching since it was not the only site of metastasis and presented after the development of metastasis in other sites that were not cured with any of your systemic regimens. So it seems natural that the longer the patient lived, the more sites within the body would become involved. You could have easily made this a case report about scalp metastasis.

Authors response: Among metastatic site disease spectrum cardiac involvement has been selected as significant due to limited number of reported Intramyocardial ccRCC metastases and due to TKI treatment efficacy of this metastasis. No cardiac metastases TKI treatment monitoring was described before.

Nevertheless, I agree that cardiac involvement is rare but since it was just one of many sites affected and its involvement did not alter systemic treatment recommendations, it is just an interesting footnote.

Authors response: TKI based treatment could have not been modified in a sense of selecting best drug for this metastasis location, since no reports on TKI efficacy in intramyocardial lesions are known until now. In the future it may be expected that more tailored treatment may be available if more data will be reported (this and other cases) and more drugs (TKI or other) will be in the market. At the same time drug may be selected based on toxicity profile (i.e. pazopanib not relevant for patients with liver disease), but again no data on was available for this setting. In this case analysis we have shown that pazopanib is effective and may be well tolerated in cardiac metastases treatment. Intramyocardial metastases were selected as point of discussion also due to expected fatal disease course in subjects with cardiac involvement and possible cardiac toxicity following treatment with tyrosine kinase inhibitors. We aim to present intramyocardial metastases as relatively good prognosis (PFS 4 months) and support further treatment approach in such cases.

A few typographic errors with spacing which may be due to issues with my word processing software,

Authors response: Typographical errors have been corrected.
Also in the body of your manuscript, you describe Table 2 before Table 1, so recommend changing the order of your table in the manuscript or simply make Table 2 number 1 and vice versa.

Authors response: Tables order has been changed.
Reviewer: Zachary Smith

General comments:

It is astounding how much this patient had done to him. This is not standard treatment in the United States. Metastatectomy isn't done for all of those lesions as you presented. But interested, nonetheless.

Authors response: Lesions were removed in order to confirm ccRCC and exclude secondary cancer. Moreover skin lesions removal also increased QoL of the patient. Femoral bone metastasis removal enabled to keep activity of the patient, who was able to walk without walking aid (cain, crutches or walker) until final deterioration. After bi-lobectomy of the right lung and total right hip replacement the patient was disease free.

Major compulsory revisions:

1. The title is misleading. The use of "presenting with" makes it sound like the patient presented with cardiac mets as his initial symptom. It should read as "Renal cell carcinoma with intramyocardial metastases."

Authors response: the title has been corrected.

Minor Essential Revisions:

1. You mention Table 2 in your text prior to mentioning Table 1 (page 5, lines 77-79).

Authors response: As requested by other reviewer tables have been renumbered.

2. You don't first spell out ccRCC in the abstract before using that abbreviation. It is done in the text, but the abstract is a stand-alone entity and must be treated as such. No abbreviations should be used unless spelled out first in the abstract.

Authors response: ccRCC was spelled out in the abstract.

3. The last two sentences on page 5 (lines 83-86) are inappropriately placed. You should not make recommendations in the "Background" section. This should be in the discussion.

Authors response: Sentences have been placed in discussion.
Discretionary Revisions

1. The first paragraph on page 5 (lines 68-75) are not very applicable in their context. Maybe in the discussion they would be, but remember, your paper isn't about IVC thrombus.

Authors response: This data has been moved to discussion.

2. Page 6, lines 91 and 95, you use centimeters to measure size and then millimeters. May want to just choose one for consistency

Authors response: Centimeters have been used for consistency.