Author’s response to reviews

Title: SURGICAL TREATMENT OF ENDOPERITONEAL METASTASES FROM LUNG CANCER: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

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Author’s response to reviews:

Dear Editor, thank You again for giving us the opportunity to revise our manuscript as suggested by the reviewers. We hope it could be now considered for publication.

Sincerely,

the authors
Reviewer #3:

1. Do you believe the case report is authentic?
   
   Yes

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.
   
   Comments:

3. Does the Introduction explain the relevance of the case to the medical literature?
   
   Y

4. Does the article report the following information? Where information is missing, please specify.
   
   a. The relevant patient information, including:
      
      - De-identified demographic information (age, gender, ethnicity)
      - Main symptoms of the patient
      - Medical, family and psychosocial history
      - Relevant past interventions and their outcomes

   b. The relevant physical examination findings

   c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.
d. Diagnostic assessments, including:
   - Diagnostic methods
   - Challenges (e.g., financial, language/cultural)
   - Reasoning and prognostic characteristics (e.g., staging), where applicable

e. Types and mechanism of intervention

f. A summary of the clinical course of all follow-up visits

Comments:

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?

Comments:

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.

   Yes/No

7. Is the Abstract representative of the case presented?

   Comments: Needs Revision

   R.: The abstract has been revised.

8. Does the case represent a useful contribution to the medical literature?

   Comments: Yes, for a limited subset
9. Additional comments for the author(s)?

1. Language and grammar needs extensive editing and revision.
R.: language and grammar have been edited by English mother tongue.

2. Rephrasing some aspects of case summary and discussion is suggested.

3. Background needs revision and rephrasing.
R.: Background has been revised and rephrased.

4. Page 3-
HIPEC has not been evaluated in setting of peritoneal metastasis from lung cancer.
It doesn't deserves a mention in the background of mentioned cases.
R.: Thank You for the comment. According to your correct suggestion, the phrase about HIPEC has been amended in the background section.

Page 9; lines 37-40
"therefore cytoreductive surgery and HIPEC treatment protocols could be indicated in highly selected cases"
HIPEC is being proposed in peritoneal mets from lung cancer.
The authors must provide reference of any case where HIPEC was used in peritoneal mets from lung cancer to substantiate their proposal; though it has been used malignant pleural effusion.
R.: Thank You. We think data in this filed are to scarce to state about the possible role of HIPEC in these patients so far. The phrase was referred to other kinds of primary tumors in which HIPEC has been employed as investigational treatment. We corrected the mistake and clarified this in the text.
5. Page 4, lines 14-20

Taxol is perhaps a brand name - replace with generic name or give credit to the brand.

Taxol was replaced by gemcitabine will be better.

R.: Also according to other reviewer comment, the term “taxol” has been replaced with “paclitaxel”. Rephrased as suggested.

6. Page 5

"Chest x-ray showed a "ground glass" picture of left lung and bloodstream cultures were positive for candida albicans spp."

Was this patient immunocompromised ?

Did sputum or expectorate examination also showed Candida ?

R.: The patient was not immunocompromised. Also expectorate cultures were positive for candida. This has been added in the text.

7. Page 6; lines 33-43

Cytological examination of fluid is repeated.


8. Page 7

"these are the first literature report of diffuse peritoneal spread from lung cancer."

It doesn't appears diffuse as CC score was zero and it involved multiple sites in a segment.

R.: Thank You for the comment. In the first patient, peritoneal metastases were found in omentum, right, transverse and left colon, as well they interested the spleen. So debulking surgery was extensive and aimed to remove all the visible disease (CC-0). Indeed, in the second patient, peritoneal involvement was confined to the right colon. Nevertheless, the phrase has been changed in the text.
"indicated in isolated peritoneal metastases from lung cancer"

Here it is isolated mets.

R.: The term “isolated” has been deleted, since in the first patients, there were multiple peritoneal metastases.

9. The need for HPE picture of lung pathology and vis a vis peritoneal pathology would have added more substance.

R.: Thank You. Indeed we strongly agree with you but we weren’t able to retrieve pictures of HPE of lung cancer since the two patients underwent thoracic surgery in different hospitals from ours and, although we repeatedly asked for them, we did not have any answer from them.

Reviewer #5:

1. Do you believe the case report is authentic?

No

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.

Present

3. Does the Introduction explain the relevance of the case to the medical literature?

Yes
4. Does the article report the following information? Where information is missing, please specify.

a. The relevant patient information, including:
   - De-identified demographic information (age, gender, ethnicity)
   - Main symptoms of the patient
   - Medical, family and psychosocial history
   - Relevant past interventions and their outcomes

b. The relevant physical examination findings

c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.

d. Diagnostic assessments, including:
   - Diagnostic methods
   - Challenges (e.g., financial, language/cultural)
   - Reasoning and prognostic characteristics (e.g., staging), where applicable

e. Types and mechanism of intervention

f. A summary of the clinical course of all follow-up visits

Comments: Above mentioned information was reported

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?

Well balanced
6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.

Yes

7. Is the Abstract representative of the case presented?

Yes

8. Does the case represent a useful contribution to the medical literature?

Yes

9. Additional comments for the author(s)?

Interesting case reports. Please consider modifications as discussed below.

Abstract introduction -

Line 3-6
Lung cancer is one of the most common neoplasms in the world with early metastases and is associated with poor prognosis in advances stages

Line 17
But - add comma - But, Its
R.: Thank You, added
Background - Line 14
Spelling needs to be changed to Pseudomyxoma
R.: The phrase was changed and “primary peritoneal malignancies” cited.

Line 34 - the literature instead of literature

Case report -

Change Taxol to Paclitaxel through out the case report
R.: Changed

Sm needs to changed to m2
R.: Changed

Line 23 Case report - 39 year instead of years
R.: Corrected

Line 51 - Considering the previous toxicity to taxol no other drug was associated - what does this mean - ?? Considering previous toxicity to Paclitaxel - no other drug was used.
R.: Corrected. Thank You
Discussion -

Line 23 - a poor prognosis

Line 28 - please consider changing to - mostly from the breast cancer (40.8%), followed by lung cancer (25.6%)

Line 34 - series, this - add comma

Line 37 - It is, therefore, possible - add commas

Line 46 - history of a pleural - remove a

Line 48 - 51 - but to our knowledge, these are the first literature report of diffuse peritoneal spread from lung cancer.

I saw in the discussion - In the recent review from Balla et al. (15), the reported patients with clinically obvious peritoneal metastases from lung cancer

How can this be the first report

R.: Sentence has been changed and better explained: in our knowledge, there is no case in literature similar to our first patient who had a wide extension of the peritoneal disease and underwent an extensive debulking surgery, very unusual for lung cancer metastatic patients, even in the most consistent literature experiences.

Line 43-51
In the recent review from Balla et al. (15), the reported patients with clinically obvious peritoneal metastases from lung cancer are 191, and disparity with autopic series suggest that most cases are asymptomatic or unreported (16,17).

Sentence needs clarification - I reviewed the article and there were 91 patients and 2 patient did have peritoneal metastasis. This contradicts the earlier statement made by authors [but to our knowledge, these are the first literature report of diffuse peritoneal spread from lung cancer]

Autopic need to be changed to autopsy
R.: The reported number of patients was a typo. Sentence has been clarified.

Line 51-60

Similarly to our patients, the emergency onset with bowel obstruction and/or bowel perforation make the surgical treatment necessary and explains, together with the concomitant presence in more than 60% of the patients of associated extrabdominal metastases (11,12), the poor prognosis

Please break it down into two sentences to make it simple.
R.: The sentence has been rephrased and made simple.

References need to be adjusted as per JCMR format
R.: References have been checked and revised.