Peer review file

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Reviewer A

I appreciate the author's effort in writing up this interesting and rare case reported related to the extraintestinal manifestation of TB.

Please, refer to the attached pdf for comments/suggested corrections.

Comments 1: “She started anti-tuberculosis and somatostatin analogue therapies, the tuberculosis treatment was considered completed and the somatostatin analogue therapy was continued for 21 months providing stable and symptom-free disease”. Rewrite this highlighted sentence for better comprehension.

Reply 1: We have modified our text as advised (See Page 3, lines 49-54).
Changes in the text: “Anti-tuberculosis treatment was prescribed, and somatostatin analogue therapy was introduced one month later. The tuberculosis treatment was finished, and the patient remained on somatostatin analogue for 21 months. During this time the symptoms of abdominal pain and diarrhea disappeared, and her body weight increased 35% over her baseline weight”.

Comments 2: “…was again a response for more than a year…” (Page 3 Line 54) Describe response.

Reply 2: We thank the reviewer you for this comment. The sentence was rewritten in order to make it clearer (See Page 3, lines 57-59).
Changes in the text: “She was forwarded to another Hospital to be treated with 177Lu-DOTATOC. The symptoms improved and the patient remained symptom free for more than a year…”.

Comments 3: “The SA therapy was returned, and she presented with controlled disease

for more 18 months when a new progression was documented". Rewrite this sentence correcting the grammar.

Reply 3: We thank the reviewer you for this comment. The sentence was rewritten in order to make it clearer (See Page 8, lines 173-176).
Changes in the text: "The SA treatment was reintroduced and resulted in controlled disease; however, a new disease progression was documented 18 months after the reintroduction of SA therapy."

Comments 4: In addition, would recommend adding more recent references if appropriate.
Eg: 1. Chakinala RC, Khatri AM. Gastrointestinal Tuberculosis. In: Stat Pearls. Treasure Island (FL): StatPearls Publishing; May 30, 2020. (https://pubmed.ncbi.nlm.nih.gov/32310575/).

2. Chakinala RC, Farkas ZC, Barbash B, et al. Gastrointestinal Tuberculosis Presenting as Malnutrition and Distal Colonic Bowel Obstruction. Case Rep Gastrointest Med. 2018;2018:2808565. Published 2018 Feb 27. doi:10.1155/2018/2808565 (https://pubmed.ncbi.nlm.nih.gov/29682364/).

Reply 4: We thank the reviewer for this comment. We included these references in the manuscript. The reference list has been updated.

Reviewer B

Thank you for this interesting and rare case report. Here are a few comments to help improve the article before approval.

A) Major revisions

Comments 1: The authors should better highlight in the abstract and in the main text (especially in the conclusion section) why this case report is interesting. It is not only a

matter of association of EPT and immunosuppression/cancer, it is also a matter of differential diagnosis (briefly mentioned in the abstract). Occlusion is often the consequence of a midgut NET (intestinal), and since here we conclude in a small bowel G2 NET it was quite remarkable to find CT instead to explain the occlusion. That does not exclude the presence of an unseen intestinal lesion by the way....

Reply 1: We thank the reviewer for this substantial comment. We agree with the reviewer's comment that this topic could have been better explored in the abstract and conclusion section. As suggested, these topics were detailed accordingly (See Page 3, lines 42 and 43. Pages 3 and 4, lines 62-65. Page 12, lines 252-254).

Changes in the text:

Abstract section:

"Here we present a rare case of intestinal subocclusion that was supposed to be caused by cancer and was indeed caused by colonic tuberculosis (CT) in a patient with metastatic neuroendocrine tumor (NET)".

"We must keep this hypothesis in the differential diagnosis of our patients since symptoms of CT are usually nonspecific. At colonoscopy, radiological features are strictures, colitis and polypoidal lesions and complications such as bowel perforation or fistula must be in mind. It is particularly important those with advanced disease in endemic areas of tuberculosis".

Conclusion section:

"The importance of this report is to raise the suspicion of EPT, in particular IT. Another point to be highlighted is the differential diagnosis of intestinal occlusion in cancer patients. In the presented case, the finding of IT causing the occlusion instead of a most probable cancer cause was unexpected and exceptional. The combination of..."

Comments 2: Why was the colonoscopy performed before the computed tomography?

Reply 2: We thank the reviewer for this comment. We suggested a small sentence to be added (See Page 6; lines 112 and 113).

Changes in the text: The patient was referred to our hospital to perform a hepatic biopsy based on previous abdominal images that revealed multiple liver nodules and weight

loss. The initial work-up of consumptive syndrome…"

Comments 3: Figure 2 legend is a little confusing regarding timing. Please also specify here that A and B are baseline images.

Reply 3: We thank the reviewer for this comment. The sentence was rewritten in order to make it clearer (See page 15, lines 314 and 318).
Changes in the text:
"Figure 2. Baseline and follow-up imaging studies:
Baseline (2A and 2B): 2A) Dynamic contrast-enhanced CT scan during the portal phase showed a 10,3cm mass with necrosis in segment VIII of the liver; 2B) Diffuse parietal thickening with submucosal edema and mucosal contrast enhancement in the transverse colon. Follow up (2C and 2D): 2C) Dynamic contrast-enhanced CT scan during the portal phase showed a partial response of the larger mass in segment VIII of the liver 5 years after diagnosis; 2D) Heterogeneous tumoral enlargement of both ovaries 5 years after diagnosis".

Comments 4: Was any baseline functional imaging performed? before or after urgent surgery? If yes, what type and please give results. Especially in the context of occult NET. Also, it would be interesting to have the results regarding tuberculosis lesions uptake.

Reply 4: We thank the reviewer for this comment. No, it was not available in our institution at the time of diagnosis. A functioning imaging was performed after progression and before 177Lu- DOTATOC therapy when there was no active tuberculosis anymore. "We can add this statement (see Page 8; lines 163 and 164).
Changes in the text: "Functional imaging was not performed because it was unavailable at our hospital in that time."

B) Minor revisions

Comments 1: Please check again for English language. Here are some remarks/mistakes

Line 39: 'is often associated with"

Line 53: "she was referred to receive"

Line 162 "for 18 more months"

Line 178: "but also a clinical manifestation"

Line 205: "the most probable source

Line 207: "the entire population is probably..."

And others I certainly missed

Reply 1: We thank the reviewer for these remarks. They were replaced accordingly.

Changes in the text:

Line 39: “is often associated with"

Line 57: "she was forwarded to another hospital to be treated with…"

Lines 173-176: “the sentence was rewritten according to reviewer #1 “The SA treatment was reintroduced and resulted in controlled disease; however, a new disease progression was documented 18 months after the reintroduction of SA therapy.”

Lines 193-195: "The cachexia could be a consequence of the untreated carcinoid syndrome and NET as well as a consequence of advanced tuberculosis.”

Line 214: “rheumatic disease”

Line 216 “and hemodialysis”

Line 221: “The most probable source”

Line 225: “food policies in the risky populations”

Comments 2: Please specify in the main text that the G2 NET lesion showed indeed well differentiated morphology

Reply 2: We thank the reviewer for this remark. This was replaced accordingly (see Page 3, line 48).

Changes in the text: “The liver biopsy revealed a well differentiated grade 2 NET and the mycobacterial culture…”