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Beijing, China

Nov 3, 2019

Dear Editors:

We are resubmitting our manuscript titled *"Rare adult jejunum lymphangioma manifested as gastrointestinal bleeding with hypogammaglobulinemia: A case report and literature review "(No. 51563)* to be considered for publication in *World Journal of Clinical Cases.* We have addressed all the comments of the reviewers and editors in our point-by-point response below.

We thank you for your considerations and look forward to publishing our findings in *World Journal of Clinical Cases*.

Sincerely,

Bei Tan, MD and Jia-Ming Qian, MD, on behalf of the authors
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Point-by-Point Responses:

Reviewer #1:

Q1. This is a very interesting Case Report of a very unusual benign tumor of the jejunum. The description is very clear and well done. The figures are of good quality. The review of the literature is good and the proposed way of acting is very useful.

A1. We appreciate the reviewer for this positive comment.

Reviewer #2:

Q1. In the manuscript entitled, "Rare adult jejunum lymphangioma manifested as gastrointestinal bleeding with hypogammaglobulinemia: A case report and literature review", the authors present a case of a patient with obscure overt bleeding who ultimately was found to have a cavernous lymphangioma in the jejunum. The case is generally written well and describes a fairly rare scenario.

A1. We thank the reviewer for this comment.

Q2. Some clarification is needed in various parts of the manuscript. Additional comments and suggestions, many of which can be easily resolved and are intended to strengthen the manuscript, are provided below: Title: -It is difficult to read, in part because it is so long. Please consider revising, e.g. to "Jejunal cavernous

lymphangioma manifested as gastrointestinal bleeding with hypogammaglobulinemia: a case report and literature review" Abstract: -A comma is not needed in this sentence as there is only one independent clause: "We also summarize and analyze all 22 reported cases from 1961 to 2019, and propose an algorithm for identification and management of small bowel lymphangioma." - "We present a case of 29-year-old female, initially presenting…" should be changed to "We present the case of a 29-year-old female initially presenting…"

A2. Thank you so much for your kind suggestion.

We revised the title as "Jejunum cavernous lymphangioma manifested as gastrointestinal bleeding with hypogammaglobulinemia in adult: a case report and literature review", as the reviewer suggested. Pls kindly allow me to reserve the word "adult" in the title, for this disease is especially rare in adult patients.

According to the reviewer's kind suggestion, we revised the abstract as "We also summarize and analyze all 23 reported cases from 1961 to 2019 and propose an algorithm for identification and management of small bowel lymphangioma.", the comma was deleted. And the words were modified to "We present the case of a 29-year-old female initially presenting with persistent melena and iron-deficiency anemia accompanied with hypogammaglobulinemia."

Q3. There is no mention of the source of bleeding/melena. How do the authors know it was from a lymphangioma?

A3. Thank you for this inquiry. Since the capsule endoscopy assessed the whole small intestine, both the capsule endoscopy and double-balloon enteroscopy (DBE) revealed the primary lesion with visible fresh blood stains, and all other bleeding sources from upper/lower GI were already first excluded by the esophagogastroduodenoscopy (EGD) and colonoscopy, therefore we believed the primary lesion of 3×2cm in the middle jejunum with visible fresh blood stains was the source of bleeding/melena.

Q4. It's odd that the authors would write, "CT and capsule endoscopy/enteroscopy as first- and second-line examination, followed by curative surgery with histological diagnosis will be ideal algorithm." even though CT (enterography at that!) was falsely negative for tumor.

A4. Thank you for your kindness to point this out. We rewrote the abstract conclusion part as "We first recommend CT to identify or exclude the possibility of intussusception, as well potential discovery of lesion with two-fifth chance. Then, we recommend capsule endoscopy and enteroscopy following negative CT to identify and mark the lesions. Finally, laparoscopic surgery with histological diagnosis is the ideal curative method."

Q5. Core tip: Needs extensive English language review. Text: Needs extensive English language review.

A5. Thank you for your suggestion. The English language of core tip and text were re-reviewed and polished again, pls check.

Q6. Can the authors comment on the difference between a lymphangiectasia, lymphangioma, cavernous lymphangioma, and lymphangiosarcoma, and which of these (if not all) can be found in the GI tract?

A6. We are very grateful for this suggestive comment. The following sentences were added to the DISCUSSION (line 248-255).

"Since lymphangioma in adult can be asymptomatic and varied, we need to distinguish it from lymphangiectasia. The superficial mucosal layers and consists of confluent dilated spaces with a smooth muscle component are more involved in lymphangioma. While lymphangiectasia consists of more widely spaced mucosal and submucosal cystic spaces, which lack smooth muscle and prominent endothelial lining. Hence, lymphangioma can be reliably distinguished from lymphangiectasia by pathologic characteristics [26]. However, lymphangiosarcoma scarcely involves gastrointestinal tract in adult."

Q7. How did the authors find/search for the previous cases? What were the search criteria? Was this case overlooked?
https://www.ncbi.nlm.nih.gov/pubmed/28270661

A7. Thank you so much for pointing out this missed case. It was added as case 4 in Table 1 and Reference 5, also included into the further summarized and analyzed in the DISCUSSION part. The search strategy was described in the INTRODUCTION part as follows:

"We searched 'lymphangioma', 'small intestine', 'small bowel', 'jejunum' and 'ileum' as key words in MEDLINE and PubMed from inception up to September 1, 2019 with full text available. The patients with mesenteric lesions were excluded, and no language limitation was set. Totally, 23 reported cases were included for further summarized and analyzed, aiming to propose our suggested algorithm for identification and management of small intestine lymphangioma. "