November 29th ,2020

Dear Editors of *World Journal of Gastroenterology,*

We are pleased for the opportunity to submit a revised version of our manuscript entitled “Primary Intestinal Lymphangiectasia in an adult patient - Case Report and literature review of a symptomatic chameleon”. We are grateful for the comments of the reviewers and the editors. Please find a detailed response letter addressing each of the mentioned points attached.

We strongly believe that our manuscript is of interest for readers of *World Journal of Gastroenterology,* and are looking forward to receiving your editorial decision.

Sincerely,

Rudolf Huber and Christian Datz,

on behalf of the co-authors

Reviewer#1: Dear editor, I'm glad to have chance to review the manuscript. Actually, the author showed us a very good clinical case of primary intestinal lymphangiectasia, providing a practical approach to facilitate diagnosis and therapy of PIL in adults. However, several questions are needed to be answered, which may make the case more complete.

1. Is there internationally recognized criterion of the diagnosis of PIL?

R: We want to thank reviewer#1 for these encouraging words. Unfortunately, there are no established criteria for the diagnosis of PIL. However, as stated by previous reviews on this topic, the requirement for histological diagnosis is essential.

The author showed that the diagnosis of primary intestinal lymphangiectasia was established after 22 weeks by histological analysis of biopsy samples obtained via enteroscopy? Why it is 22 weeks?

R: Thank you for this point. As highlighted in our literature review, the mean time to diagnosis in PIL was 3 (0-40) years according to the published case reports. However, this is mainly influenced by the onset of symptoms and the individual patient's perception, and likely explains the large variation. In our patient, symptoms started at the age of 12, and final diagnosis was established at the age of 34. The patient initially underwent a thorough medical examination in another hospital. At our institution, 22 weeks passed by until the correct diagnosis was established following computed tomography, magnetic resonance imaging, gastroduodenoscopy, colonoscopy, video capsule endoscopy and double-balloon enteroscopy.

2. Scales are needed for the figures.

R: We have provided scales for the figures in the respective legends.

3. If the author could provide the review result of colonoscopy and pathology results for comparison after 2-year- follow-up, this case will be more complete.

R: We have established the diagnosis of PIL in this patient in December 2018, hence nearly two years ago. Although endoscopic reevaluation to investigate histological changes would be desirable, this was refused by the patient due to several reasons: Firstly, due to the significant improvement of her clinical situation, she is free of

symptoms now, and thus does not feel the need for an endoscopic intervention with potential complications. Secondly, due to the recent birth of her second child, she is still breast feeding. Understandably, she refuses to take this additional risk of potential side-effects also affecting her child. Thirdly, due to the COVID-19 situation, resources are limited for “elective” procedures. Thus, only essential endoscopic procedures are performed since April 2020. Therefore, we are unable to provide data on histological and endoscopic follow-up, although we would be very interested in these data ourselves.

Reviewer#2: This case report and review about the characteristics and treatment of primary intestinal lymphangiectasia (PIL) is instructive and beneficial. PIL is an uncommon disease in clinical work and the author has introduced this disease in detail to us. Here are my recommendations after revising the paper.

（1） The author should present us how the patient’s condition changed during the 8 weeks of follow-up after treatment. Actually, the author has given us an introduction in detail about the patient’s symptoms and examination results and told us the procedure of how PIL was diagnosed. But as to the treatment of this patient, the words can’t let us know what happened after treatment in this case report. Did the medium-chain triglyceride (MCT) diet work after a short or a long time? Maybe the author could show us what happened to this patient during the 8 weeks of follow-up.

R: We want to thank reviewer#2 for his critical review of our case-report. We further interviewed the patient and found that symptoms disappeared continuously, being markedly improved from week 4 after initiation of MCT-diet. Until today, symptoms nearly completely resolved with only mild lower limb edema between the end of breastfeeding period and a second pregnancy, while abdominal discomfort, fatigue and nausea significantly improved.

（2） The author could give us your own thoughts and experience about how to diagnose this disease and develop a treatment strategy. PIL is so rare that the gold standard and treatment strategy have not been raised yet. The author has

met it, reported it and reviewed it. Combined with this case, I think the author could present some suggestions that how to make a diagnosis and cure PIL.

R: Thank you for this point. Since we also felt that a clear strategy to diagnose PIL is missing, we have provided an extensive literature review and systematically assessed the published literature to guide decision making. Please find a strategy for diagnosis and treatment in the Graphical Abstract, as well as the evidence behind these steps in the Discussion section and the supplementary materials.

Reviewer #3: I am pleased to be invited to review this prominent work, and it makes me step foreward in gastric diseases. Like many age-related diseases, PIL has the prevalence in childs and youngersters. Among adults it is rare. In this article, a 34-year woman suffered from PIL was reported completely through symptoms to pathological diagnosis, and compared with other diseases with same conditions. It is very good. It is well written and organized, nearly has any shortages in grammar or language need to be changed. Only the limitation I suggest is the examples fo literature review is relatively less, if possible, authors should amend it as large as possible.

R: Thank you for your review of our manuscript. Since the number of references is recommended to be between 30-60 for a case report, we did not include all evaluated case reports in the main manuscript (in total, these include 61 studies alone for the literature review). However, we addressed your point and included all references included in the literature review on diagnosis and therapy to the main file.

Reviewer #4: Rudolf et al. present the case of primary intestinal lymphangiectasia in a 34-year-old woman, and the diagnosis was performed on histological and immunohistological analyses from jejunal biopsies. At the same time, they provided a literature review of the pubslihed case reports, and assessed the clinical presentation. Therfore, the paper will provide a practical approach to facilitate diagnosis and therapy of PIL in adults.

R: Thank you for these encouraging words.

Science editor: 1 Scientific quality: The manuscript describes a case report of the primary intestinal lymphangiectasia. the topic is within the scope of the WJG. (1) Classification: Grade A, Grade B, Grade B and Grade C; (2) Summary of the Peer-Review Report: The author showed us a very good clinical case of primary intestinal lymphangiectasia, providing a practical approach to facilitate diagnosis and therapy of PIL in adults. However, several questions are needed to be answered. Scales are needed for the figures. If the author could provide the review result of colonoscopy and pathology results for comparison after 2-year- follow-up, this case will be more complete. The questions raised by the reviewers should be answered; and (3) Format: There is 1 table and 3 figures. A total of 16 references are cited, including 3 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A, Grade A, Grade A and Grade A. 3 Academic norms and rules: The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, written informed consent, and fill out the CARE Checklist–2016 with page numbers. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJG. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (2) I found the "Case Presentation" did not meet our requirements. Please re-write the "Case Presentation" section according to the Guidelines and Requirements for Manuscript Revision. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

R: We want to thank the scientific editor for reviewing our manuscript. We have answered all questions raised by the reviewers, and included COI forms, a Copyright License Agreement, and the CARE Checklist–2016 within our revised version. Furthermore, we provide all figures using PowerPoint, and re-arranged the section "Case presentation" accordingly.