Author’s response to reviews

Title: A literature review and case report of severe and refractory post-colectomy enteritis

Authors:

Yingyun Yang (yingyunyang@126.com)
Yuan Liu (ly880817@126.com)
Weiyang Zheng (oven186@126.com)
Weixun Zhou (zweixun@163.com)
Bin Wu (wubin0279@hotmail.com)
Xiyu Sun (sunpumch@126.com)
Wei Chen (chenw@pumch.cn)
Tao Guo (guoqiong990@126.com)
Xiaqing Li (lixiaoqing20060417@126.com)
Hong Yang (hongy72@163.com)
Jiaming Qian (qianjiaming1957@126.com)
Yue Li (yuelee76@gmail.com)

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Author’s response to reviews:

Dear Editor,

We would like to thank the editors for giving us a chance to resubmit our paper, and thank the reviewers for giving us such constructive suggestions which helped us in improving the quality of our manuscript. Here we submit a new version of our manuscript with the title “A literature review and case report of severe and refractory post-colectomy enteritis”, with revisions according to the reviewers’ suggestions. Efforts were also made to improve language of the paper, with the help of language editing services.

The following is a point-to-point response to the reviewers’ comments.

And wish you all a happy new year!
Sincerely yours,
Yue Li

Reviewer #1
General comments: The case is interesting but there are numerous things that needs to be revised in my opinion. The English language needs to be revised by a native English speaking. It is right now quite difficult to follow the history of the case after IPAA surgery was performed.
Response: Thank you so much for mentioning the problem of English language quality. To improve our manuscript and to make it easier understood by potential readers, we have used Nature Research Editing Service’s language support to edit our manuscript, and the certification file is attached.

Comment 1: Was the inflammation in the diverted pouch only or truly a pan enteritis? If it was the previous, I can understand why a closure of the stoma would possibly work but not in the case of a pan enteritis.
Response: Thanks for raising this important question. To explain this, actually we not only noticed inflammation in diverted pouch, but also noticed inflammation in tissue biopsies taken in both duodenum and pre-stomal ileum. Thus, we infer the inflammation was truly a pan enteritis. To make it clearer stated, we rewrite some sentences in the Case Presentation part, paragraph 2, line 23-30.

Comment 2: Were the stool cultures taken from the diverting ileostomy and/or from the diverted pouch? E.g. a bacterial over growth in the diverted pouch has triggered the inflammation?
Response: Thanks for this great comment. The stool cultures were taken from the diverting ileostomy stoma. We revised the sentence in the Case Presentation part, paragraph 2, line 11-13. And we do appreciate the thought of bacterial overgrowth triggered inflammation, we think this is one possibility. However, could bacterial overgrowth in the diverted pouch trigger inflammation just in the pouch or could also trigger pan-enteritis is unknown yet, and unfortunately couldn’t be implied from this case. If we could luckily meet another similar patient, we will try to do more stool tests from both sites. And we added this to the Discussion Part, paragraph 5, line 7-11.

Comment 3: The included endoscopic findings seems a bit unclear and I would like to have seen the diverted pouch endoscopically as well as histologically and compared with the ileum proximal of the stoma.
Response: Thanks for this valuable comment. We only chose endoscopic photos of the duodenum and neo-ileum before and after ileostomy closure (Figure 2). The pictures of the diverted pouch were not shown in the manuscript. Following are photos of the diverted pouch. Although there is patchy inflammation in the pouch body, it could not explain the high volume of output from the ileostomy. That’s the reason why we did not include these in the manuscript. (The pictures please see the supplemental files.)

Comment 4: Was it ever tried to feed the diverted pouch with luminal content, nutrition or at least rinsed?
Response: Thank you for raising this important question. Since this patient’s major symptom was
watery stool from ileostomy stoma not her diverted pouch, we never feed the diverted pouch. There was no symptom related with her diverted pouch throughout.

Comment 5: Apart from stool cultures, were there viral analyses performed, especially as she previously was suffering from CMV?
Response: Thanks for this comment. This is an important supplement. In fact, we have performed the tests of CMV-DNA, CMV-pp65 and EBV-DNA which all came out negative. We have added these results to the second part of Case Presentation, paragraph 2, line 14-15.

Comment 6: Were she on any medications prior to admittance, e.g. NSAIDs that can alter the mucosal barrier?
Response: She was not on any medication that may influence the mucosal barrier, including NSAIDs. Her steroids were stopped before the end of April 2015. We make sure this point is clarified in the second paragraph of Case Presentation, paragraph 2, line 15-16. Thanks for this kind remind.

Comment 7: Please discuss if this could have been a secondary reaction to a long term electrolyte and/or fluid deficit due to border limit high stoma output for an extended time leading to secondary intestinal failure?
Response: Thanks for proposing the possibility of secondary intestinal failure here. Since the patient went through severe disturbance of hemodynamics. It is very difficult to rule out the impact of electrolyte and/or fluid deficit on intestinal failure. However, considering the patient’s symptoms, lab results endoscopic and histologic findings and reactivity to treatment collectively. We believe that post-colectomy pan enteritis is the true diagnosis to this case. We are glad to leave the possibility of secondary intestinal failure in discussion and have already added it to the discussion part accordingly, in paragraph 13-16.

Comment 8: The discussion lacks a discussion on possible causes and why a closure of the stoma was discussed as well as why it might have worked.
Response: In paragraph 5 of discussion and conclusion part, we preliminarily discuss the possible causes including inflammatory response, change of fecal stasis after ileostomy and post-surgical ischemia. We believe there may be varied causes of post-colectomy enteritis that are not fully understood, because some of the cases reported are more severe and complicated than others. In our case, the patient benefited from closing of her ileostomy indicating that reestablishment of nature fecal stream might have played a positive role. We have emphasized this point in the discussion part. More cases and fundamental research are required to investigate the pathogenesis of this condition.

Reviewer #2
Comment 1: The authors have reviewed the literature, but the paper would benefit from adding more detail on the search strategy used, so that other researchers could replicate the search. For example, what time period for publication was considered? Which languages were searched? What was the date of the search? Were there any exclusion criteria?
Response: We searched PubMed, Medline and EMbase databases, for case reports and case series by the combination of ‘ulcerative colitis’ and ‘post-colectomy enteritis’ or ‘pan-enteritis.’
Since there is a literature review of 42 cases published in 2008, we include 10 other cases that have been reported together with our case from 2008-1-1 to 2018-6-17 which are published in English or with an English abstract. There are no other exclusion criteria. We have clarified in the paper, in Discussion and Conclusion part, paragraph 2, line 3.

Comment 2. The authors have proposed a diagnostic algorithm and treatment strategy based on a very small number of case reports. It would be valuable for readers if the authors could expand in the discussion on how the evidence they have supports this algorithm, and what experiments would be able to provide evidence to support its use (RCTs, observational studies etc.).
Response: Great thanks for this valuable comments. Diagnostic algorithm and treatment strategy based on few cases are surely limited in application. Here we raise merely a proposal. A positive result of a RCT or observational study will be extremely helpful in empowering the conclusion. Unfortunately, post-colectomy enteritis of UC patients is a relatively rare condition. Study based on cases is much more feasible in reality. We explain in the discussion part how the available evidence supports our algorithm, in paragraph 4.

Comment 3. The authors should add descriptive captions or titles to each figure, to clarify what each panel shows and make it more comprehensible to readers.
Response : Thanks to this comments. Adjustments have been made accordingly.

Comment 4. The current way the timeline of the case is presented was confusing to this reader. Please consider labelling the colour of the boxes and making the grey timeline linear.
Response : Great thanks for reminding us this problem. We made some adjustments, including adjusting the timeline figure to horizontal and adding some arrows, trying to make it easier to understand.