

Dear Editor,

Thank you very much for your decision letter and advice on our manuscript entitled “Unexplained septic shock after colonoscopy with polyethylene glycol preparation in a young adult”. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our study. We have addressed the comments raised by the reviewers which we hope meet with approval, and the amendments are highlighted in yellow in the revised manuscript. In addition, our point-by-point responses to the comments are listed below in this letter. Thank you very much.

Yours sincerely,

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## Response to Reviewer 1

What is Tezhixing authors need to clarify agent for western readers 2. Clearly this patient had issues" not necessarily healthy" belching diarrhea ect authors should discuss abnormalities in Gut microbiome as a predisposing factor 3. what were pts risk for bacterial translocation? what were albumin levels any pre colonoscopy labs.

**Response:** 1.The author of this article mainly wants to clarify that if septic shock occurs after gastrointestinal endoscopy, PEG maybe the murderer after excluding common factors.

2. The author also considered that the patient may have a basis of intestinal flora imbalance, which is explained in the DISCUSSION Paragraph 2.

3. In the DISCUSSION Paragraph 2 Line 14-17 and Line 20-22, We added risk explanation for gut bacterial translocation. In the History of past illness, we listed laboratory examinations including albumin as normal.

## Response to Reviewer 2

1: [...] The male's previous physical examination showed no abnormal indicators and colonoscopy showed normal [...] Please specify to what do you refer as "normal"..

**Response:** We listed in the History of past illness that the patient's previous laboratory examinations and imaging examinations were normal and added description of the patient's normal colonoscopy result.

2: [...] Immediate resuscitation and intensive care with appropriate antibiotics [...] Please provide the class of antibiotics used or the association of classes. Later on, in the Case Presentation section, you mention only one antibiotic (Tezhixing) so where is the plural coming from?

**Response:** This patient received two antibiotics, including levofloxacin and Piperacillin Sodium and Tazobactam Sodium for Injection, which were described in detail in FURTHER DIAGNOSTIC WORK-UP.

3: [...] After reviewing the literature [...] Please provide the methods used for literature review: databases used, terms, operators, restrictions on search results (if any), range in years for the timespan.

**Response:** We have provided the methods used for literature review in INTRODUCTION.

4: [...] The results of gastroscopy showed: hiatal hernia, [...] Please clarify if the patient did undergo both upper digestive endoscopy as well as lower digestive endoscopy (colonoscopy) in the same session, and if so, what investigation was the first. This is important for the differential diagnosis..

**Response:** The patient underwent gastrointestinal endoscopy including both gastroscopy and colonoscopy. We did the gastroscopy first, then the colonoscopy. Detailed description has been added in History of past illness.

5: [...] multiple polyps in the fundus (removed by biopsy forceps [...]) Please provide more details regarding this finding: number of polyps, dimensions, aspect, grouping. Did you send the resected specimens for pathology examination and if so, what was the result? Was it an all-cold biopsy or some sort of electroresection was also involved? These are important in discussing the differential diagnosis..

**Response:** There were 2 gastric polyps (0.2-0.3 cm) in total, all of which were Yamada type II. We used biopsy forceps for all-cold biopsy and the pathological diagnosis was fundic gland polyps. Detailed description has been added in History of past illness.

6: [...] without coffee-like substances [...] Please clarify this statement. What do you mean by this term?

**Response:** The author wanted to express that the patient did not vomit blood, now we changed coffee-like substances to haematemesis.

7: [...] straight bile [...] Please use standard medical terms for the fractions of Bilirubin, such as: conjugated/direct bilirubin or unconjugated/indirect bilirubin.

**Response:** We have made normalized changes.

8: [...] stomach protection, liver protection [...] Please provide full medication (active principles and dosage) administered to the patient as this is also an important point of discussion.

**Response:** We have added detailed description in FURTHER DIAGNOSTIC WORK-UP.

9: [...] with severe infection, septic shock, and multiple organ failure, then transferred to the intensive care unit (ICU) [...] Based on what criteria? For the panel provided so far in the text, the patient should have not been diagnosed with septic shock or MOF. Also, please provide other important details such as

SpO2, acid-base balance, etc.

**Response:** We found that the patient had a progressively elevated body temperature, persistently high leukocyte index, and the presence of metabolic acidosis. The patient's oxygenation was maintained at 100% under 2 L/min nasal cannula oxygen inhalation, but the patient's respiratory rate increased to a maximum of 25 per min, heart rate was 124 per min, blood pressure was 94/62 mmHg, and the systemic inflammatory response was obvious. At that time, it was considered that the patient may have septic shock possible. In addition, the patient developed acute renal insufficiency and hepatic insufficiency, and the patient was considered to be complicated by multiple organ failure. Therefore, he was immediately transferred to the intensive care unit (ICU). Detailed description has been added in FURTHER DIAGNOSTIC WORK-UP.

10: [...] Tezhixing [...] Please provide the active drug and class of medication instead of the commercial name of the drug. Also, dosage is important and ways of administration Please provide, either in full text or in the form of a table, the complete list of differential diagnosis for this case, besides an infection with intestinal point of origin..

**Response:** The specific description of the Tezhixing has been modified. Differential diagnosis for this case has been added in DISCUSSION Paragraph 3. The authors also considered whether it was other factors induced to severe infection. First, we suspected whether it was a potential diverticulum perforation by colonoscopy or perforation by polyp cold biopsy; second, whether it was a pulmonary infection caused by reflux aspiration during anesthesia examination; third, whether it was an unclean diet resulting in acute gastrointestinal infections after gastrointestinal endoscopy. However, through a series of examinations and medical history inquiries, they were all denied.

11: [...] however, this case also provided some caution [...] Please state what the cautions should be, since the patient did not had any flags in his medical history and no associated comorbidities. Provide some sort of criteria to be monitored in order to identify the risk of developing septic shock after PEG preparation for colonoscopy.

**Response:** Because the patient has no underlying disease and no warning factors, this case report suggested that if septic shock occurs after gastrointestinal endoscopy, PEG maybe the murderer after excluding common factors. Detailed description has been added in DISCUSSION Paragraph 4.