

Peer Review File

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Reviewer A

The case report titled "Diagnosis of Inverted Meckel's Diverticulum by Double Balloon Enteroscopy: A Case Report" presents an insightful analysis of a challenging diagnostic case involving a 12-year-old male child with recurrent abdominal pain and gastrointestinal symptoms. The authors discuss the limitations of conventional diagnostic methods and emphasize the role of double-balloon enteroscopy (DBE) in diagnosing Meckel's diverticulum (MD), particularly in cases with atypical presentations and negative technetium-99m pertechnetate scanning. The report highlights the significance of accurate diagnosis for MD, the diagnostic value of DBE, and the complexities associated with inverted MD.

Strengths:

- Clinical Relevance: The case report addresses a clinically important scenario involving recurrent abdominal pain and gastrointestinal symptoms in a pediatric patient. It underscores the diagnostic challenges associated with MD, particularly when conventional methods yield inconclusive results.
- Comprehensive Presentation: The authors provide a detailed description of the patient's medical history, clinical presentation, diagnostic journey, and treatment. This comprehensive approach enhances the reader's understanding of the case's complexity and the significance of DBE in diagnosis.
- Visual Aids: It is interesting the inclusion of histopathological images and endoscopic images to visually illustrate the diagnostic process and the appearance of the inverted Meckel's diverticulum during double balloon enteroscopy. Well structured and summarized the clinical history of the patient on the ending timeline
- Importance of DBE: The report effectively highlights the advantages of double-balloon enteroscopy in diagnosing MD, especially when traditional diagnostic tools fail to provide clear results. The discussion on the value of DBE in visualizing the diverticulum, performing biopsies, and guiding surgical decisions is well-presented.

- Discussion on Inverted MD: The authors offer a thorough analysis of the unique presentation of inverted MD in the context of this case. They discuss how the diverticulum's inversion led to diagnostic challenges, the limitations of various imaging methods, and the contribution of DBE in overcoming these challenges.

Suggestions for Improvement:

- Structural Clarity: The report offers valuable insights; however, there is room for improvement in the organization of specific sections. Particularly, the discussion regarding the timing of surgery and the utilization of additional diagnostic tools requires further clarity. For instance, it is essential to address why the patient was discharged during the initial hospitalization without undergoing further diagnostic examinations. In the context of the second hospitalization, despite the patient's symptoms and clinical presentation, the report could delve deeper into whether the information gleaned from the initial and subsequent diagnostic images (before DBE) was insufficient to warrant a surgical decision.

- Comprehensive Examination: The inclusion of bone marrow examination in the diagnostic process raises questions for clarity. Was there a suspicion of lymphoma prompting this test? Furthermore, the report mentions abnormalities in the cytology results. Providing details about the nature of these abnormalities could enhance the reader's understanding and shed light on the decision-making process.

- Enhanced Explanation of Surgical Approach: A more detailed explanation behind the decision to transition from laparoscopy to open surgery would be valuable. Currently, the motivations for this change remain undisclosed, and shedding light on these factors would provide readers with a clearer insight into the surgical treatment choice.

Conclusion: The case report "Diagnosis of Inverted Meckel's Diverticulum by Double Balloon Enteroscopy: A Case Report" effectively addresses the complexities of diagnosing MD, particularly when traditional diagnostic methods are inconclusive. By presenting a comprehensive clinical case, the report emphasizes the significance of DBE as a diagnostic tool, especially for atypical cases and those with inverted MD. While some structural improvements could enhance clarity, the report contributes valuable insights to the medical literature.

Reply: Thank you for your kind feedback. Your suggestions are very constructive, and we have added a paragraph in red text to explain that (lines 296-332). We have added further clarifications

why the patient was discharged. We suggested double-balloon enteroscopy or laparotomy, but the child was discharged due to the good treatment response during the first hospitalization, and the family members refused further examination (lines 305-308). We have further elaborated on the judgement made based on the scenario and diagnostic images from the second hospitalization. MRE of the small intestine during the second hospitalization suggested uniform thickening of the unsegmented ileum wall and ileo-colonic intussusception, indicating possible inflammation or tumor. The second $^{99}\text{Tc}^{\text{m}}\text{O}_4$ - SPECT / CT imaging result remained negative and still did not support Meckel's diverticulum. We suggested double-balloon enteroscopy or surgical exploration to determine the nature of the lesion. After consultation, the medical staff and the family members decided to choose double balloon enteroscopy, which is a less invasive procedure. The results indicated that the mass of the upper ileum was found, and the pathological return was gastric mucosal tissue. At this time, we considered the Meckel's diverticulum with ectopic gastric mucosa. The medical staff and the family members explained the condition, and the family members agreed to explore and remove the lesion (lines 309-319). We performed bone marrow examination during the course of the patient's diagnosis because the repeated routine blood tests of the child indicated decreased leukocytes and hemoglobin, and we wished to exclude hematological diseases (lines 300-305). There was significant difficulty to locate the lesion in this case. Moreover, the double-balloon enteroscopy suggested that the lesion was an intestinal lumen mass without a typical diverticulum opening. We believe that identification of Meckel's diverticulum or tumor is necessary. Therefore, based on the purpose of surgical exploration, we first chose laparoscopic combined colonoscopy to avoid a large incision to explore the abdominal cavity, and to avoid missing colonic lesions, when the diverticulum is found after open diverticula and intestinal anastomosis (lines 319-332).

Reviewer B

1. Figures, tables, and videos should be cited **consecutively** in the text and numbered in the order in which they are discussed. Therefore, Figure 1A should be cited before Figure 1B; Figure 2A and 2B should be cited before Figure 2C and 2D. Please check **through** and revise.

Reply: We have modified the images order.

2. Figures

- Figure 1C-D: Please if it is necessary to remove or mask any information which may reveal the patient's privacy.
- Figure 1E-F, 2E-F: Please indicate staining or observation method in the legends.

Reply: We have checked and modified it. The images did not contain any information that might reveal the patient's privacy

3. Please check if any references should be added since you mentioned *studies*.

- Some *studies* have suggested that the application of this method in the detection of ectopic gastric mucosa with small tissue ($< 1.8 \text{ cm}^2$), vagal diverticulum and rapid gastrointestinal bleeding often results in false negative results [7].
- Other *studies* have also found that when anemia caused by lower digestive tract bleeding reaches a certain level ($\text{Hb} < 110\text{g/l}$), the diagnostic sensitivity of $^{99}\text{Tc}^{\text{m}}\text{O}_4$ -nuclide scanning imaging in patients with ectopic gastric mucosal imaging Meckel diverticulum is lowered to 60% [8].
- Some *studies* have shown that it is difficult to distinguish obvious ectopic tissue in surgical operations (62% of the ectopic tissue of diverticulum is nonpalpable) [15],....
- *Studies* have found that ectopic tissue is found in about 29% of MD [15],....

Reply: We have checked and modified it.