

PEER-REVIEW REPORT

1、Reviewer's code: 00038617

(COMMENTS TO AUTHORS)

The authors reported a rare case of primary gastrointestinal amyloidosis with multiple nodular protuberances in the digestive tract, with controllable moderate abdominal discomfort and anemia and a benign course. Enteroscopy with biopsy and endoscopic ultrasonography played an important role in the diagnosis of primary gastrointestinal amyloidosis. This case is certainly a rare and unique case with a benign nature. However, the authors should investigate the subtype of amyloidosis, and examine bone marrow to rule out multiple myeloma. Previous reports revealed that there were cases of AL amyloidosis resulted from multiple myeloma in which serum and urine protein electrophoresis were both negative for monoclonal gammopathy. In this paper, discussion section should be written more briefly.

Answer: Thanks for your positive comment on our work. We agree that subtype of the amyloidosis should be investigated to rule out multiple myeloma. We indeed tried to persuade the patient to take bone marrow examination during the course, but the patient refused. Nevertheless, there was no manifestation of multiple myeloma during the 3-year follow-up, and thus multiple myeloma could be ruled out. Accordingly, we have added this important point in the revised version of the manuscript (Page 9, Lines 17-21). In addition, we have already mentioned in the original version of the manuscript that to test this hypothesis, we will continue to closely follow up the case and conduct protein mass spectrometry analysis to identify the deposited proteins and genetic analysis to explore the genes involved in the development of amyloidosis (Page 10, Lines 6_10). In addition, the Discussion section has been more concisely written.

2、Reviewer's code: 00036517

(COMMENTS TO AUTHORS)

To editor, I think this case is rare and can be accepted to the journal with some additions. I suggest that authors need to add endoscopic findings in follow up period. I want to know the reason the use of PPI for the patient.

Answer: Thanks for understanding the merits of our case report. We agree that it will be more informative to add endoscopic findings in follow up period, but due to the space limitation for a case report, we cannot add additional images in the paper. Moreover, there appeared no changes in the endoscopic findings during the follow-up, which has been clearly described in the text. The use of PPI, namely esomeprazole magnesium (Nexium®), was used for treatment of abdominal discomfort, which has

been clearly stated in the revised version of the manuscript (Page 6, Lines 21-22;Page 7,Lines 1).

Dear Editor,

Thanks for your further evaluation of our manuscript, with a few more comments.

We have responded, point-by-point, to these constructive comments below. Accordingly, we have addressed these important points, and highlighted all changes in red in the newly revised manuscript.

We hope that the newly revised manuscript is now ready for publication.

With kind regards,

Yan-Qing Li,

The corresponding author

Point-by-point responses to the editor

My evaluation

The article is aimed to report a rare case of primary gastrointestinal amyloidosis in a stable condition after being followed up for three years. The title is “**Rare case of primary gastrointestinal amyloidosis diagnosed with enteroscopy and endoscopic ultrasonography**”.

1. This is a case report.

Answer: Yes, this is a case report.

2. Several factors influence the diagnosis. Please discussion these factors.

Answer: Thanks for your thoughtful comment, and suggestion. Accordingly, we have addressed this important issue in the Discussion of the newly revised manuscript (Page 9, Lines 14-21).

3. This procedure needed special equipment and an experienced endoscopist. It could not apply in the other settings.

Answer: We agree with your comment and have now stated this point clearly in the newly revised manuscript (Page 9, Lines 21-23). What we can learn from this case is that it is important for a physician, especially a gastroenterologist, to be aware of the existence of digestive tract amyloidosis and refer the suspected patients to enteroscopy and endoscopic ultrasonography in clinical practice in order to diagnose or rule out amyloidosis of the digestive tract. This point is also made clear in the in the newly revised manuscript (Page 9, Lines 23-28).

4. What are the new knowledges from this report?

Answer: The new knowledges from this report is that a patient with long-term moderate abdominal discomfort and anemia may have primary gastrointestinal amyloidosis, with controllable symptoms and a benign course, and enteroscopy and endoscopic ultrasonography play an important role in the diagnosis of primary gastrointestinal amyloidosis. These points have been stated in the Conclusion of the manuscript (Page 11, Lines 3-9).

5. Please also recommend the readers “How to apply this knowledge for routine clinical practice?”.

Answer: Thanks for your insightful suggestion. In fact, we have addressed this important issue in the previous manuscript. Accordingly, we have made this more clearly as recommendations on how to apply this knowledge for routine clinical practice in the Discussion of the newly revised manuscript (Page 9, Lines 10-13).

Dear Editor,

Thanks for your further instruction on addition of more figures for endoscopic findings in follow up period.

Accordingly, we have added the figures (Figures 5A-C), and highlighted all changes in red in the newly revised manuscript (Page 8, Lines 25-26).

We hope that the newly revised manuscript is now acceptable for publication.

With kind regards,

Yan-Qing Li,

The corresponding author