Answering Reviewers

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Persistent Diarrhea with Petechial Rash: Unusual Pattern of Light Chain Amyloidosis Deposition on Skin and Gastrointestinal Biopsies Case Report

Reviewer #1:
Scientific Quality: Grade D (Fair)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: The authors present a case report of persistent diarrhea with petechial rash that was revealed to be a AL amyloid deposition on skin and on gastrointestinal biopsies. The title is complete according to the CARE checklist and the core of the manuscript as the abstract. The introduction section is complete and informative.

- In case presentation section more: why if the symptoms were suspicious of crohn disease, why were antibiotics prescribed and additionally why he wasn't he admitted in the first place with this history?
    - **Response**: We have clarified the patient's timeline of initial presentation and work up in the case presentation section of the manuscript. The patient was stable and discharged after his initial colonoscopy at an outside institution with a scheduled follow-up appointment for long-term management of suspected Crohn disease. At presentation to our institution, the patient was admitted and started on empiric antibiotics due concern for sepsis.
- This part is incomplete: "Initial labs revealed anemia (values must be added), among other markers suggestive of hypovolemia. How many platelets? Inflammatory markers were within normal limits. How was calcium, and creatinine levels? Protein and albumin? Labs showed high stool lactoferrin of 332.15 μg/mL (normal range 0 – 7.24 μg/mL) and high pro-BNP of 10,212 pg/mL (ERROR, this value is low) (normal range < 125 pg/mL). Folate and thiamine labs were low. Urinalysis was remarkable for proteinuria of 100 mg/dL and the presence of numerous hyaline casts and coarse granular casts.
    - **Response**: We have added the values to include the patient's CBC, calcium, creatinine, protein, and albumin.
- In the CT, the bones were normal? The discussion is incomplete. The diagnostic process is very poor.
    - **Response**: We have added to the description of the CT, "No bone fractures or suspicious osseous abnormalities seen on any imaging".
- "Upon extensive chart review, the patient presented to an outpatient clinic with diarrhea and hematochezia seven months prior to the patient's first colonoscopy. At that time, the patient's symptoms were attributed to probable hemorrhoids". In a patient with hematochezia and diarrhea and 18 kg weight loss, the first diagnostic hypothesis can't be hemorrhoids. The diagnostic process in case of weight loss, diarrhea and hematochezia should be described better. Even if the case is interesting, the diagnostic approach was really poor.

- **Response**: We have clarified and elaborated on the diagnostic approach, and included alternative diagnoses considered at the time of his initial presentation to his primary care provider (PCP) with symptoms of diarrhea, intermittent scant hematochezia and no weight loss. The patient was referred for colonoscopy at the time of his initial presentation to his PCP, but this was not performed at that time.

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: It is a very good paper, with clear importance for the everyday practice (family doctors; gastroenterologists) Some suggestions:

1. No explanation of the acronym AL amyloidosis (amyloid-light chain): please add one at the start of the article.
    a. **Response**: We have added this explanation at the beginning of the article.
2. What do you mean 'outpatient daratumumab'? Is that a treatment the patient had once discharged from the hospital? The two-word combination makes little sense.
    a. **Response**: Yes, the plan at the time was to begin this treatment outpatient upon discharge from the hospital. We have amended the treatment section to be more clear.
3. Both images on histopathology (Figure 3, Figure 5) shown no magnification at all. What was the microscopic magnification of the images?
    a. **Response**: We have added the magnification to the figure legends. Please see below:
    b. Figure 3. Histopathology of abdominal fat pad biopsy. (A) H&E stain at 4X of skin biopsy with eosinophilic deposits in the upper papillary dermis and periadnexal dermis. (B) PAS stain at 10X shows the deposition to be negative for lipoid proteinosis. (C) CK5-6 immunostain at 10X is blush positive but interpreted as negative, an important stain considering differential includes primary cutaneous amyloidosis of macular or lichen subtype. (D) Congo red stain at 4X under polarization showing apple green birefringence, rarely seen in cutaneous amyloidosis but always present in AL amyloidosis.
    c. Figure 5. Histopathology from colon biopsy. (A) H&E stain at 4X of colon biopsy shows fragments of colonic mucosa with amorphous homogenized pink material. (B) Congo red stained colon tissue at 4X shows the classic salmon-color (C) Congo red stain colon tissue at 4X under polarization shows apple green birefringence.