Author’s response to reviews

Title: Infantile-onset inflammatory bowel disease in a patient with Hermansky-Pudlak syndrome: a case report

Authors:

Jun Ishihara (jun_ishihara@med.kurume-u.ac.jp)
Tatsuki Mizuochi (mizuochi_tatsuki@kurume-u.ac.jp)
Takashi Uchida (uchitakamehameha@yahoo.co.jp)
Yugo Takaki (takaki_yuugo@med.kurume-u.ac.jp)
Ken-ichiro Konishi (konishi_kenichirou@med.kurume-u.ac.jp)
Masahiko Joo (masahiko.kyu@gmail.com)
Yasuhiro Takahashi (yshk.takahashi@gmail.com)
Shinichiro Yoshioka (yoshioka_shinichirou@kurume-u.ac.jp)
Hironori Kusano (kusano_hironori@med.kurume-u.ac.jp)
Yoji Sasahara (ysasahara@med.tohoku.ac.jp)
Yushiro Yamashita (yushiro@med.kurume-u.ac.jp)

Version: 2 Date: 25 Nov 2018

Author’s response to reviews:

BMC Gastroenterology Editorial Office

Dear Editor and Reviewers:

RE: BMGE-D-18-00323R1

Infantile-onset inflammatory bowel disease in a patient with Hermansky-Pudlak syndrome: a case report
Thank you very much for your letter of November 6, 2018. Based on your kind suggestions concerning the above manuscript, assigned the number BMGE-D-18-00323R1, my coauthors and I have made revisions as summarized below. We also indicated changes made based on these comments in the revised manuscript with red lettering.

Additionally, we added 2 co-authors, Shinichiro Yoshioka and Hironori Kusano, because they contributed to the revised manuscript.

Response to Editor Comments:

1. Addition of any further details on endoscopy of terminal ileum and upper GI tract, as well as on imaging studies.

   We added an endoscopic image of the terminal ileum as Figure 1B and its description in lines 96-97, as well as in the Figure Legend. We did not perform upper endoscopy.

   Abdominal ultrasonography and computed tomography were carried out in this child. We added the sentence, “Abdominal ultrasonography and computed tomography showed bowel wall thickening in the transverse and descending colon,” in lines 94-95.

2. Update on genetic panels in accordance with more recent genotypic information on HPS and IBD.

   We added details of the genetic panel as Additional File 1 and the description of genes examined in lines 111-112. We now have a more advanced genetic panel including additional genes related to very early onset IBD. However, we cannot include this new genetic panel in the present case report because we are in the midst of preparing a separate research article concerning it.

Technical Comments:

1. Please move the list of abbreviations to after the conclusion section.

   We moved the list of abbreviations to follow the conclusion section.

2. Please include the heading Declarations at the start of this section.

   We added the Declarations heading in line 162.
3. Under the heading Authors’ Contributions in the Declarations, JM is listed as an author, please confirm whether this was meant to be MJ (Masahiko Joo).

We changed “JM” to “MJ” in line 181.

4. “Figure 1” title should be removed from the graphic file.

We removed the “Figure 1” title from the graphic file.

5. When describing patient, you state: "A Japanese boy...was born with whitish skin, hair, and eyelashes and gray irises.". Can you please rephrase this to a more scientific description of the typical albino features.

We changed “whitish skin, hair, and eyelashes and gray irises” to “chalky white skin, silvery-white hair, and gray eyes” in lines 47 and 85.

Response to Reviewer #1 Comments:

1. When the colonoscopy was done, was the terminal ileum intubated and what were the findings?

We added an endoscopic image of the terminal ileum as Figure 1B and a corresponding description in lines 96-97 and in the Figure Legend.

2. Was an upper endoscopy done at the time, and if so, what were the findings?

We did not perform upper endoscopy.

3. No imaging was mentioned, this should be clarified.

4. Was any imaging done on the child?

Abdominal ultrasonography and computed tomography were carried out in this child. We added the sentence, “Abdominal ultrasonography and computed tomography showed bowel wall thickening in the transverse and descending colon,” in lines 94-95.
5. Most important, in view of the great interest in very early onset IBD, the authors should include the specific panel that was done looking for primary immunodeficiency and IBD. There reference is from 5 years ago and there have multiple gene discoveries in this area.

We added details of the genetic panel as Additional File 1 and a description of genes examined in lines 111-112, as per a recent article (new Reference 9). We now have a more advanced genetic panel including additional genes related to very early onset IBD. However, we cannot include this new genetic panel in the present case report because we are in the midst of preparing a separate research report concerning it.

Response to Reviewer #2 Comments:

1. In the abstract (line 43), the authors state that the patient "was diagnosed with Crohn's-like inflammatory bowel disease at 11 months." Information should be added to the abstract to describe the basis for establishing this diagnosis.

We added the phrase, “based on the endoscopic finding of longitudinal ulcerations in the colon and the histopathologic finding of nonspecific chronic inflammation without granulomas,” in lines 49-51.

2. The authors describe the endoscopic biopsy findings (lines 87-88). The report would be improved by adding this description to the abstract and showing the histopathologic images in a figure.

We added a mention of “histopathologic findings of nonspecific chronic inflammation without granulomas” in the abstract (lines 50-51) as well as a histopathologic image (Figure 1C) with added description in the Figure Legend.

3. The authors state in the Discussion (lines 111-112), "IBD is more common in HPS-1, -4, and -6;" but do not indicate what it is more common than. Perhaps the authors should consider revising the statement to "IBD is reported in patients with HPS-1, -4, and -6; …"

We changed "IBD is more common in HPS-1, -4, and -6" to “IBD has been reported in patients with HPS-1, -4, and -6” in line 122.

4. Genetic analysis is a useful diagnostic modality for many inherited disorders, as exemplified by this case. In this case, clinical features (e.g., oculocutaneous albinism with nystagmus) are
consistent with an underlying diagnosis of HPS. This report would be strengthened by the addition of a short discussion of the differential diagnosis of infantile-onset IBD, and clinical features that aid in diagnosing specific etiologies of infantile-onset IBD.

We added these sentences: “In this patient, the clinical features of oculocutaneous albinism with nystagmus are consistent with an underlying diagnosis of HPS [1]. Such characteristic features may aid in diagnosing specific etiologies of infantile-onset IBD” in lines 145-148.

My coauthors and I thank you again for your helpful suggestions, and hope that the resulting improvements have rendered our report suitable for publication in your journal.

Sincerely,

Tatsuki Mizuochi, MD, PhD
Department of Pediatrics and Child Health
Kurume University School of Medicine
Kurume, Japan