Peer Review File

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Responses to Reviewer A Comments

Thank you very much for reviewing our paper throughout.

Comment 1: How about the effect of TCZ in UC in this case? Past reports describing TCZ with TAC in UC patients are also of interest. The authors should review and discuss past cases treated with TCZ in patients with TAK complicated by UC in a table (clinical features, treatment, outcome etc.).

Reply 1: This point is touched on in the Discussion. "In the present case, tocilizumab was administered for more than 4 years before the current relapse. Therefore, it seems unlikely that tocilizumab played a critical role in the current relapse."

There are only three reports are available including a reference cited in this paper in which tocilizumab was used in a patient with TAK and UC. The effect of tocilizumab on UC is inconsistent. I have modified a sentence and added two references.

Change in the text: The effect of tocilizumab on UC is contradictory in cases with TAK associated with UC: improvable (22) and detrimental (23). In another case in quiescent phase, tocilizumab was not detrimental (24).

Comment 2: The use of Infliximab seems to be successful for TAK as well as UC in this patient, why infliximab is stopped and changed to TCZ again?

Reply 2: We published that our modality, i.e., infliximab and plant-based diet as first-line (IPF) therapy, showed lower relapse rates in the medium and long term without infliximab maintenance therapy both in UC and Crohn's disease compared to those of the current standard. Therefore, we use infliximab only for induction. I have added our observations in the 2nd paragraph in Discussion.

Change in the text: Our modality, i.e., infliximab and plant-based diet as first-line (IPF) therapy, showed lower relapse rates in the medium and long term without infliximab maintenance therapy both in UC (15) and Crohn's disease (21) compared to those of the current standard.

Comment 2: Why infliximab is changed to tocilizumab again?

Reply 2: TAK was controlled well by tocilizumab, and tocilizumab did not seem to be detrimental to UC. Therefore, it is reasonable to resume tocilizumab for TAK. I have added this in the last sentence in Discussion.

Change in the text: Because TAK was controlled well by tocilizumab, and tocilizumab

did not seem to be detrimental to UC, tocilizumab will be continued for TAK.

Comment 3: English editing in native-speakers are required in entire manuscript.
Reply 3: A professional native English speaker edited our manuscript.

Responses to Reviewer B Comments
Thank you very much for reviewing our paper throughout.

Comment 1: What was the disease activity of TAK at the time of UC exacerbation? As the authors mentioned, CRP and ESR would not be indicators of activity due to the influence of oral medications such as Tocilizumab. Did the authors perform FDG-PET or other evaluations?
Reply 1: I have added the following sentence in the first paragraph in Case presentation.

Changes in the text: FDG-PET performed in May 2021 showed complete remission of TAK.

Comment 2: Are there possibility that discontinuation of Tocilizumab may have been benefit? The authors mentioned that the referring physician also managed the patient relapses by drug holidays of Tocilizumab. What were the patient's UC symptoms at that time?
Reply 2: I have inserted symptoms of relapses of UC.

Changes in the text: there were a few mild relapses, i.e., blood attached to stool and/or loose stool, recently.

Comment 3: What were the patient's HLA-B52, IL12B?
Reply 2: I have added the following sentence at the end of Case presentation.

Changes in the text: A genetic study was not undertaken.

Comment 4: The authors need to rule out infection in the patient. Was there any possibility of infectious enteritis?
Reply 4: Infectious colitis was unlikely based on the endoscopic findings and the results of laboratory studies for pathogens. I have added other tests done to exclude possibility of infectious enteritis.

Changes in the text: Stool culture for pathogen, CD Chek (Techlab C. Diff Quik Chek Complete; Techlab Inc, VA, USA), COVID-19 antigen test (HISCL; Sysmex, Kobe, Japan), and cytomegalovirus antigenemia (13) were negative.

Comment 5: What about the possibility of ischemic enteritis? It was stated that there was stenosis in the abdominal aorta due to TAK. Has intestinal blood flow been evaluated?
Reply 5: As stated in the text, inflammation was diffuse in the left colon. There were no longitudinal ulcers indicating ischemic colitis. Intestinal blood flow was not evaluated.

Comment 6: The authors mention in the text that there was a lesion in the left colon, but there is no description of the lesion site in the Legend of Figure 2. Please describe the site of observation in the Legend.

Reply 6: I have added the colon site to the figure legend.

Changes in the text: Colonoscopic images in the distal descending colon

Responses to Reviewer C Comments

Thank you very much for reviewing our paper throughout.

Comment 1: As the authors describe in the manuscript, TAK is not considered an extraintestinal complication; however, not a few cases of IBD with TAK have been reported. Although this case was valuable to consider the pathology based on inflammatory signals, such as IL-6 signaling and TNF-α signaling, the authors did not discuss the patient's pathology. Moreover, tocilizumab and infliximab are the standard treatments for TAK and IBD, respectively, but the guideline recommends that infliximab be used for remission and maintenance in IBD treatment. The authors should describe more details of infliximab discontinuation in this patient.

Reply 1: We partly describe the reason why infliximab was discontinued in the last paragraph in Discussion: "This dietary change together with anxiety over her father's condition seemed to be a critical factor in the current relapse. Further appreciation of the role of diet in the present relapse will enhance self-management skills and prevent another relapse." I have added our observations, i.e., low relapse rates with our modality without infliximab maintenance, in the 2nd paragraph in Discussion.

Change in the text: Our modality, i.e., infliximab and plant-based diet as first-line (IPF) therapy, showed lower relapse rates in the medium and long term without infliximab maintenance therapy both in UC (15) and Crohn's disease (21) compared to those of the current standard.

Comment 2: The authors describe details about the case with clinical findings with figures and episodes which could be the triggers of relapse, such as the dietary change and anxiety; however, the disease activity index, the level of fecal calprotectin, or trough levels of tacrolimus should be added for the case presentation of ulcerative colitis.

Reply 2: Disease activity of UC was evaluated based on the patient's condition, stool condition including bloody stool, endoscopic findings, and fecal occult blood test. These are described in the text and Figures 1 and 2. Tacrolimus was used for TAK by the referring physician, and it was not a critical agent in the induction phase of UC in the present case. Therefore, trough levels of tacrolimus were not examined. Fecal occult blood test is a conventional biomarker for UC activity, and its significance is almost equal

to fecal calprotectin test.

Minor comment:
Reply: I have deleted the initials of the physician's name.