Author’s response to reviews

Title: A girl with protein-losing enteropathy during ketogenic diet: a case report

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Author’s response to reviews:

Response to the Editors and reviewers

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “A girl with protein-losing enteropathy during ketogenic diet: a case report” (ID: BPED-D-19-00527R1). Your valuable comments have helped us revise and improve our manuscript, in addition to being an important guidance to our researches. We have studied the comments carefully and have made corrections in the manuscript accordingly. The revised portions have been marked in red. The manuscript has been reviewed by native English speakers, and we hope that it is now suitable for publication in your journal. The main corrections in the manuscript, and the responses to the reviewer’s comments, are detailed below.

Editor Comments (Please rewrite your discussion section in original language. Currently, it contains an unacceptable overlap in text with previously published sources. In addition, please copyedit the text to improve the standard of written English. I suggest that you ask a native English-speaking colleague to help you with this.)

Response: Thank you for pointing out the overlap and errors in writing. We have rewritten this part according to your suggestion, and the manuscript has been reviewed by native English speakers.

Reviewer #1:

Dear professor Nur Arslan:
We sincerely appreciate your constructive suggestions, which have helped us improve the quality of the work. We have carefully considered the comments and revised the manuscript accordingly. Changes made in the revised manuscript have been highlighted in red.

Response to comments

1. Response to comment: (problems with grammar and writing).
   Response: Thank you for pointing this out. We have corrected the issues with grammar and writing, and the manuscript has been reviewed by native English speakers.

2. Response to comment: (Case section should be shortened)
   Response: We agree with your assessment, and have shortened this section.

3. Response to comment: (Discussion should be shortened. The Authors should discuss the original findings, main case reports related with PLE, pathogenesis of PLE and treatment modalities of PLE. A conclusion paragraph should be added to the end of the discussion section.)
   Response: Thank you for your detailed suggestions. We have rewritten this part accordingly.

   We have discussed the original finding: this patient is the first one reported who did not discontinue the KD. We find that decreasing the ketogenic ratio maybe a feasible way of managing PLE. There have been two published case reports of PLE occurring upon initiation of the KD, and both the patients had discontinued the KD. Mucosal injury by viral infection, and secondary lymphangiectasia aggravated by KD were frequently suspected as the mechanisms of PLE.

   We have also added a conclusion paragraph at the end of the discussion section.

   We have improved the manuscript by making substantial changes based on the reviewers’ comments, but these changes have not altered the content or framework of the manuscript. We have not listed these changes in detail in our replies, but have marked them in red in the revised manuscript.

   We greatly appreciate the editor’s and reviewers’ comments and suggestions, and hope that the corrections in our manuscript will be met with approval.

Reviewer #2:

Dear professor Biswaroop Chakrabarty:
We sincerely appreciate your constructive suggestions, which have helped us improve the quality of the manuscript. We have carefully considered the comments and have revised the manuscript accordingly. Changes made in the revised manuscript have been highlighted in red.

1. Response to comment: (Case summary maybe omitted)

Response: We have added this section as suggested.

2. Response to comment: (Details should have more clarity in terms of which epilepsy syndrome, point at which it was labeled as drug refractory, any neuroimaging changes.)

Response: Thank you for your detailed suggestions. We have rewritten this part accordingly.

3. Response to comment: (What ketogenic formulation was used and whether urine ketone monitoring was being done?)

Response: Thank you for pointing this out. We have added these details in the revised manuscript. We obtained the milk formula from the Zeneca Biological Technology Company, China. We did not monitor the urine ketone levels, but we monitored the blood ketones regularly.

4. Response to comment: (at what age ketogenic diet was initiated and what investigations were sent and what modifications done prior to starting KD)

Response: We have added these details in the revised manuscript. When the patient was 3 months old, her urine organic acids, serum amino acids, complete blood count, serum liver and kidney tests, and abdominal B-scan ultrasound results were all normal. We therefore treated her with the KD.

5. Response to comment: (How was the diagnosis of PLE established)

Response: We have rewritten this part to explain the diagnosis. We found no common causes of protein loss in the skin, urine, and blood tests, echocardiograph, stool screening for pathogens, or abdominal ultrasonography. Meanwhile, the EGD revealed edematous mucosa in the duodenum, and the biopsy results revealed lymphocytes and plasma cells infiltrating the lamina propria, which was different from lymphatic ectasia. These findings were consistent with intestinal lymphangiectasia as a presentation of PLE, and thus, we diagnosed PLE.

6. Response to comment: (Whether interstitial lymphangiectasia is a cause of PLE or its effect, that needs clarification, and its relation to KD, needs clarity)

Response: Thank you for your suggestion. We have added these details in the revised manuscript. Food-induced enteropathy can cause PLE, and intestinal lymphangiectasia has been reported in children following a high-fat diet. Our patient had no history of intestinal disease and showed hypoproteinemia and intestinal lymphatic changes after starting the KD. The hypoproteinemia improved after adjusting the ratio of the KD, indicating that the intestinal lymphangiectasia was secondary to the KD.
Response to comment: (How was the patient monitored on KD and mention of other side effects should also be done)

Response: Thank you for this suggestion. We have added this section to the manuscript. In the follow-up clinic visits, we found no side effects on the height, weight, BMI, blood test, urine test, abdominal ultrasonography, hepatic and renal functions, or microelements of the patient.

Response to comment: (The EEG images should be more clear with appropriate figure legends)

Response: Unfortunately, the original computer data was lost. We tried our best to recover it, but failed. Therefore, the EEG images are paper reports from the parents.

We have improved the manuscript by making substantial changes based on the reviewers’ comments and suggestions, but these changes have not altered the content and framework of the manuscript. We have not listed the changes in detail in our replies, but have marked them in red in the revised manuscript.

We greatly appreciate the editor’s and reviewers’ comments and suggestions, and hope that the corrections in our revised manuscript will be met with approval.