**Author’s response to reviews**

**Title:** Delayed Diagnosis of Acromegaly in a Patient with Focal Segmental Glomerulosclerosis: A Rare Case Report and Literature Review

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Dear Editor,

RE: BNEP-D-19-00343R1, entitled "Delayed Diagnosis of Acromegaly in a Patient with Focal Segmental Glomerulosclerosis: A Rare Case Report and Literature Review".

Thank you for giving us the opportunity to revise our above referenced manuscript. We have revised the manuscript carefully according to the Editor and Reviewers’ comments and recommendations. All the revisions were clearly highlighted, using the "Track Changes" function in Microsoft Word, so that changes are easily visible to the editors and reviewers. The response to each question or comment of the reviewers is listed point-by-point in the attached pages. We hope the revised form is suitable for publication in your journal.

Thank you for your consideration.

Yours sincerely,
Responds to the reviewer’s comments:

Editor Comments:

Please rewrite your background section in original language. Currently it contains an unacceptable overlap in text with multiple previously published sources.

Response: Thank you. We have re-written the background section to avoid unnecessary overlap in text with previously published sources (Page 3).

Reviewer reports:

Howard Trachtman (Reviewer 1):

This is a very interesting case report of an adult with acromegaly and FSGS. The authors make the reasonable claim that the excess GH contributed to the development of FSGS based on the absence of response to standard therapy and improvement with resection of the GH producing lesion.

I think the case is well documented, the manuscript is clearly written and the interpretation is justified. My only suggestions would be to (1) clarify whether ACEI/ARB were prescribed (2) include the following reference Trachtman H, Futterweit S, Schwob N, Maesak J, Valderrama E. Recombinant human growth hormone exacerbates chronic puromycin aminonucleoside nephropathy in rats. Kidney Int. 1993 Dec;44(6):1281-8. which supports a deleterious effect of GH on glomerular structure in an animal model of FSGS and (3) consider adding a speculation on why the association is so rare (lower GH levels in acromegalic patients versus experimental animals, lack of awareness, low-grade versus nephrotic range proteinuria).

Response: We thank the reviewer for the great comments and the suggested reference. (1) No ACEI/ARB were prescribed in our presented patient. (2) In our revised manuscript, the above reference has been included in Discussion as “In addition, Trachtman H et al. found a deleterious effect of GH on glomerular structure in an animal model of FSGS [18]” (Page 7). (3) A speculation on why the association is so rare has been discussed in our revised manuscript as “We speculate the scarcity of the association between excessive GH and glomerular sclerosis may be due to lack of awareness, lower GH levels in patients with acromegaly versus experimental animals, and low-grade proteinuria in most patients versus nephrotic syndrome in this case” (Page 7).
Changli Wei (Reviewer 2):

It is very rare to have focal segmental glomerulosclerosis (FSGS) in patients with acromegaly, vice versa. This report by Zheng et al presents a 63-year old man with 2 history of nephrotic syndrome refractory to prednisone. While kidney biopsy indicated FSGS, physical examination suggested acromegaly with MRI showing pituitary macroadenoma. Surgical removal of the tumor led to a partial remission of proteinuria, suggesting FSGS in this case is most likely secondary. The authors went on to discuss the relationship between FSGS and acromegaly, and the possible mechanisms how growth factor excess could contribute to kidney injuries. This is a very well-presented rare case, which reminds us nephrologists of the possibility of primary growth factor disorders in patients presented with nephrotic syndrome.

Minor comments:

In order to be more accurate, the authors are suggested to add such words as "So far with our knowledge" in front of "there are only two cases---", the first sentence of paragraph two on Page 6.

Response: Thank you. In the revised manuscript, we have added "So far with our knowledge" in front of "there are only two cases---" to be more accurate (Page 6).