Responses to comments from the reviewers

1. **Comment 1：** The problem for me is that it is unclear the real/clinical impact of such secondary effect. All along the manuscript, it is clear the pharmacological mechanism explaining histopathological findings, but it is not clear the potential clinical effects (Is the renal effect relevant? Reversible?) … And, the most important thing is that it is no clear if pharmacological renal lipidosis has any relevant clinical relevance.

   Reply: In the revised manuscript we have added that deposition of the substrates induced by hydroxychloroquine in kidney lead to renal dysfunction, such as glomerulosclerosis, thickening of glomerular basement membrane and increase of mesangial matrix. All of these renal pathological changes ultimately cause proteinuria and hematuria. It indicates that renal effects of hydroxychloroquine are relevant to renal histopathological changes.

2. **Comment 2:** On the other hand, the authors indicate that it is a case report and bibliographic review. However, I do not see the part related to the review, not at least in a specific way. In the actual manuscript, it seems to be a qualitative comment of the presented case more than a review. It lacks more specific “numerical” data obtained from existing bibliography.

   Reply: Because the main contents of manuscript involve in a case of hydroxychloroquine-induced renal phospholipidosis, we have adjusted type of the manuscript to a case report rather a review in the revised manuscript.

3. **Comment 3:** In my opinion the way for it would be another renal biopsy, although for ethical reasons probably the correct way would be periodical monitoring of proteinuria as well as hematuria, and only in the case of persistence of initial alterations after a reasonable time period (6-12months) to repeat renal biopsy to discard other causes of renal disease.

   Reply: The patient had returned to her native place, and we keep in touch with her. The patient went to the local hospital for examination in April 2019, urine test showed hematuria and proteinuria decreased. Although the patient had already decided not to repeat renal biopsy, we will continue to monitor the conditions of this patient.

4. **Comment 4:** Another point to illustrate when considering published bibliography is the effect and indication of enzyme replacement with pharmacological enzymes.

It is not clear in the manuscript, in which in a first time the authors establish that it is indicated but later, when commenting bibliography, it seems that it is not.

Reply: In the discussion section of article, we just wanted to present a variety of treatment methods and some doubts about the enzyme replacement. Because enzyme replacement was not applied in this case and also generates uncertainties during clinical use, we had decided not to involve the treatment method of enzyme replacement in article.

5. **Comment 5:** In relation with formal aspects of the actual text, in my opinion authors repeat too much times the reasons to discard Fabry disease.

   Reply: Redundant statements about the reasons to discard Fabry disease had been reduced.

6. **Comment 6:** In the actual manuscript the conclusion/s is very poor and it is not clearly identificable as such. I do not know, after Reading the actual work which is its originality in the field. I do not know how to manage this finding.

   Reply: Apparently, the significance of article is that our presentation provides further evidence of the side effects of hydroxychloroquine. It demonstrates that we should pay more attentions to application of hydroxychloroquine. Furthermore, drug-induced renal phospholipidosis should be considered as a differential diagnosis, especially when zebra bodies and myelin figures are found in renal biopsy samples.

7. **Reply to specific comments**: We had modified contents of the manuscript in detail according to specific comments from reviewers, such as lots of inappropriate expressions put forward by reviewers.