Author’s response to reviews

Title: Insulin autoimmune syndrome induced by exogenous insulin injection: a four-case series

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Author’s response to reviews:

Dear editor,

Thank you for your review of and response to our manuscript “Insulin autoimmune syndrome induced by exogenous insulin injection: four-case series”. We are enclosing a revised manuscript in which we have addressed the comments of the reviewers, and we hope that this manuscript will meet the standards for publication. Revised portions of the manuscript are highlighted in red, and our responses to specific comments of the editors and reviewers are noted below. The authors thank the editors and the reviewers for their pertinent and constructive comments.

Reviewer 1:

Case 1: Author should present complete history of patient especially the comorbidities and the oral treatment used. Since the patient was diabetic for ten years, it is important to know about basic case information in the beginning. Author has mentioned later about renal insufficiency, it should be mentioned in the beginning along with other co-morbidities.

Answer: Thanks for your suggestion. We have mentioned the comorbidities and the oral treatment used in the beginning of case 1.

Line 4: Recently LISPRO has been added, this statement is vague. The way author has mentioned, it seems that due to LISPRO patient had renal insufficiency and that's why LISPRO has been changed to other treatment. There should be clarity in text.

Answer: Thanks for your advice. The treatment changed from metformin to LISPRO due to the patient’s renal insufficiency. And as a result of the fluctuated glucose concentration, LISPRO has been changed to other treatment. We have revised the sentence to reduce the misunderstanding in the case 1.
Authors should follow a uniform pattern to present their cases, a good example of case presentation can be following article:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5118974/.

Answer: Thanks for your helpful suggestion. We have referred to this article and improved our case presentation in the revised version.

Authors should justify need of this case series review since there is sufficient data about insulin autoimmune syndrome and its cases in literature.

Answer: Thanks for your advice. Although there is a few of data about insulin autoimmune syndrome and its cases in literature, there has few reported cases about exogenous insulin injection induced IAS. In this study, we come up with a new concept of non-classical IAS which is caused by exogenous insulin injection. Our study discusses the clinical manifestation, potential mechanism and the therapy about classical and non-classical IAS. Moreover, we also differentiate classical and non-classical IAS as well as other hyperinsulinemic related disease.

Reviewer 2:

More detailed description of typical IAS cases might be a plus. If possible, typical cases of IAS might be added in Table 1.

Answer: Thanks for your suggestions. Our study aims to introduce the exogenous insulin injection induced IAS and the Table 1 summarizes the characteristics about 4 non-classic IAS patients. And the difference between classic and non-classic IAS is discussed in the discussion and conclusion part. Therefore, we thought it is not necessary to add the typical case of IAS in Table1.

In Table 3, "extremely high" and "high" should be defined, as well as doses of glucocorticoid.

Answer: Thanks for your comments. We revised the "extremely high" and "high" as "serum insulin concentration &gt;1000pmol" in the Table 3. Moreover, as for the doses of glucocorticoid, the oral prednisone 30-60mg per day can be the useful adjunct therapy in classical IAS based on the previous study. And approximately 15mg per day prednisone initially through our experience is preferred for the non-classical IAS.

The following sentences need to be rewritten, "...insulin concentrations were 11 1567.44/1493.06/1370.20/1616.43/1812.01 pmol/L at 0/30/60/120/180 minutes, and C-peptide 12 concentrations were 3.41/3.68/3.95/4.56/4.51 nmol/L at 0/30/60/120/180 minutes...”.

Answer: Thanks for your suggestion. We have rewritten the sentence in the revised version.
The section of Discussion and Conclusions should be more concise.

Answer: Thanks for your suggestion. We have corrected the section of discussion and conclusions in the revised version.

This manuscript needs editing by native English speaker or by someone who is involved in scientific writing as the way of presentation of cases is bit weak (reviewer1).

There are some spelling errors, such as "While" in Line 23 on Page 6 should be in small case (reviewer2)

Answer: Thanks for your reminds. We have corrected it in the revised manuscript. And the language of this version has been re-edited by “CACTUS”, and proof is attached below.