Author's response to reviews

Title: Tubulointerstitial nephritis complicating IVIG therapy for X-linked agammaglobulinemia

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Date: 14 April 2014

Author's response to reviews: see over
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Prof. Guy Neild
Editor-in-Chief, BMC Nephrology

Dear Prof. Neild
Thank you for your letter of March 29, 2014 regarding our manuscript (MS: 1365747672121644). We appreciate the editor’s and reviewer’s assessment of the work. Please find the revised manuscript enclosed. Particular attention was focused on the following points, and corrections were indicated by underline.

Author's response to reviews

**Tubulointerstitial nephritis complicating IVIG therapy for X-linked agammaglobulinemia (MS: 1365747672121644)**

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Version: 2 Date: 14 April 2014

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For editor
Thank you for your suggestion. According your comment, we included acknowledgement and e-mail address of all authors in the manuscript.

For reviewer 1
We very much appreciate for your kind suggestions. According to the comments, we added new data and sentences, and also we removed redundant phrases and shortened discussion.
1. According your suggestion, we carried out determination of cell type infiltrating in the tubulointerstitium. We performed immunohistologic staining using antibodies
for T-cell specific surface antigen, CD3, and IgG4. The results indicated that the predominant tubulointerstitial infiltrating cells are T-cell, while IgG4-bearing B cells were only few (P.6 lines 15 to 17). These finding indicated that the Patient's TIN is not IgG4-related glomerulopathy. We added new photographic findings of CD3 staining (Figure 1e) and IgG4 staining (Figure 1f).

In addition, we included serum IgG4 concentration (P.5 line 19) and also added phrase to explain for exclusion of Casleman’s disease and malignant lymphoma (P.6 line 5 to 6).

2. We deleted redundant phrases and shortened manuscript.
3. We added important normal value for laboratory examinations (IgG, IgM, Ccr etc.)
4. According to your comment, we added new phrase concerning the immune complex-mediated TIN (P.8 line 2 to 7).

For reviewer 2

We very much appreciate for your kind suggestions. According to the comments, we added new data and sentences.

1. According your suggestion, we carried out determination of cell type infiltrating in the tubulointerstitium. We performed immunohistologic staining using antibodies for T-cell specific surface antigen, CD3, and IgG4. The results indicated that the predominant tubulointerstitial infiltrating cells are T-cell, while IgG4-bearing B cells were only few (P.6 lines 15 to 17). These finding indicated that the Patient’s TIN is not IgG4-related glomerulopathy. We added new photographic findings of CD3 staining (Figure 1e) and IgG4 staining (Figure 1f).

2. Thank you very much important information about TIN associated with IVIG for hypogammaglobulinemia. We cited this case report (reference #7) and included additional phrase regarding this patient's condition in discussion and (P.7 lines 8 to 12).

3. We substituted pathogen for antigen (P.7 line 22).

4. Thank you very much for your comment. I am very sorry, I don't have clear answer for your question. We employed venilon® (Teijin pharma., Tokyo, Japan) for IVIG. Venilon is prepared from healthy volunteers without any chronic diseases including collagen diseases like RA.