Reviewer’s report

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

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Reviewer: Stephen Walsh

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Review of Tubulointerstitial nephritis complicating IVIG therapy for X-linked agammaglobulinaemia

Sugimoto et al report a case of tubulointerstitial nephritis (TIN) apparently caused by therapeutic IVIG. They make a strong case that the IVIG was pathogenic, and include evidence that the patient had immune complex deposition in the tubular basement membrane.

The case is interesting and well written and is deserving of publication.

I have a few comments:

1. Given the distinctive IgG complex deposition in the tubular basement membrane, and the fact that exogenous IgG is the presumed pathogenic agent, there should be some consideration given to the measurement of the IgG4 subclass in both the infused IgG as well as on the renal biopsy. IgG4 disease can also give rise to membranous changes in the glomerulus; which, interestingly is also reported with IVIG. This should be mentioned in the discussion also.

2. Although there are no other reports of TIN with IVIG in XLA, there are in other conditions and these should be mentioned in the discussion; as XLA is unlikely to be relevant to the TIN. (An example is Tanaka et al Tohoku J Exp Med 1999, 155-161).

3. page 8 para 1 line 6-9: “...immune complex formation by interactions between a pathogen present in the patient and the IgG...” should read “...immune complex formation by interactions between an antigen present in the patient and the IgG...”

4. page 8 para 1 line 13-15. If there was autoantibody production against exogenous IgG, there should be detectable rheumatoid factor, and possibly a cryoglobulin, if these were not detected, that would weigh against this suggestion.

Overall, I think that this case report is novel and interesting and worthy, after these minor revisions, of publication.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests