Author's response to reviews

Title: Severe refractory autoimmune hemolytic anemia with both warm and cold autoantibodies: complete response to Rituximab

Authors:

Shilpi Gupta (drshilpigupta@gmail.com)
Anita Szerszen (aszerszen@aol.com)
Fadi Nakhl (fnakhl@hotmail.com)
Seema Varma (svarma@siuh.edu)
Aaron Gottesman (agottesman@siuh.edu)
Frank Forte (fforte@siuh.edu)
Meekoo Dhar (mdhar@siuh.edu)

Version: 3 Date: 30 June 2010

Author's response to reviews: see over
Dear Editor

Sub: Manuscript revision for MS: 7623694637727906, Severe refractory autoimmune hemolytic anemia with both warm and cold autoantibodies: complete response to Rituximab

We would like to thank you for considering our paper for publication in your journal and for the excellent critique provided. We have incorporated all the recommended changes and hope that our paper will be accepted for publication.

These are the changes recommended and the actions taken.

1) Table 1 does not add substantially to the report and duplicates some of the data already in the text. The relevant post-rituximab data could easily be summarized in the text.

We have removed the table from the manuscript.

2) There is some inconsistency in reported units; haemoglobin reported as both g/dl (text) and mg% (figure 3) similarly proteinuria is reported as g per day (text) and mg/24 dl (table 1). The more usual units are those in the text and the others should be amended.

The differences have been changed and we have used ‘g/dl’ in the text as well as the graph.

3) The statement "...the possibility of an underlying immunocompromised state were ruled out." is too euphemistic to be clearly understood. If the authors mean the patient was HIV seronegative this should be clearly stated (or whatever the meaning may be).

The statement has been re-written to state that our patient was HIV negative.

4) Follow up of case is slightly confusing regarding the time scale: abstract states 8 months post rituximab he is in CR (ABSTRACT; CASE PRESENTATION 2nd paragraph), within the main paper (CASE REPORT last paragraph) it refers to 2 year follow up (which I am assuming includes initial presentation and steroid use; I feel at this point clarification within text of CR at 8 months follow up post rituximab should be made, as it is stated in the abstract.
We apologize for the confusion and the text has been amended to indicate that patient was stable after 2 years of follow up.

5) Figure 1: initial LDH rise post rituximab could be commented on within the text

The initial rise in LDH has been discussed in the text.

6) Minor comments (not for publication) spellings of oedema, haemolysis, haemaglobinuria, stabilised: clarification regarding American/English spelling with journal.

We have not changed the spelling but if needed we will make the changes in the way certain words are spelt as required by the journal.

7) Top of page 5: Clarification of the timing of plasma exchange in relation to rituximab, as plasma exchange would remove rituximab. How many days of plasma exchange were given? What volumes were used?

The appropriate information has been incorporated in the text of the manuscript.

8) Middle of page 5: The nodular sclerosis on renal biopsy is interesting. Was the patient diabetic or obese? Was he HIV positive? Was this an FSGS type pattern? If so, what kind of FSGS? Could the authors include light microscopy of the biopsy? The authors suggest that the nephrosis is secondary to AIHA: it would be interesting if they could speculate a mechanism.

We have addressed the points raised and have tried to explain the possible mechanisms for the renal pathology. Also the light microscopy findings have been included.

9) Top of page 6: I’m not sure of the relevance of the use of rituximab to treat membranous nephropathy if there was no evidence of the disease on light microscopy or EM. However, there is a body of evidence regarding the use of rituximab with anti-virals in the treatment of cryoglobinaemia which should be mentioned.

As advised, the role of Rituximab in treatment of viral associated nephropathy has been included and we have rephrased the text in the areas where nephropathy and Rituximab is discussed.
10) The last sentence should be moderated – a single case is not sufficient to claim that rituximab is an effective treatment for AIHA.

The sentence and conclusion has been rephrased.

We would like to thank the reviewers for their comments and observation.

We look forward to the final decision regarding our submission.

Thank you
Shilpi Gupta.