Author’s response to reviews

Title: Enhanced serum immunoglobulin-G clearance in myotonic dystrophy-associated hypogammaglobulinemia: a kindred of two patients and review of the literature

Authors:

Sarah Sasson (ssas7805@med.usyd.edu.au)
Alastair Corbett (alastair.corbett@sydney.edu.au)
Andrew McLachlan (andrew.mclachlan@sydney.edu.au)
Renfen Chen (Ren.Chen@health.nsw.gov.au)
Stephen Adelstein (stephen.adelstein@sydney.edu.au)
Sean Riminton (sean.riminton@sydney.edu.au)
Sandhya Limaye (Sandhya.Limaye@health.nsw.gov.au)

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Author’s response to reviews:

Dear Prof Kidd,

Thank you for the correspondence regarding our report entitled: “Enhanced serum IgG clearance in myotonic dystrophy-associated hypogammaglobulinemia: a kindred of two patients and review of the literature” for consideration for publication in the Journal of Medical Case Reports.

I have read the Reviewer comments and made the following changes in line with their suggestions:

1. Page 3 and Page 4: The 2 cases are now presented separately under sub-headings.

2. Case 1: The report of findings has been re-organised and Past Medical History clearly sign-posted in Line 70. Family History has been signposted in Line 74. Social History has been signposted in Line 76 and includes the employment and environmental exposure history in Lines 77-78.

3. Case 2: The report of findings has been re-organised and Past Medical History sign-posted in Line 90. Family History has been signposted in Line 97 and Social History in Line 98. The social history now includes an employment and environmental history in Lines 99-101.
4. As stated in both Case Reports, the low serum IgG in both patients was found as the result of routine screening, and so it is difficult to describe the symptomology over time. A significant history of infections could only be elicited by a careful Past Medical History. Indeed, at the time of diagnosis Patient II-1 was asymptomatic and Patient III-1 had recurrent bowel obstructions with no identified pathogens. This has been added to Line 109.

5. The infective histories of both patients are included in the Past Medical Histories. Patient II-1 was relatively well despite a profoundly low IgG, however of note did have recurrent upper respiratory tract infections requiring tonsillectomy and adenoidectomy as a child, which is relevant. As these were distant infections treated in Ireland, records of causative agents could not be found. Patient III-1 had recurrent otitis media as a child requiring grommet insertion, however no records with positive microbiology could be obtained. Patient III-1 also had ongoing small bowel obstruction with no identified pathogen, both of these features are consistent with an underlying antibody deficiency.

6. Table I (new): As requested a new Table I has been created summarising the demographics, presenting features, past medical history and management of infectious illnesses for both patients.

7. Both presented patients were managed in the outpatient setting. Detailed neurological, cardiopulmonary and gastrointestinal examination findings have been included for Patient II-1 (Lines80-86) and Patient III-1 (Lines 123-128).

8. Full medication lists have been included for Patient II-1 (Lines 79-81) and Patient III-1 (120-122).

9. Table II (new): A new Table II has been inserted containing the requested tests (FBC, EUC, LFT and urine tests) and reference ranges. The additional requested serology tests (Pneumococcal, Tetanus and Haemophilus influenzae IgG) have been inserted alongside the other immunological tests in Table III.

10. The fact the genes for FcRn and DMPK are co-located on Chromosome 19 is raised in the Discussion as point of research interest. As there is no currently validated diagnostic tests for DM-1-associated hypogammaglobulinemia, no testing of Chromosome 19 was requested.

11. A new paragraph has been added to the opening of the Discussion (Lines 155-161) that summarizes the case, its contribution to the literature and unique features.

12. The Conclusions and future directions have been separated from the rest of the Discussion as requested.

I look forward to further correspondence,
Yours Sincerely,

Dr Sarah C. Sasson (Corresponding Author)

Nuffield Department of Medicine,  
University of Oxford,  
Level 5, John Radcliffe Hospital,  
Headington, United Kingdom  
OX3 9DU  
Phone (+44) 01865 220663  
Fax (+44) 01865 222737  
Email: ssas7805@med.usyd.edu.au