Author's response to reviews

Title: Anti-hLAMP2-antibodies and dual positivity for anti-GBM and MPO-ANCA in a patient with relapsing pulmonary-renal syndrome.

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Author's response to reviews: see over
Dear Mrs Chap

Thank you for your positive response to our revised manuscript “Anti-hLAMP2-antibodies and dual positivity for anti-GBM and MPO-ANCA in a patient with relapsing pulmonary-renal syndrome”. Please find enclosed the second revision of the manuscript. We hope that we have addressed adequately the minor concerns of the reviewer and that the revised paper is now acceptable for publication in BMC Nephrology.

Sincerely,
Christoph Etter and Clemens D. Cohen

Reviewer 1: Thomas Hellmark


Thank you for your positive response. We are happy to change the name of the disease according to the recently suggested new nomenclature.

Reviewer : Alenka Vizjak

The authors have adequately responded to the comments. However, I one minor concern: The text of Legend to Table 1 is inconsistence. The normal values for all clinical and serologiac data, listed in the table, should be indicated.

Thank you for your support. We have added normal values to Table 1.

My additional suggestion is: Insert Abbreviations: CRP = C-reactive . . .

Abbreviations are now avoided where possible or are given in the table legend.

Furthermore, there is a mistake in the last paragraph of Background: . . . immune deposits instead of depots

We deleted this typo.

Reviewer 3: Agnes Fogo

It remains incongruous why the authors do not explicitly even mention in the abstract or the Introduction, and continue to focus almost exclusively on the combination of antiGBM and MPO-ANCA, and do not include the very rare co-occurrence of a membranous nephropathy. Their response that they “prefer to focus on the clinical course and serology” does not make sense- the patient had significant proteinuria at presentation, and definite biopsy evidence of membranous nephropathy- and they did not test the serum for e.g . anti-PLA2R antibodies. The addition of one sentence stating that antiGBM disease and MN has been well recognized does nto adequately address the unusual occurrence of apparently three different types of injury.

We have added membranous nephropathy to the abstract and highlighted it in the introduction. Following the reviewer's suggestion we emphasize now the co-occurrence of all
three potential disease processes. We also discuss now shortly the potential clinical implications of subepithelial immune complex deposits in CGN. However, we do not believe that most readers would appreciate a broader discussion of membranous nephropathy or even anti-PLA2R antibody results in the context of this case-report.

The authors’ added statement that plasmapheresis was discontinued, because of the the anti-MPO titers increased and the presence of anti-hLAMP2 antibodies led to a diagnosis of relapsing ANCA-associated SVV is difficult to understand on what basis did they at that time make any conclusion that anti-hLAMP2 indicated relapsing disease, independent of the presence of anti-MPO –linked disease? Please explain this- what is the evidence that anti-hLAMP2 antibodies more specifically is associated with relapsing disease, independent of PR3 or MPO ANCA antibodies, or more so that in patients with the latter antibodies?

At time of relapse plasmapheresis was initiated immediately for treatment of a potential anti-GBM positive glomerulonephritis. As the renal biopsy showed no typical linear positivity the treatment was successfully changed to standard therapy of ANCA-positive vasculitis with crescentic glomerulonephritis, serum creatinine below 500 µmol/l, and no active pulmonary hemorrhage, i.e. cyclophosphamid and steroids but no plasmapheresis (Mukhtyar C et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2009; 68:310-7.)

The authors’ conclusions still reach far beyond what one can even speculate from this case- and their continuing reference to dual disease and dual positivity is not accurate- this is a patient with 3 disease processes, it appears.

We feel it has been adequately emphasized already in the first revision that this is an uncommon single case. And we clearly state that no firm conclusion can be drawn from a case-report. However, we believe that the report of this patient’s history together with the novel data on anti-hLAMP2 antibodies is of importance in the field.