Letter: In Reply to IgG4-Restricted Anti-Glomerular Basement Membrane Autoantibodies Targeting Quaternary Epitopes of Native alpha 345(IV) Collagen

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In Reply to: IgG4-restricted anti-GBM autoantibodies targeting quaternary epitopes of native α345(IV) collagen

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We have with interest read Dr Borzas comment on our report. The cases we described in our manuscript exhibited several features distinguishing them from other patients with anti-GBM disease, this included features related to demography, clinical presentation, autoantibody specificity, autoantibody subclass distribution as well as clinical outcome\(^1\). We do not know which of these features that occurred together by chance and which features that are linked by a pathogenetic mechanism forming a syndrome within the syndrome. Dr Borzas comment focuses on autoantibody specificity and IgG subclass distribution, as two of our mainly IgG4-antiGBM sera reacted better with non-denatured antigen, which presumably is a consequence of reactivity with an epitope requiring the intact alfa3,4,5-hexamer of the NC1-domain of Type IV collagen. We apologize that we failed to recognize Dr Borzas manuscript describing a serum with such specificity and IgG4 predominance\(^2\). We think, however, it is too early to make conclusions regarding the clinical significance of such antibodies or their IgG subclass distribution in general, even though Dr Borza provides interesting data from his animal model. It is an intriguing possibility that anti-hexamer autoantibodies might be less toxic to renal capillaries, and maybe more toxic to the lung capillaries, but such a hypothesis definitely requires to be addressed in larger studies.
