Reviewer’s report

Title: A case of atypical anti-GBM disease complicated by CMV pneumonitis and massive hemoptysis

Version: 1 Date: 06 Jan 2019

Reviewer: Scott Wenderfer

Reviewer's report:

The manuscript describes an interesting case of glomerulonephritis and subsequent CMV infection with pneumonitis and viremia that fortunately the patient survived but unfortunately resulted in progression to ESKD. The case and discussion nicely address (i.) the challenges of detecting in blood the autoantibodies implicated in anti-GBM disease, and (ii.) the importance of distinguishing disease recurrence vs. secondary infection after initiation of therapy.

The following suggestions might increase the impact of the manuscript:

1. It is important to distinguish, when possible, the etiology of hemoptysis when reporting on patients with anti-GBM disease. The manuscript suggests the patient never had Goodpasture disease, and that the hemoptysis on initial presentation was mild and likely due to hypervolemia from severe GN. It then implies that the second episode was due to pulmonary hemorrhage secondary to CMV pneumonitis. Was there evidence of diffuse alveolar hemorrhage on any of the BALs (hemosiderin-laden macrophage >20%, or elevated Golde score [see article by De Lassence, Fleury-Feith, et al. Alveolar hemorrhage. Diagnostic criteria and results in 194 immunocompromised hosts. American journal of respiratory and critical care medicine 1995])? Is it correct that bronchoscopy was not performed upon initial hospitalization? Etiology of hemoptysis should be clearly stated in discussion and title should be changed to "A case of atypical anti-GBM disease complicated by pulmonary hemorrhage from CMV pneumonitis" if appropriate.

2. Is there evidence that the CMV infection exacerbated the GN and contributed to the progression to ESKD? Or do authors think that viral sepsis and anemia secondary to the hemoptysis led to pre-renal AKI that in combo with GBM disease caused the ESKD? A third possibility was that the ESKD was inevitable after an initial modest improvement from the GBM disease, completely unrelated to the CMV infection. Answering this in the discussion would help readers form an opinion on the efficacy and safety of the initial immunosuppression regimen prescribed.

The following minor issues should be considered:
3. Page 6, lines 105-106 and page 9, line 184: statement "EM did not show any immune complex-type powdery linear densities along the GBM" from discussion should also be included in the pathology section of the case report.

4. Page 7, line 120: Please clarify: was patient treated with plasma exchange (with FFP as replacement fluid)? Or plasmapheresis with albumin as replacement fluid?

5. Page 7, line 122 and 132: Was CMV assayed in BAL at time of initial bronchoscopy, or only at time of 2nd bronchoscopy? Any negative blood tests for CMV prior to onset of viremia?

6. Page 7, line 134: should serum CMV viral load be greater than 10^6 instead of 2^6?

7. Page 9, line 180 - page 10, line 199: could be abbreviated, since these differential diagnoses do not relate to the CMV infection or progression to ESKD.

8. Fig 1: add arrows/arrowheads to identify (1) the mesangial hypercellularity, (2) the endocapillary hypercellularity, (3) the nodular mesangial sclerosis, and (4) the disruptions in Bowman's capsule. It might help to crop the images in A, B, and D to include all of each glomerulus, as was done for Fig1C.

9. Are Fig 1C and 1D stained with PAS or silver stain? If 4 glomeruli are to be included in the figure, it would be nice to show one with a necrotizing lesion and one with the focal GBM duplication.

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- Are the description of any error bars and probability values appropriate?

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