Reviewer's report

Title: Validation of a newly proposed histopathological classification in Japanese patients with anti-neutrophil cytoplasmic antibody-associated glomerulonephritis

Version: 2 Date: 15 October 2012

Reviewer: Leal C Herlitz

Reviewer's report:

Major revisions:
1) Your criteria for enrollment in the study are very unclear. You need to say how you identified people, what biopsy findings and serologic parameters needed to be met for inclusion into the cohort etc.

2) I find the description of how the SMA positivity was evaluated to be very confusing. You speak of >50% cytoplasmic staining defining a cell as positive. Are you referring to some kind of intensity measure or are you just looking at a cell to see whether it looks like half the cell is positive? You then talk about calling a glomerulus positive even if the staining area was very small. I would be unable to duplicate these methods as described. An additional figure showing a range of findings and how they were interpreted may help clarify.

3) In your section titled “immunohistochemical study” you talk more about SMA staining. You begin by saying that because you could not differentiate the mixed and crescentic classes in terms of renal outcome, you turned to SMA staining. You state that SMA reactivity differed substantially between each patient. Do you mean group? If so, what group? Are you looking at just patients with crescentic or mixed biopsies or are you looking at all patients? If there are “substantial” differences between the groups (as claimed), they should be detailed here. Instead, you speak about differences in SMA in patients who reach ESRD and non-ESRD. Are you looking at all who progressed to ESRD or not, or are you restricting this to certain subgroups (i.e. crescentic, mixed etc)?

4) In your discussion you bring up the important point that cyclophosphamide is less commonly used in Japan. I think that this is a significant point that should be underscored and this may indeed explain why after 1 year, prognosis of crescentic and mixed groups does not differ. It would also be important to know in this study, how many patients received cyclophosphamide and whether this treatment had an impact on outcomes.

5) You state in your abstract that SMA positivity was associated with a poor renal prognosis (P<0.05) but at the end of your discussion you say that SMA positivity was not correlated with outcome at 1 year after diagnosis. Outcomes, endpoints, groups etc are all very confusing and very poorly defined here. A clear question is never asked and a clear answer is never given.

Minor revisions:
1) In background you say no “active” lesions such as fibrous crescent formation or glomerulosclerosis are observed – these are chronic lesions

2) Methods: you say EM was not performed except in difficult cases. You need to say how many cases had EM and if/how EM contributed in these cases.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare I have no competing interests.