Reviewer’s report

Title: Picking Transplant Glomerulopathy out of the CAN: Evidence from a Clinico-pathological Evaluation

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Reviewer: Tibor Nadasdy

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Authors compare clinicopathologic features of patients with transplant glomerulopathy and chronic allograft nephropathy (CAN). Although the manuscript is interesting, it is mostly confirmatory. In its present form, it does not truly provide new relevant information regarding transplant glomerulopathy.

Major comments

1. One interesting observation is that patients with transplant glomerulopathy had a higher incidence of glomerular IgA deposition. IgA nephropathy is a quite common glomerular disease in China, most likely secondary to genetic susceptibility of the population. It would be interesting to know if authors have data in China whether hepatitis C infection is associated with higher incidence of mesangial IgA deposition in native kidney. Theoretically, it is possible that impaired hepatic function in hepatitis C positive patients is responsible for the increased incidence of glomerular IgA deposition in patients with transplant glomerulopathy. Authors need to provide more detailed data on the hepatitis C infection related transplant glomerulopathy patients. It would be important to know the viral load, liver function tests, rheumatoid factor tests, presence or absence of cryoglobulinemia. Hepatitis C infection is commonly associated with cryoglobulinemia, which can be transient. Cryoglobulinemia associated renal disease may have overlapping features with transplant glomerulopathy, particularly after repeated episodes of cryoglobulinemia. A detailed workup of hepatitis C infection related transplant glomerulopathy cases would greatly enhance the manuscript; in fact, this could be the focus of this manuscript.

2. Authors do not present data on donor specific antibodies. In the materials and methods sections, they indicate that they considered patients to be anti-HLA antibody positive if the flow PRA at the time of the biopsy was above 10% for anti-MHC class I or II antibodies. This definitely does not mean that these antibodies were donor specific. If they cannot perform donor specific antibody testing retrospectively, they should indicate whether these anti-MHC antibodies were de novo, appearing after transplantation or were they pre-existing.

3. It is unfortunate that authors did not perform ultrastructural examination. Detailed morphologic workup of biopsies with transplant glomerulopathy cannot be performed in the absence of ultrastructural examination. This is particularly relevant in hepatitis C positive patients who could have overlapping features of
cryoglobulinemia. Also, without electron microscopy, authors cannot comment on microvascular damage in peritubular capillaries.

Minor comments

1. In the Materials and Methods sections, authors indicate that 43 biopsies with transplant glomerulopathy were included in the study. Were these from 43 different patients?

2. Although the manuscript is easy to understand, it will need a thorough editing for English grammar.

Level of interest: An article of limited interest

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

Statistical review: No, the manuscript does not need to be seen by a statistician.