Reviewer's report

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

Version: 2 Date: 12 June 2012

Reviewer: Tibor Nadasdy

Reviewer's report:

Authors’ revised manuscript improved substantially; however, I still have several comments.

Major Revision

Authors apparently have a misconception about IFTA. The Banff group eliminated the term “chronic allograft nephropathy (CAN)” because the impression was that CAN is being used as a separate entity. Therefore, IFTA is not the same as CAN and IFTA does not represent a separate entity. IFTA represents interstitial fibrosis/tubular atrophy. Throughout the manuscript, authors interchangeably use IFTA and CAN, somewhat confusingly, and consider IFTA as an entity. I think the two main study groups should be called the transplant glomerulopathy (TG) group and the non-TG group. Also, in the text, the sentences where authors compare the entities of TG and IFTA should be eliminated/revised. The title of the manuscript sounds very interesting, and I do not want to suggest changing it. However, briefly in the introduction, authors need to explain, as they do, that CAN is now not an accepted entity.

Throughout the text, the term “C4d deposition” is used. This is incorrect, because I believe authors mean peritubular capillary (PTC) C4d deposition. C4d deposition is frequently present outside the peritubular capillaries (for example, mesangial and arteriolar staining by immunofluorescence are a nonspecific finding). Also, in TG, glomerular capillary staining for C4d is frequently strong in the absence of PTC C4d staining. Therefore, wherever they indicate C4d staining and they mean PTC C4d staining, authors should put the abbreviation PTC in front of the C4d.

Minor revisions

The abbreviation of PTC is confusing and incorrect, in my opinion. PTC in most manuscripts and texts is the abbreviation for peritubular capillary. The authors use this abbreviation (PTC) for peritubular capillaritis throughout most of the text. However, later in the Results section (in the paragraph on pathologic features), they use PTC as an abbreviation for peritubular capillary. The abbreviation of PTC should be used for peritubular capillary not for peritubular capillaritis. In the Banff scoring system, the PTC score refers to the inflammation in the peritubular capillaries, so they should use the PTC score as they use it in the text. The term “peritubular capillaritis” could be used but it should not be abbreviated, or authors
should use the terminology “PTC inflammation” or “PTC margination of inflammatory cells.”

Several times in the manuscript authors use the terminology “clinical histological entity.” It would be more appropriate to use the term “clinicopathological.”

In the Materials and Methods, in the second paragraph, authors indicate that “patients who suffer from acute rejection were excluded from both groups”. They probably mean that patients who suffered from acute rejection at the time of the biopsy were excluded.

In the results section, the anti-HLA antibody paragraph is unclear. Authors indicate that 30 patients with TG and 23 patients with IFTA had anti-HLA antibody and then they were “classed as” positive in 20/30 and 5/23. This is unclear; this paragraph should be clarified.

How did authors define PTC C4d positivity? Did they consider biopsies with over 50% PTC C4d as positive?

It is only mentioned in the Discussion that the distribution of IgA staining was not different between HCV positive and negative TG patients. This should be mentioned in the Results as well.

The legend of Figure 5 should be more detailed. It is unclear what the numbers on the Y axis mean, for example.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I have no conflict of interest to declare