Reviewer's report

Title: An unusual case of glomerulonephritis in a patient with Non-Hodgkin Mucosal Associated Lymphoid Tissue (MALT) B-cell lymphoma

Version: 2 Date: 21 March 2013

Reviewer: Joachim Velden

Reviewer's report:

Major compulsory revisions to the Authors' reply (numbered)

1. „As requested by the reviewer, all IMF photos are now incorporated into Figure 2.“
   
   Revision to this point:
   
   This is appreciable, but it is very speculative to call these findings a „full-house pattern“ for the following reasons: First, C1q and C4 show only incomplete and trace positivity which may be due to an unspecific trapping phenomenon. This must not be scored as 2+ for C1q and 1+ for C4, particularly in comparison with IgG and IgA, which are both scored 2+. Second, lambda light chain staining is completely negative and does not justify 1+ score as claimed by the authors. Hence, these data and their interpretation by the authors are inconsistent. This is a major point of criticism because the authors claim the „lupus-like“ features of the GN based on this immunofluorescence pattern.

2. „Figure 3 has been replaced with another electron micrograph that demonstrates both sub-endothelial and intraluminal deposits.“
   
   Revision to this point:
   
   The deposits are still subendothelial but not intraluminal. The lumen is narrowed because of the subendothelial deposits and augmented extracellular matrix which also entraps some cytoplasm (presumably of mesangial cell origin) and some red blood cell fragments. The figure shows the typical EM findings of membranoproliferative GN.

Comment to the legend to figure 4: Insert electron DENSE deposits, and delete either DELICATE or THIN.

3. „We accept the reviewer’s point that Richmond’s study is from an autopsy series and may not be clinically relevant currently. We have re-written that portion and included a review of 700 patients with clinical renal manifestations. As this is a case report, the manifestations of plasma cell myeloma and other B-cell neoplasms including
monoclonal gammopathy is beyond the scope of this manuscript.“

Revision to this point:

The authors' statement that „kidney involvement in NHL is …. most commonly due to direct infiltration of lymphoplasmocytic cells within the renal parenchyma“ (first sentence of Abstract) is highly questionable since it neglects the „non-cellular“, paraneoplastic involvement of the kidney e.g. in productive B-NHLs such as plasma cell myeloma, which indeed represent a substantial portion of all non-Hodgkin lymphomas, and cause common paraneoplastic renal sequelae (cast nephropathy, AL amyloidosis, MIDD/LCDD, hypercalcemic acute tubular injury). Undoubtedly, the details of such sequelae clearly exceed the scope of this case report.

4. „We agree with the reviewer’s comments and have removed the following statement from page 8 - “The absence of a MPGN pattern or an immunotactoid glomerulonephritis picture, which is often the histology compatible with cryoglobulinemic glomerulonephritis, also refutes such a diagnosis.”“

Accepted.

5. „We accept the reviewer’s comments and have removed the portion on the pathogenesis of lupus nephritis and HIV-associated immune complex GN. Focus is now placed on the differential diagnosis of the renal biopsy, as suggested.“

Revision to this point:

DISCUSSION:
The last sentence on p.7 (starting „The rare occurrence...“) continued on p.8 needs linguistic revision.

The following sentence „The paraneoplastic nature...“ (p.8) contains a contradiction: „Spontaneous remission“ cannot follow therapy because „spontaneous“ means „without prior therapy“. Apart from that, this sentence is speculative because rituximab and cyclophosphamide are well known to be also effective in lupus nephritis.

The next sentence „Consequently, the similar hyperactive...“ needs explanation of what is meant.

P.9 (4th paragraph): A low or negative anti-dsDNA titer renders the diagnosis of proliferative lupus nephritis less likely. but does not preclude lupus nephritis.

P.10/11: „Likewise, the anti-dsDNA titers would represent a false positive serology arising from polyclonal B-cell activation in the setting of B-cell lymphoma, which would become undetectable immediately with treatment of the malignancy“. Please cite at least one convincing reference that supports this claim.

P.10: „... suggesting the production and deposition of immune complexes arising
from polyclonal immunoglobulins**: Polyclonal immunoglobulins should contain both kappa and lambda light chains. But lambda is negative in Figure 2 whereas kappa is strongly positive. How do the authors explain this discrepancy? It does not fit their argumentation.

P.10, last sentence of paragraph Discussion: What is „unique“ about the morphological pattern of glomerular immune complex deposition in the reported case?

CONCLUSION: The authors provide a summary but not a conclusion. A good conclusion should state a take-home message. The last sentence („Unfortunately,...“) is neither summarizing nor concluding – and hence does not belong here.

REFERENCES: There is at least one double reference (#1=#7 Da'as et al.) Please check reference list for further potential doublettes or inconsistencies.

6. „Normal ranges had been included in page 4 of the manuscript. Blood cell counts are now only represented in cells/uL. (Page 4)“ Accepted.

7. „Serum leukocyte count has been replaced with blood leukocyte count. (Page 4)“ Accepted.

8. „Proliferation of endothelial cells has been replaced with endothelial cell damage and activation on page 5.“ Accepted.

9. „The absence of extraglomerular immune deposits involving tubular basement membranes and vessel walls would be unusual in severe lupus nephritis.” has been removed in page 6.“ Accepted.

10. „Suggestion by reviewer “MPGN has been the most commonly reported histological TYPE OF GLOMERULONEPHRITIS…” is now incorporated in page 7.“ Accepted.

11. „The spelling error was corrected to “Kowalewska” in page 7.“ Accepted.

12. „The findings does not add to the discussion and differential diagnosis, and hence was
not imaged and shown in a figure."

Accepted.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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 declare that I have no competing interests.