Author’s response to reviews

Title: IgG4-related kidney disease (IgG4-RKD) with membranous nephropathy as its initial manifestation: report of one case and literature review

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Author’s response to reviews:

To Reviewer 1

Dear Mihir Ravi Atreya, MD, MPH,

Thank you for your comment, which is as follows:
“1. Line 44-45 of Page 2. Please specify which medication was stopped-corticosteroids, cyclophosmaide or both. 2. Table 2: Clarify line on "Hormone Dosage" and what the authors are referring to.”

Response:
1. Prednisone acetate and cyclophosphamide were discontinued, and irbesartan was administered for maintenance.
2. Hormone dosage : Typically adequate (Prednisone dose that was 1-2 mg/kg/d) ; Generally medium and small dose (Prednisone dose that induced was 30–40 mg/d).

To Reviewer 2

Dear S. Bardak,

Response: IgG4-RD is a cause of secondary MN. A meta-analysis showed that the sensitivity and
specificity of serum anti-PLA2R antibody were 68% and 97% in the differential diagnosis of primary MN and secondary MN, respectively. In our current case, PLA2R was negative during both attacks. Thus, patients with PLA2R-negative MN should be further examined to identify IgG4-RKD and other secondary MN. Based on the immunohistochemical findings and clinical manifestations, and other secondary factors that were excluded, a diagnosis of IgG4-TIN accompanied by MN was made.

To Reviewer 3

Dear Tatar Bengu,

Response: For the first attack, we administered prednisone acetate (60 mg/day for 8 weeks, then reduced it by 5 mg every 4 weeks as the patient’s condition permitted) and cyclophosphamide (0.6 g/month by intravenous injection, to a total of 6 g). After 11 months of treatment, the patient’s condition was completely relieved. The prednisone acetate and cyclophosphamide were discontinued, and irbesartan was administered for maintenance.

For the second attack, prednisone acetate and cyclophosphamide were administered in accordance with the previous treatment regimen. A further 6 g of cyclophosphamide was then administered (to a total of 12 g), and the prednisone acetate was continued at 10 mg/day for maintenance.

During the second attack, based on the immunohistochemical findings, clinical manifestations, and exclusion of other secondary factors, a diagnosis of IgG4-TIN accompanied by MN was made.

During both attacks, the patient displayed evidence of chronic bilateral lacrimal gland inflammation, with exophthalmos, tearing, and bulbar conjunctival hyperemia. Unfortunately, we do not have a lacrimal gland biopsy. However, this does not prevent our results from providing a clue for suspecting that the patient had IgG4-RD.

To Reviewer 4

Dear Udayan Bhatt,

Thank you for your comments.

To Reviewer 5

Dear Abhilash Koratala,
Response: Because of our laboratory conditions and our experience in the diagnosis of MN, tissue PLA2R testing was not performed.

During the patient’s first hospitalization, his serum creatinine increased progressively, his albumin levels were extremely low, the edema gradually worsened, and his urine output was low. To prevent further deterioration of renal function and secondary thrombosis, we administered prednisone acetate (60 mg/day for 8 weeks, then reduced it by 5 mg every 4 weeks as the patient’s condition permitted) and cyclophosphamide (0.6 g/month by intravenous injection, to a total of 6 g). After 11 months of treatment, the patient’s condition was completely relieved. The prednisone acetate and cyclophosphamide were discontinued, and irbesartan was administered for maintenance.

During the patient’s second hospitalization, he had acute kidney injury and was in critical condition. Prednisone acetate and cyclophosphamide were administered in accordance with the previous treatment regimen. A further 6 g of cyclophosphamide was then administered (to a total of 12 g), and the prednisone acetate was continued at 10 mg/day for maintenance. His renal function returned to normal after 2 months, and nephrotic syndrome was ameliorated after 5 months.

During the two attacks, the patient displayed evidence of chronic bilateral lacrimal gland inflammation, with exophthalmos, tearing, and bulbar conjunctival hyperemia. Unfortunately, we did not have a lacrimal gland biopsy. However, this does not prevent our results from providing a clue for suspecting that the patient had IgG4-RD.

Studies have shown that rituximab is effective in the treatment of IgG-RD, but it was very expensive for this patient. Thus, we did not consider using this drug.

We have revised the Figures in the article.

Yours sincerely,