Defining the Incidence, Pathology and Clinical Outcomes of Kidney Disease Related to Waldenström's Macroglobulinemia and IgM MGUS

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Key points

- Related kidney disease complicated WM/IgM MGUS in approximately 3% of cases in our cohort.
- There was a wide range of kidney pathology associated with WM/IgM MGUS.
- Renal function improved or remained stable in the majority of treated patients.
- Outcomes seem worse in patients with renal amyloidosis or light chain deposition disease.

Background & Methods

Background While kidney disease (KD) occurs in up to 40% of multiple myeloma (MM) patients, the incidence, pathology, and clinical correlations of KD in patients with Waldenström's Macroglobulinemia (WM) or IgM MGUS remain to be clarified.

Methods Out of 1,738 patients with consensus criteria defined WM (N=1,665) or IgM MGUS (N=83) diagnosis who were evaluated at the Bing Center for WM from 2001-2015, we selected those individuals with at least one of the following abnormalities: serum creatinine ≥1.3, estimated GFR (eGFR) <60; or proteinuria. Patients with non-WM/IgM MGUS related KD were excluded.

Results - Crude incidence

Renal impairment and/or proteinuria were present in 259 patients. In 183 cases, this was unrelated to WM/IgM MGUS. We excluded 15 patients with urological carcinoma, and 4 patients with peri-renal diffuse large B-cell lymphoma. In 31 patients, the kidney biopsy was not available. In 6 patients, the disease was considered “renal amyloidosis” and included the diagnosis of light chain deposition/Cryoglobulinemia. Capillaries were occluded by large masses of PAS-positive protanocous material (“pseudothrombosis”). The lower panel shows the reactivity for this material as well as the electron microscopy appearance of the endothelial deposits. The deposits were reactive for kappa and not for lambda light chains (not shown).

Results - Kidney Pathology

Kidney Biopsy Pathology

Kidney Biopsy: TMA

Interestingly, in 3 patients thrombotic microangiopathy was identified as the renal diagnosis. To our knowledge, no cases of TMA have previously been reported in association with WM. TMA has been reported in MM and CLL, although in most cases related to chemotherapy. However, the 3 WM patients presenting with TMA were all previously untreated. The pathophysiological process leading to TMA associated with WM is unknown. Several mechanisms could be suggested, including paraprotein- or tumor cell-related activation of the complement and/or coagulation cascades.

Results: Outcomes

The median follow-up was 17 months (range 1-162). A synchronous diagnosis of WM and KD was made in 17 patients (41%), while in the remaining 24 patients the median time to KD following the WM diagnosis was 29 months (range 5-88). KD was diagnosed mostly in untreated patients (N=29; 70%), while the remaining 12 patients had a median of 2 prior therapies. Thirty-six patients were treated after their kidney biopsy, regimens were as follows: proteasome-inhibitor based (N=19; 46%); alkylator based (N=15; 27%); nucleoside analogues (N=4; 10%); and rituximab monotherapy (N=2; 5%). Additional plasmapheresis was employed in 12 (31%) patients. WM treatment responses based on consensus criteria were as follows: CR (N=1; 3%), VGPR (N=4; 11%), PR (N=27; 75%), MR (N=1; 3%) progressive disease (N=3; 5%), or not evaluable (N=5; 14%). Renal outcomes for the 36 treated patients based on at least a 10 ml/min/1.73m2 change in eGFR were as follows: improved (N=14; 31%); stable (N=12; 29%); decreased (N=9; 22%) and unknown (N=1; 2%). Patients with either amyloid or light chain deposition (N=16) showed worse outcomes: 1 died of refractory nephrotic syndrome; 5 went to dialysis. None of the patients with other renal pathology either died of renal complications or required dialysis.

Conclusion

KD complicates WM/IgM MGUS in approximately 3% of cases and shows a wide range of kidney pathology. Patients with amyloidosis or light chain deposition disease show worse outcomes, including the requirement for dialysis. Establishing the underlying WM-related kidney pathology may help direct appropriate therapeutic interventions.