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Proliferative glomerulonephritis with non-organised monoclonal immunoglobulin deposits (PGNMID): a single-centre retrospective study

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Introduction

Proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) is a rare glomerular disease1. It is most often seen in the context of monoclonal gammopathy of renal significance (MGRS), a group of disorders in which a circulating monoclonal immunoglobulin causes renal injury, but where diagnostic criteria for multiple myeloma or lymphoma are not met2. At present, optimal treatment for most subtypes of MGRS, including PGNMID, is not known3. We performed a retrospective, study of patients with PGNMID managed at our tertiary referral centre.

Methods

All native renal biopsies performed at the Hammersmith Hospital over a 12-year period (2006-2017) were analysed. 15 cases of PGNMID were identified. Baseline characteristics and clinical outcomes during follow-up to January 2019 are summarised in Table 1. Renal response to treatment was defined according to changes in eGFR and uPCR at follow-up (Table 1).

Results

In our cohort, mean age at presentation was 61, 33% were men, mean eGFR was 49 mL/min/1.73m2 and mean uPCR 384 mmol/mol. A circulating paraprotein was detectable in 5 (33%) of the 15 patients. Most patients (80%) underwent bone marrow aspiration and trephine (BMAT), with a clone identified in two of these 12 (17% of those tested). One had a plasma cell clone and did not receive specific treatment, with early requirement for dialysis. The second patient had a B cell clone, and achieved complete remission of proteinuria and stabilisation of eGFR with prednisolone and rituximab. These patients had variable renal function and amount of glomerulosclerosis (GS) and interstitial fibrosis and tubular atrophy (IFTA) at baseline. The treatment non-responder presented with an estimated glomerular filtration rate (eGFR) of 7 mL/min/1.73m2 and 50% IFTA, whilst the responder had an eGFR of 83 mL/min/1.73m2 and 0% IFTA.

Three (20%) patients had a detectable paraprotein but no clonal population on BMAT, and all received treatment. Two patients received steroids, rituximab and cyclophosphamide; neither responded to treatment and both progressed to ESRD. One patient received clone-directed therapy with steroids, MMF, rituximab and bortezomib. They initially achieved complete renal remission, but relapsed following cessation of bortezomib after three cycles due to peripheral neuropathy.

10 of 15 (67%) patients had no detectable paraprotein at diagnosis. Of these, 80% had partial or complete renal remission at follow-up. Treatment of this group was variable, from conservative management including renin-angiotensin-aldosterone system inhibition, to empiric immunosuppression. None had clone-directed therapy. One case was lost to follow-up post renal biopsy.

Discussion

Our cohort of PGNMID patients corroborates the previously described low rate of detection of circulating paraprotein and pathogenic clones on BMAT4. Patients with detectable clones at presentation or those with a higher burden of GS and IFTA on biopsy may have lower treatment response rates and worse clinical outcomes. This highlights the need for the development of tools to enable early diagnosis.

Treatment remains varied in this population. In our centre, an individualised approach is taken, with multidisciplinary involvement from nephrologists, haematologists and histopathologists. Further collaborative studies are required to establish the safety and efficacy of clone-directed therapy, and to guide optimal management in patients with PGNMID.