Introduction and Aims: DDD and C3 nephropathy (C3GN) are rare forms of glomerulonephritis associated with glomerular deposition of complement factors due to dysregulation of the alternative pathway of complement. Functional inhibition of the complement regulating proteins may result from monoclonal gammopathy. Proliferative glomerulonephritis tends to recur in the graft (recurrence rate up to 50%) and the risk of recurrence is higher when circulating monoclonal immunoglobulin are present in serum.

Methods: We describe the case of a 65 year old men with ESRD due to DDD and a previous diagnosis of monoclonal gammopathy of undetermined significance (MGUS) at bone marrow biopsy: 8% plasmacells, serum monoclonal component (CM) 30%. In 2014 he received a deceased donor kidney transplantation (Induction immunosuppression: basiliximab, mycophenolate and steroid; maintenance therapy: tacrolimus and steroid). At hospital discharge: serum creatinine - sCr 1.5 mg/dl, proteinuria 0.1 g/24h. C3 was 61 mg/dl (72-150).

Results: One month after, sCr increased to 2.5 mg/dl. A renal biopsy (RB) demonstrated an early DDD recurrence at electronic microscopy and immunofluorescence. CM was 23%. No evidence of complement mutation and of abnormal values of C5b9 were found. A pulse steroid therapy obtained a poor response. According to a newly described entities of MGUS associated C3 glomerulopathies, we proposed, after a haematologic counseling, a treatment with plasmapheresis (5) and chemotherapy, initially with bortezomib (1.3 mg/m²/week subcutaneously) and desametasone, and subsequently, owing a CM increase, with cyclofosfamide (400 mg/week orally) for 3 weeks monthly for 6 months. Reduction of tacrolimus levels was performed (5 ng/mL). After 6 months: sCr 1.4 mg/dl, no adverse event, CM 14-7%. A protocol RB was performed after 4 months of therapy and the graft picture was unchanged.

Conclusions: Monoclonal gammopathy-associated glomerulonephritis is a newly described entity; particularly DDD and C3GN may result from the direct glomerular deposition of monoclonal Ig that cause the activation of the alternative pathway of complement, with in renal deposition of complement-regulating proteins. Treatment should be aimed at eradicating the population of clonal cells responsible for the offending Ig. Currently, optimal approach is unknown. The association of bortezomib, dexamethasone and cyclophosphamide is reported and appears a reasonable option in presence of M protein in serum and urine and/or a proliferative glomerulonephritis with Ig deposits at immunofluorescence staining. In our patient this therapy was associated with an improvement of renal function and a CM reduction. In consideration of the well known slow progression of the glomerular disease we cannot establish the real impact of the therapy. Yet, the approach seemed to us promising for the close linked hemathological and nephrological disease.

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