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NEPHROLOGY - LETTER TO THE EDITOR

# Why renal biopsy is crucial in monoclonal gammopathy of renal significance (MGRS)

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Dear Editor,

Monoclonal gammopathy of renal significance, from now on MGRS, is a hemato-nephrological meta-entity caused by monoclonal immunoglobulins or humoral factors secreted by B cell lineage clones which do not meet hematological criteria for treatment (mostly small clones) [1–4].

Among paraprotein-related diseases, nephropathies that belong to MGRS meta-entity (with the exception of amyloidosis) are the ones in which the role of the nephropathology is more relevant when it comes to deciding the specific treatment [2].

To our knowledge, only one retrospective study has evaluated the prevalence of paraprotein-related kidney diseases, including MGRS. This pioneer study had two limitations driven from the moment it was written. One of the selection criteria was M-component detected by serum or urinary electrophoresis; thus, patients with positive immunofixation or abnormal serum kappa/lambda ratio, but normal electrophoresis were ruled out. The other limitation was that only five nephropathies were considered as paraprotein-related kidney diseases: monoclonal immunoglobulin deposition disease, light chain amyloidosis, cryoglobulinemia, light chain tubulopathy with crystals and light chain cast nephropathy. Nevertheless, this study documented that at least one-third of the patients who had paraproteinemia and kidney disease had a paraprotein-related kidney disease [1, 4, 5].

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Renal biopsy is the only way to determine the specific pattern of kidney injury. As a result, the association between the paraproteinemia and the nephropathy can be proven in most cases. The exceptions are basically two: first, C3 glomerulopathy and atypical hemolytic uremic syndrome, the ones in which ordinary techniques do not demonstrate the presence of monoclonal immunoglobulins in renal tissue, and second, POEMS syndrome nephropathy related to humoral factors. In fact, there are cases of MGRS in which monoclonal immunoglobulins are detected neither in serum nor in urine. In this cases, monoclonal immunoglobulins can only be identified by restrictive immunoglobulin deposits in renal tissue. Renal biopsy also allows to rule out other nephropathies that could appear alone or associated to MGRS in patients with paraproteinemias. The usefulness of renal biopsy in MGRS prognosis is based on its role for diagnosing the specific nephropathy as well as determining the severity and chronicity of the lesions in all the renal compartments, which is needed to ponder clone directed therapy. The significance of renal rebiopsy in MGRS has yet to be established. Like with other kidney diseases, as lupus nephritis or IgA nephropathy, renal rebiopsy is a strategy to be considered [1–3, 6, 7].

It has been demonstrated that renal biopsy does not have more complications in patients with paraproteinemias than in general population. Moreover, it has been proven that renal biopsy does not have more complications in very elderly patients than in general populations, which is especially important considering that the prevalence of paraproteinemias rises with age [1, 8, 9].

Although the main causes of renal replacement therapy in adulthood are diabetic nephropathy (DN) and nephroangiosclerosis, these diagnoses are not always certain since sometimes they are not based on renal biopsy, and in fact some of them could be masked cases of MGRS. In this sense, it has been showed that among type II diabetic mellitus patients with kidney disease, one-third had a DN alone, another third had DN plus another nephropathy and the last third had a

nephropathy non-related to diabetes. Even more, light chain deposition disease has been diagnosed thanks to renal biopsy in patients with hypertension, mild proteinuria (≤ 0.5 g/day), and reduced glomerular filtration rate, even though nephroangiosclerosis was initially suspected [10, 11].

In spite of being an invasive tool, renal biopsy is the only alternative to get an accurate diagnose. Even though one of the trends is toward using kidney biomarkers to avoid renal biopsy when it seems reasonable, the other one is towards a more exhaustive evaluation of kidney tissue based on precision nephrology [12].

In conclusion, renal biopsy should be performed in those patients who might benefit from the specific treatment as MGRS is suspected.

## Compliance with ethical standards

**Conflict of interest** All the authors declare that they have no conflict of interest.

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