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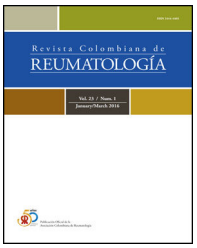

Editorial

Another step in lupus nephritis

Un paso más en la nefritis lúpica

The follow-up and treatment of systemic lupus erythematosus (SLE) have progressed significantly in recent years. In this sense, new therapeutic targets have been developed, including anifrolumab, obinutuzumab or voclosporin, among others, and new treatment strategies such as Treat to Target (T2T), and new monitoring tools have been implemented to define both remission and low disease activity. All these strategies are ultimately intended to prevent organ damage, including kidney damage, as well as to reduce mortality.[1]

It is well known that the appearance of lupus nephritis (LN) is one of the main determining factors in the prognosis of patients with SLE; therefore, the identification of clinical and immunological factors related to the development of LN is a crucial issue.

In the present volume, Téllez Noriega et al.[2] analyze a cohort of 87 patients with SLE from Argentina, mostly of mixed race and with an average age of 25 years at diagnosis of SLE. It should be highlighted the high prevalence of LN in this cohort, close to 60%, and the high rate of development of chronic kidney disease (CKD), around 50%. These data are far above other cohorts, even above the Latin American cohorts with SLE.[3,4]

Among the factors associated with greater renal involvement, factors specific of the disease, such as the age of onset, the presence of *livedo reticularis* and serological markers such as the presence of anti-double stranded DNA antibodies and low concentrations of complement were taken into account. Among the comorbidities, hypertension was a factor clearly associated with the development of LN. Even though the presence of *livedo reticularis* was not associated with the presence of antiphospholipid antibodies, its relationship with LN may suggest the role of the microvasculature in lupus renal pathology.

As supported by literature, the presence of anti-double stranded DNA antibodies and hypocomplementemia are closely associated with the development of LN.[5] In a recent systematic review, it was reported a strong association with the decrease of the C3 and C4 complement fractions, with the subsequent risk of a flare of the disease —including a flare of LN— as well as of anti-double-stranded DNA antibodies with odd ratios of higher risk of flare ranging between 2.0 and 2.8.[6]

It is evident that the study conducted by Téllez Noriega et al. has certain limitations, not only those characteristic of a cross-sectional study and with a relatively small cohort of patients with SLE, but also the fact that in 27% of the patients classified as LN, a renal biopsy was not available.

The access to renal biopsy can sometimes be a limitation for the study of LN, not only in Latin America, but also in other latitudes. For this reason, the implementation and identification of biomarkers both in serum and in urine is an area of research with growing interest. In this regard, the Latin American Group for the Study of Lupus (GLADEL 2.0) is developing a multicenter study in more than 10 Latin American countries, which aims to analyze various biomarkers both in patients with or without LN, as well as in those with incident and prevalent kidney disease in order to more precisely stratify the risk of kidney disease in a large cohort of patients.[7]

However, it should be noted that even though the field of biomarker identification is a promising topic, it is not intended to replace renal biopsy, but rather to complement it or help reaching a diagnostic approach and perhaps a more accurate follow-up.

Renal biopsy not only provides us with relevant information regarding glomerular involvement, but also about interstitial and vascular commitment, which are also associated with a worse prognosis and a higher risk of developing CKD, as recently described.[8]

The management of LN continues to be a challenge for the clinician, and involves the control of the activity of the disease by the rheumatologist, in addition to the control of comorbidities and complications inherent to kidney involvement by other specialists such as internists or nephrologists. This multidisciplinary approach allows a stricter control of the

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disease, with a lower number of flares, less deterioration of renal function and less progression to CKD.[9]

The implementation of combined therapies (e.g., calcineurin inhibitors plus mycophenolate mofetil), or the addition of biological therapy (belimumab) has shown good results both in proliferative and in membranous forms of LN,[10] all this added to a prudent use of glucocorticoids. Beyond the immunomodulatory therapies, nephroprotective therapies such as angiotensin-converting enzyme inhibitors and more recently the use of other nephroprotective agents such as sodium and glucose cotransporter 2 inhibitors (SGLT2-i) are essential.[9]

Therefore, although the identification of factors related to LN and its treatment continues to be a challenge, it finally seems that we are moving in the right direction both in the diagnosis and in the management of these patients. This path is promising and we have already started to take great steps.

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