Essential Mixed Cryoglobulinemia and IgA Nephropathy, an Infrequent Association

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Dear Sir,

Essential mixed cryoglobulinemia (EMC) is an infrequent disease grouped together with hypersensitivity vasculitis [1]. Glomerular involvement is present in 50% of cases, morphologically identified as a membranoproliferative glomerulonephritis, and related to the presence of mixed type IgG-IgM serum cryoglobulins, less frequently with the IgG-IgG and IgG-IgA complexes [2-5]. On reviewing the literature we have found only one case of EMC type III IgG-IgA associated with IgA nephropathy (IgA N) [6]. In this paper, we describe the first case of EMC type II IgG-IgM with IgA N as renal involvement.

Our patient was a 58-year-old female with a 10-year history of arthralgia and cutaneous lesions. She was referred to our service because of urinary sediment changes; over the preceding 6 months she had experienced dark urine, and in the 3 months prior to admission arterial hypertension and general malaise, weakness and weight loss. The only noteworthy findings in the physical examination were systolic hypertension (180/90 mm Hg), mucocutaneous pallor and residual hyperpigmentation in both lower limbs. She had severe normochromic normocytic anemia (Hb 7.9 g/dl; Ht 23.9%), proteinuria (0.85 mg/min), microscopic hematuria, and a mild renal insufficiency (blood urea 83 mg/dl and creatinine 1.7 mg/dl). Serum proteins were normal, with an isolated increase of IgG: 2,210 mg/dl (normal 810-1,690); antinuclear antibodies and HbsAg were negative; C4: 8.3 mg/dl (normal 10-10); CH50: 47 U/ml (normal 150-250). Rheumatoid factor was positive; Latex was 102 IU/ml (normal 0-10). Cryoglobulins were positive in two samples; immunoelectrophoresis revealed the presence of IgM-kappa and polyclonal IgG in the cryoprecipitate. No pathological findings were detected on chest, gastrointestinal and osseous X-ray studies, abdominal echography, and bone marrow aspirate and biopsy. Renal biopsy showed glomerular mesangial matrix expansion with exudative lesions, and isolated interstitial foci of inflammatory mononuclear cells; direct immunofluorescence revealed generalized and diffuse deposits of IgA(+++) and C3(+) in the mesangium. All findings are compatible with mesangial glomerulonephritis with IgA deposits.

IgA N has been described as idiopathic or in association with a large number of systemic diseases [7]. Serum IgA is elevated in 50% of cases. Positive cryoglobulins in their serum are detected less frequently (15%), but associated with normal serum complement levels and

negative rheumatoid factor [8]. Although the typical clinical presentation is recurrent macroscopic hematuria, the final diagnosis is based on immunofluorescent demonstration of IgA deposits in mesangium despite the absence of clinical or systemic disease [7].

In the literature reference has only been made to 3 cases of EMC IgG-IgA associated with IgA deposits in renal biopsy immunofluorescence, and morphologically described as diffuse proliferative glomerulonephritis [9], rapidly progressive glomerulonephritis [10], and only one case of IgA N [6]. There has always been a close relationship between the presence of IgA in cryoglobulinemia immune complexes and its detection in glomeruli. In our patient, the unusual association of IgA N with EMC type II IgG-IgM, without any other systemic disease, can only be interpreted as a coincidence which only long-term control of clinical evolution will clarify.

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