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Membranous nephropathy with light chain restriction

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The histological pattern of membranous nephropathy with lambda chain restriction is a rare finding and a few described cases did not have any known secondary etiology. The author announces it as a quite rare entity, and emphasizes the integration of histological, clinical and laboratory findings.

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Membranous nephropathy is a frequent cause of nephrotic syndrome in adults. It results from the deposition of immune complexes along the subepithelial region of the glomerular basement membrane (1,2). In spite of membranous nephropathy is relatively frequent, its association with monoclonal gammopathy of renal significance has been poorly described (1,3,4).

The author presents a 60-year-old woman with a history of chronic myeloid leukemia (treated with IFN α 3 MU, in molecular remission), arterial hypertension and obesity who was referred to the hospital complaining of worsening lower extremity edema which has been present since 6 months ago. Initial evaluation showed proteinuria (Upt/cr: 1.80 g/g; U24h pr: 1738 mg/d), without hematuria. Hemoglobin was 13.5 g/dL, serum creatinine 0.70 mg/dL, serum albumin; 3.3 g/dL and total cholesterol 300 mg/dL. Ultrasound study showed asymmetric kidneys (right kidney 10.0 cm and left kidney 12.8 cm), with slight hyperechogenicity and loss of cortico-sinusal differentiation. Secondary work up revealed worsening of proteinuria (Upt/cr: 3.50 g/g; U24h pr: 4092 mg/d), with hypoalbuminemia (3.1 g/dL) and hypercholesterolemia (272 mg/dL). Erythrocyte sedimentation rate 48 mm/hour. Viral markers, antinuclear antibodies, anti-dsDNA, rheumatoid factor and anti-PLA2R (anti-phospholipase A2 receptor) were negative. Serum complement (C3

and C4) were in normal range. Measurement of immunoglobulins, serum free light chains, and protein electrophoresis and also serum immunofixation revealed no abnormality. Despite normal serum and urine free light chain, intense lambda band was detected in urine immunofixation study. Renal biopsy from right kidney was executed and light microscopy revealed thickening of glomerular capillary wall, vacuolization of epithelial cells and spike formations and Congo-red staining and thioflavin T staining were negative. Immunofluorescence was positive for IgG2 (2+), C3 (2+) and lambda chain (2+), with granular marking along the loops; IgM, IgA, C4, C1q, albumin, fibrinogen and anti-PLA2R were negatives. Electron microscopy showed diffuse fusion of podocyte pedicels, with thickening of the glomerular basement membrane and numerous subepithelial and intra-membranous deposits, without any fibrillar deposition, suggesting membranous nephropathy pattern. The diagnosis of membranous nephropathy with lambda light chain restriction was assumed. Endoscopy, colonoscopy, mammography and chest x-ray were normal. Hematology tests were repeated and an overlapping lymphoproliferative disease was excluded. In less than six months, spontaneous partial remission of the nephrotic syndrome was obtained, with a sustainably normal renal function (Table 1).

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Table 1. Analytical evolution

Laboratory analysis	December 2018	January 2019	April 2019
Hemoglobin (g/dL); N: 12-16	13.5	13.2	12.8
Serum creatinine (mg/dL); N: 0.51-0.95	0.70	0.86	0.88
Urine protein dipstick test (mg/dL); N: <30	30	>600	300
Upt/cr; N: <0.15	1.80	3.50	1.14
U24h protein (mg/day); N: <150	1738	4092	987
Urine sediment (µL); N: 0-20	Erit 4, Leuc 49	Erit 11, Leuc 7	Erit 105, Leuc 29
Serum albumin (g/dL); N: 3.4-4.8	3.3	3.1	3.2
Total cholesterol (mg/dL); N: 120-200	300	272	176

Erit: erythrocytes; Leuc: leukocytes.

The histological pattern of membranous nephropathy with lambda chain restriction is a rare finding (<0.95% of all this glomerulopathy cases) and few described cases didn't show a known secondary etiology (1,3).

Best Rocha et al reported the biggest retrospective study, including 28 patients with membranous nephropathy that presented light chains isotype restriction. Six patients had an underlying lymphoproliferative disease, however only one of these patients had a detectable monoclonal Ig. Kappa restriction was seen in approximately 86% of cases. Staining for IgG subclasses was realized in 19 patients, 14 of which displayed positive staining for a single subclass. Seven patients had anti-PLA2R positive. Almost a third of anti-PLA2R negative patients and more than 25% of those with positive staining for a single IgG subclass had a related lymphoproliferative disease (1).

In the literature, up to 30% of patients with negative anti-PLA2R membranous nephropathy are associated with hematological malignancy (2,4). Although not indicative of a clonal process, anti-PLA2R negativity, positive stain for a single IgG subclass and the presence of focal proliferation should motivate the investigation/exclusion of underlying lymphoproliferative disease (5,6). With the present case, which is rare, the diagnostic and orientation, reinforce the need for the integration of histological findings with clinical and laboratory data.

Authors' contribution

CIR is the first and main author. She prepared, wrote and review this manuscript. AMG, RC and AL participated in the clinical and anatomopathological approach and management of the patient reported.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

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