CHARACTERISTICS OF THE PATIENTS WITH MEMBRANOUS GLOMERULONEPHRITIS - REPORT FROM CROATIAN REFERRAL HOSPITAL

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Introduction and aims:

Membranous glomerulonephritis (MGN) still remains one of the leading glomerulonehritides in adults. This study was aimed to evaluate the demographic and clinical data, as well as pathohistological data in the patients with MGN, as well as to examine the possible differences between primary and secondary MGN.
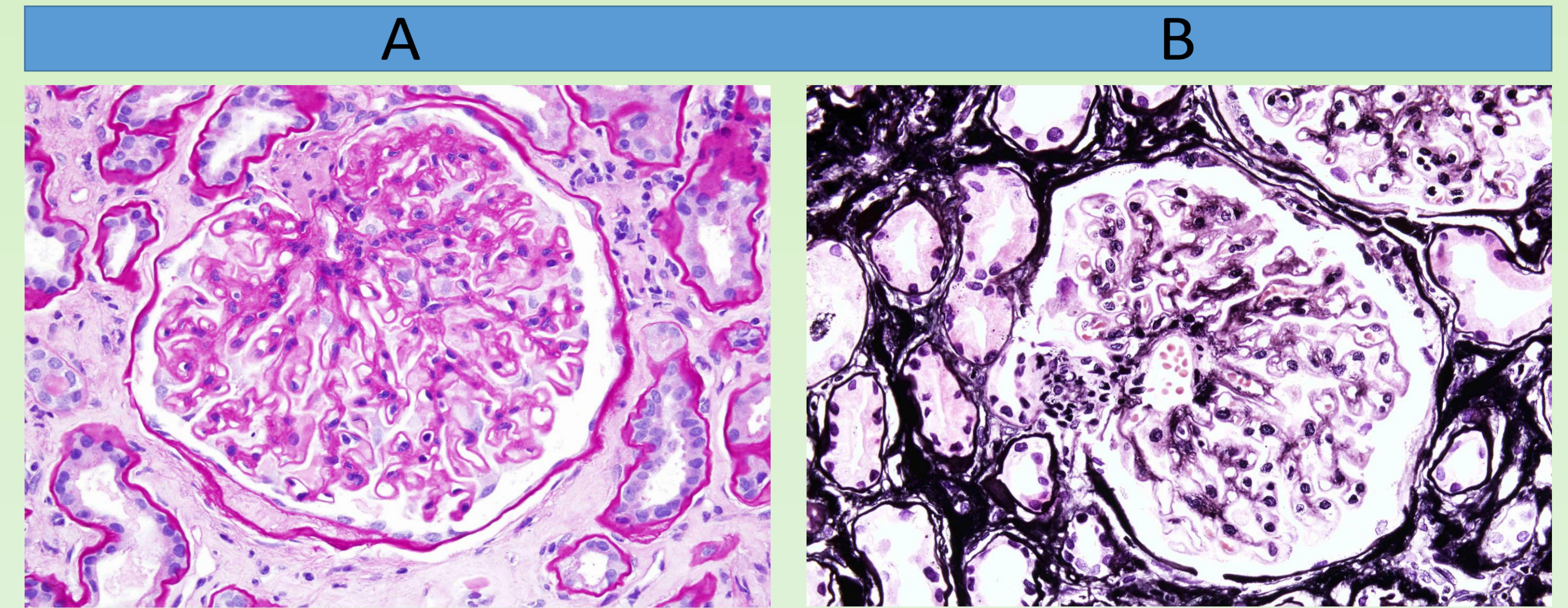

Figure 1.
Histopathology of early membranous glomerulonephritis. Mild glomerular basement membrane thickening - A) PAS stain, x400   B) Jones stain, x400
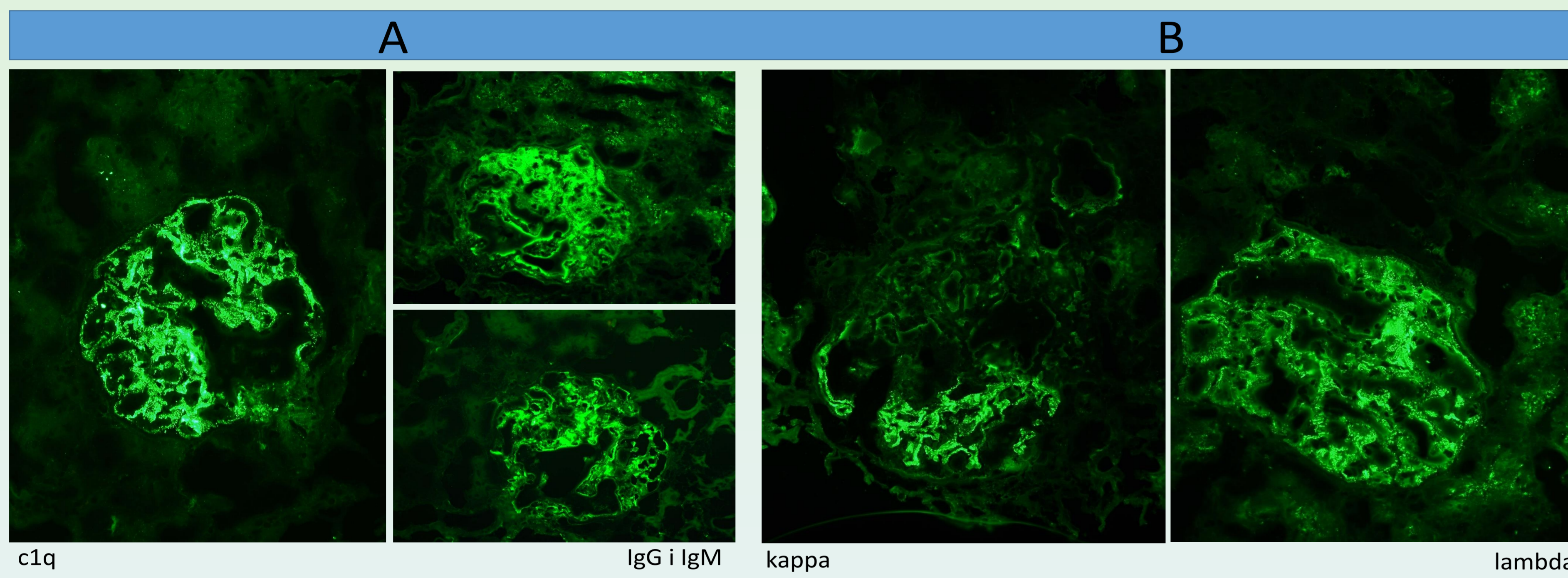

Figure 2.
Immunofluorescence staining in secondary membranous glomerulonephritis - A) Staining for C1q, IgG and IgM reveals intense, granular global subepithelial positivity involving the glomerular capillary walls (×400.)
B) Segmental granular positivity for kappa and global granular positivity for lambda light chains (x400).

Methods:

Patients who underwent kidney biopsy between 2002. and 2016., and were diagnosed with MGN in our hospital, were enrolled in our study. Demographic, clinical and pathohistological data from kidney biopsy was evaluated. Light, immunofluorescent and electronic microscopy analysis of the renal biopsy were performed. Pathological data studied were: the number of normal, focally sclerosed and globally sclerosed glomeruli, the percentage and the grade of interstitial fibrosis and tubular atrophy (IFTA), the grade of vascular changes, the grade of immunofluorescnet staining for IgA, IgM, IgG, C3, C1q, kappa and lambda chains, the degree of podocyte foot loss and finally the Ehrenreich-Churg class. The differences between primary and secondary MGN were examined with Mann-Whitney test and Chi-square or Fisher Exact test.

Results:

There were 96 patients in total, among them there were 83 patients (86.5%) with primary MGN. There were 37 women (38.5%), and the median age was 56 years (IQR 46-63). The causes for the secondary MGN were: lupus (5 patients, 38.5% of the secondary MGN), tumors (5 patients), and syphilis (1 patient, 7.7% of the secondary MGN), systemic sclerosis (1 patient) and sarcoidosis (1 patient). There were no significant differences found between patients with primary and secondary MGN regarding demographic and clinical variables (age, gender, clinical presentation, hypertension, hematuria, serum creatinine and estimated glomerular filtration rate, maximal 24-hour proteinuria, mean arterial pressure). Also, there were no significant differences found between primary and secondary MGN in forementioned pathohistological parameters.
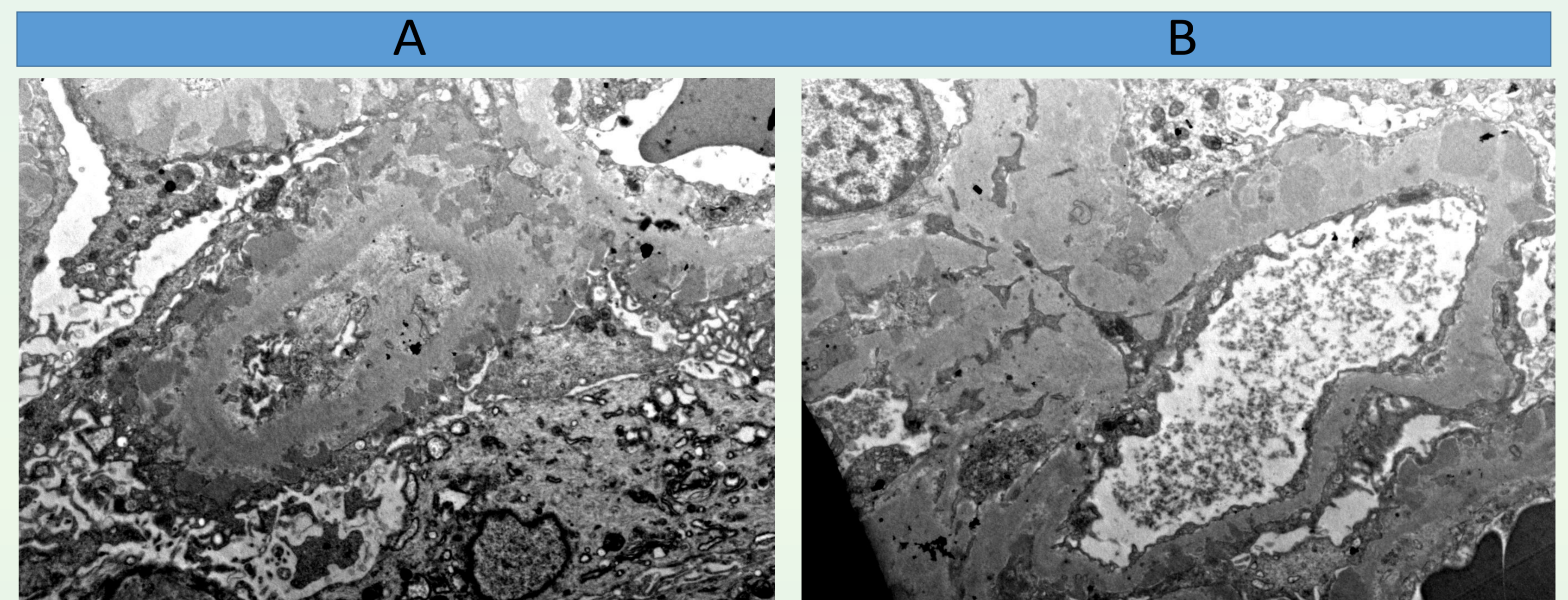

Figure 3.
Electron micrograph of membranous glomerulonephritis showing subepithelial and intramembranous electron-dense deposits.

Table 1. Clinical characteristics of patients with membranous glomerulonephritis (MGN)

	All patients (N=96)	Primary MGN (N=83)	Secondary MGN (N=13)	p
Gender (females)	37 (38.5%)	32 (38.6%)	5 (38.5%)	0.995
Age (years)	56 (46-63)	55 (46-63)	61 (46-70)	0.258
Hypertension	64 (66.7%)	54 (65.1%)	10 (76.9%)	0.534
MAP (mmHg)	106.67 (96.67-116.67)	106.67 (96.67-116.67)	103.33 (95.00-113.33)	0.362
Serum creatinine (μmol/l)	96.0 (80.0-111.0)	97.0 (79.0-110.0)	95.0 (85.0-164.0)	0.338
EGFR (ml/min)	70.51 (54.76-83.54)	70.53 (56.41-83.56)	66.31 (34.71-75.34)	0.343
24H-proteinuria (g)	9.6 (5.7-13.4)	9.7 (5.8-13.7)	8.0 (5.0-12.6)	0.467
Hematuria	66 (68.8%)	58 (69.9%)	8 (61.5%)	0.536
Hematuria (0-2 / 3-10 / 11-25 / >25E)	30 / 45 / 18 / 3 (31.3 / 46.9 / 18.8 / 3.1%)	25 / 40 / 15 / 3 (30.1 / 48.2 / 18.1 / 3.6%)	5 / 5 / 3 / 0 (38.5 / 38.5 / 23.1 / 0.0%)	0.826
Anti-RAAS therapy None / ACEI / ARB / ACEI+ARB	1 / 70 / 19 / 6 (1.0 / 72.9 / 19.8 / 6.3%)	1 / 60 / 16 / 6 (1.2 / 72.3 / 19.3 / 7.2%)	0 / 10 / 3 / 0 (0.0 / 76.9 / 23.1 / 0.0%)	0.899
Immunosupressive therapy	79 (82.3%)	70 (84.3%)	9 (69.2%)	0.237

MAP - mean arterial pressure; EGFR - estimated glomerular filtration rate (CKD-EPI formula); RAAS - renin angiotensin aldosterone system; ACEI - angiotensin-converting enzyme inhibitors; ARB - angiotensin receptor blockers
Continuous variables are presented as median (interquartile range) and compared using Mann Whitney U test and categorical variables are presented as number (%) and compared using χ2 or Fisher Exact test.

Table 2. Pathohistological characteristics of patients with membranous glomerulonephritis (MGN)

	All patients (N=96)	Primary MGN (N=83)	Secondary MGN (N=13)	p
IF-IgG (grade: 0 / 1+ / 2+ / 3+)	9 / 16 / 40 / 31 (9.4 / 16.7 / 41.7 / 32.3)	7 / 14 / 37 / 25 (8.4 / 16.9 / 44.6 / 30.1)	2 / 2 / 3 / 6 (15.4 / 15.4 / 23.1 / 46.2)	0.370
IF-IgA (grade: 0 / 1+ / 2+ / 3+)	87 / 7 / 0 / 2 (90.6 / 7.3 / 0.0 / 2.1)	77 / 5 / 0 / 1 (92.8 / 6.0 / 0.0 / 1.2)	10 / 2 / 0 / 1 (76.9 / 15.4 / 0.0 / 7.7)	0.108
IF-IgM (grade: 0 / 1+ / 2+ / 3+)	77 / 16 / 3 / 0 (80.2 / 16.7 / 3.1 / 0.0)	67 / 14 / 2 / 0 (80.7 / 16.9 / 2.4 / 0.0)	10 / 2 / 1 / 0 (76.9 / 15.4 / 7.7 / 0.0)	0.503
IF-C3 (grade: 0 / 1+ / 2+ / 3+)	25 / 40 / 21 / 10 (26.0 / 41.7 / 21.9 / 10.4)	23 / 33 / 20 / 7 (27.7 / 39.8 / 24.1 / 8.4)	2 / 7 / 1 / 3 (15.4 / 53.8 / 7.7 / 23.1)	0.178
IF-C1q (grade: 0 / 1+ / 2+ / 3+)	85 / 5 / 5 / 1 (88.5 / 5.2 / 5.2 / 1.0)	75 / 4 / 4 / 0 (90.4 / 4.8 / 4.8 / 0.0)	10 / 1 / 1 / 1 (76.9 / 7.7 / 7.7 / 7.7)	0.090
IF-kappa (grade: 0 / 1+ / 2+ / 3+)	26 / 18 / 31 / 21 (27.1 / 18.8 / 32.3 / 21.9)	23 / 17 / 24 / 19 (27.7 / 20.5 / 28.9 / 22.9)	3 / 1 / 7 / 2 (23.1 / 7.7 / 53.8 / 15.4)	0.396
IF-lambda (grade: 0 / 1+ / 2+ / 3+)	24 / 26 / 25 / 20 (25.3 / 27.4 / 26.3 / 21.1)	21 / 23 / 22 / 16 (25.6 / 28.0 / 26.8 / 19.5)	3 / 3 / 3 / 4 (23.1 / 23.1 / 23.1 / 30.8)	0.858
LM-NAS (grade: 0 / 1+ / 2+ / 3+)	42 / 34 / 13 / 7 (43.8 / 35.4 / 13.5 / 7.3)	37 / 29 / 12 / 5 (44.6 / 34.9 / 14.5 / 6.0)	5 / 5 / 1 / 2 (38.5 / 38.5 / 7.7 / 15.4)	0.597
LM-IFTA (grade: 0 / 1+ / 2+ / 3+)	55 / 22 / 12 / 7 (57.3 / 22.9 / 12.5 / 7.3)	48 / 20 / 9 / 6 (57.8 / 24.1 / 10.8 / 7.2)	7 / 2 / 3 / 1 (53.8 / 15.4 / 23.1 / 7.7)	0.633
LM-IFTA (%)	5.0 (2.0-17.5)	5.0 (2.0-15.0)	5.0 (2.0-26.0)	0.996
LM-Number of glomeruli	22 (15-28)	22 (15-28)	23 (15-32)	0.534
Glomeruli with FSGS (%)	0.0 (0.0-9.23)	0.00 (0.0-9.38)	0.0 (0.0-2.5)	0.209
Glomeruli with GGS (%)	5.63 (0.0-11.56)	5.56 (0.0-12.0)	6.25 (0.0-10.0)	0.272
EM-podocyte foot loss Focal / diffuse / unknown	13 / 81 / 2 (13.5 / 84.4 / 2.1)	11 / 70 / 2 (13.3 / 84.3 / 2.4)	2 / 11 / 0 (15.4 / 84.6 / 0.0)	0.839
Ehrenreich-Churg I / II / III / IV	14 / 46 / 30 / 6 (14.6 / 47.9 / 31.3 / 6.3)	10 / 41 / 28 / 4 (12.0 / 49.4 / 33.7 / 4.8)	4 / 5 / 2 / 2 (30.8 / 38.5 / 15.4 / 15.4)	0.082

IF - immunofluorescent microscopy; LM - light microscopy; NAS - nephroangiosclerosis and arteriolar hyalinosis; IFTA - interstitial fibrosis and tubular atrophy; FSGS - focal segmental glomerulosclerosis; GGS - global glomerulosclerosis; EM - electron microscopy; Continuous variables are presented as median (interquartile range) and compared using Mann Whitney U test and categorical variables are presented as number (%) and compared using χ2 or Fisher Exact test.

Conclusions:

In our patient cohort clinical and pathohistological characteristics of patients with primary and secondary MGN did not differ significantly. Wide range of diagnostic test and procedures is needed to differentiate between two types of MGN. Our established database of patients with MGN should serve to futher improve the management and follow up of those patients.

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