CLINICAL AND HISTOLOGICAL PRESENTATION IN ANCA-ASSOCIATED GLOMERULONEPHRITIS AS INDICATORS OF EARLY OUTCOME

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Objectives:

Antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis is a multisystem autoimmune disease with different clinical presentation and outcome. This study was conducted to determine the renal clinical disease presentation and histological indicators affecting early renal and patient outcome in ANCA-associated glomerulonephritis treated with low-dose cyclophosphamide (CyC) and methylprednisolone (MP).

Methods:

An observational single-center retrospective study was conducted in 75 patients with ANCA-associated glomerulonephritis. Renal involvement was defined by the presence of proteinuria, erythrocyturia with or without red blood cell casts, decreased calculated estimated glomerular filtration rate (eGFR) according to the Modification of Diet in Renal Disease (MDRD) equation, elevated titer of ANCA, and typical histological features of the disease obtained by representative percutaneous renal biopsy specimens.

All patients were treated according to local treatment guidelines with initial induction therapy: i.v. pulse of CyC 750 mg every 3 to 4 weeks (or 500 mg if ≥70 years old or eGFR >20 ml/min/1.73 m^2 or body weight <60 kg) and MP i.v. pulse (250-500 mg/day) for 3 consecutive days, followed by oral dose of 0.8 mg/kg body weight (or 0.4 mg/kg body weight if ≥70 years old or if eGFR < 20 ml/min/1.73 m^2 or body weight <60 kg), tapered after 4 weeks gradually to maintenance dose of 0.08 mg/kg body weight.

Renal response was evaluated after 3 months of induction therapy and was defined in patients with rapidly progressive glomerulonephritis as 30% improvement in eGFR or dialysis independence if they have been dialysis dependent at the time of diagnosis, or as stabilization or improvement of renal function in patients with chronic nephritic syndrome, with concomitant reduction of erythrocyturia (<10 red blood cells/high power field) and proteinuria (≤0.6 g/day) irrespective of clinical presentation of the renal disease. Patients fulfilling the criteria for renal response were designated as immediate responders (IR) to induction therapy, all others were designated as delayed responders (DR).

Results:

Early treatment response was attained in 48 (64%) of patients (IR group); 3 (4%) patients died, all in DR group (p=0.04). At the time of disease manifestation patients in IR group were 5 years younger than patients in DR group (p=0.04), had higher estimated glomerular filtration rate (IR 13.2 and DR 8.0 ml/min/m^2, p=0.009), lower BVAS score (IR 22, DR 28, p=0.04), but did not differ in sex and CRP (p=0.14).

Early treatment response was attained in 48 (64%) of patients (IR Kidney disease was clinically presented as:
- rapidly progressive glomerulonephritis in 85% of DR and 62% of IR (p=0.03),
- pulmo-renal syndrome in 77% of DR and 37% of IR (p=0.001),
- chronic nephritic syndrome in 17% of IR and never in DR (p=0.04).

The percent of normal glomeruli was 20% in IR and 12% in DR (p=0.06), extracapillary proliferation 50% in IR and 66% in DR (p=0.04), interstitial fibrosis 60% in IR and 77.5% in DR (p=0.07), thrombotic glomeruli 23% in IR and 58% in DR (p=0.007), extraglomerular vasculitis in 80% in IR and in 64% in DR (p=0.05), and acute with chronic lesions in 47% in IR and in 72% in DR (p=0.05) (picture 1).
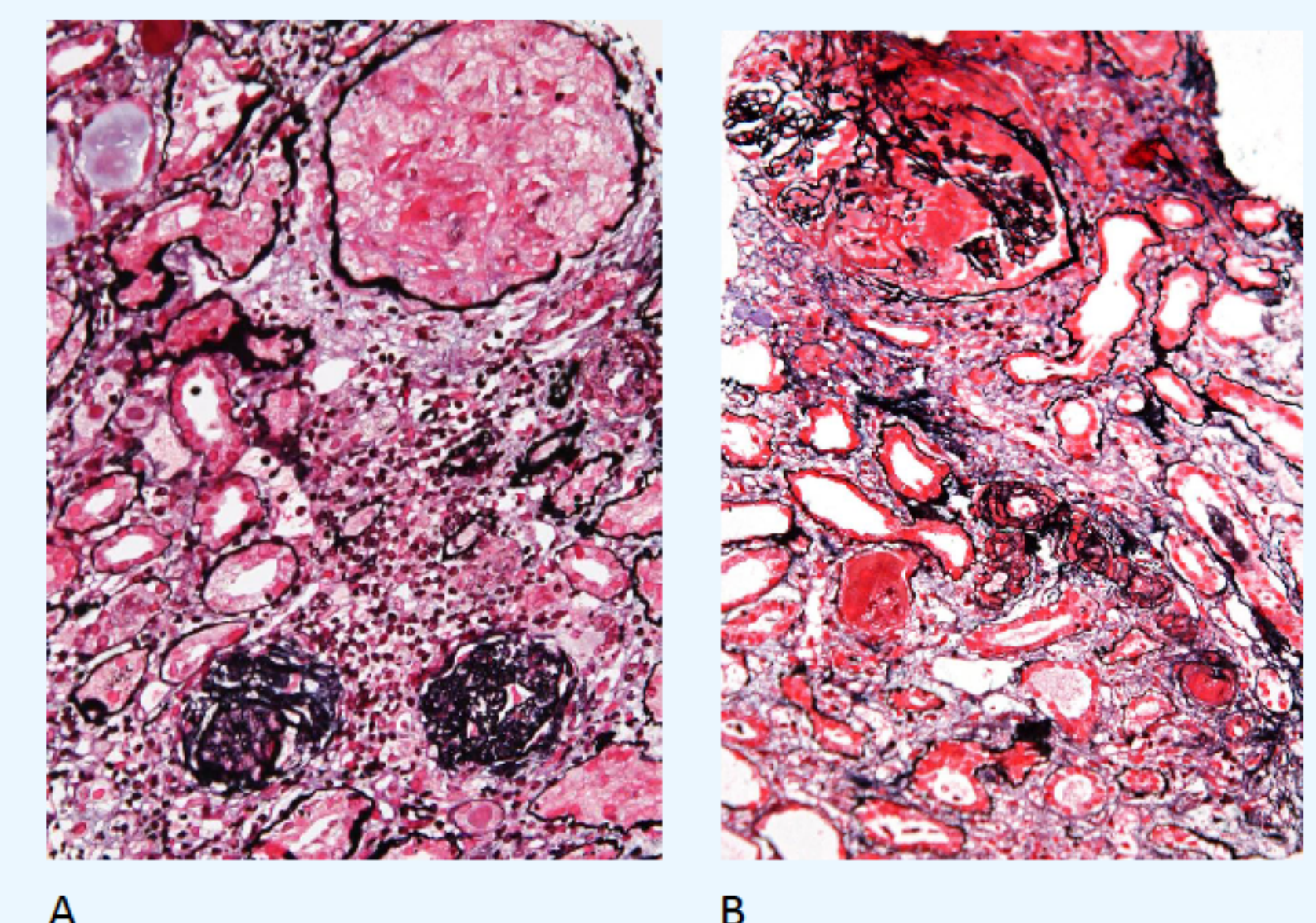

Figure 1. Kidney biopsy in ANCA vasculitis. A - lesions of different age with cellular crescents, fibrous crescents and glomerular sclerosis; B - extraglomerular vasculitis.

Comparing clinical presentation and histologic findings, pulmo-renal syndrome was associated with the presence of thrombotic glomeruli (odds ratio 4.8, p=0.01).

Performing logistic regression, delayed treatment response was independently associated with pulmo-renal syndrome (p=0.01) and the need of hemodialysis at the time of disease presentation (p=0.01) (R^2=0,449, odds ratio 6.9 and 5.0).

Conclusions:

Early treatment response to induction therapy in our patients with ANCA-associated glomerulonephritis was associated with younger age, better renal function at the time of disease manifestation and less severe systemic disease presentation.

Chronic nephritic syndrome is a possible manifestation of ANCA-associated glomerulonephritis with favorable renal and patient outcome. It was associated with higher percentage of normal glomeruli, less severe acute tissue inflammation and scaring and higher percentage of extraglomerular vasculitis.

Delayed treatment response was the hallmark of pulmo-renal syndrome, rapidly progressive glomerulonephritis and dialysis dependency at the time of disease presentation with increased mortality in the course of disease. It was associated with higher percentage of concomitant acute and chronic lesions, extracapillary proliferation, tissue scaring and thrombotic glomeruli, especially in patients with pulmo-renal syndrome, denoting the relapsing nature of ANCA-vasculitis, that was probably diagnosed late in the course of disease.

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