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CHALLENGES IN THE DIAGNOSTIC WORKUP OF RENAL AMYLOIDOSIS

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Relevance. When a renal biopsy arrives with a clinical history of proteinuria and declining kidney function, amyloidosis is often on our differential. But confirming the diagnosis is only half the battle – distinguishing AA from AL is where the real challenge lies, because the two entities demand completely different management. AA typically arises from chronic inflammation, AL from a plasma cell dyscrasia. Misclassification can lead to delayed or inappropriate treatment. With this in mind, we reviewed amyloid cases to identify histological and clinical clues that help us reliably separate the two.

Aim: we aimed to compare AA and AL cases in our biopsy series and highlight features that aid in subtype differentiation.

Material and method. We retrospectively analysed 15 renal biopsies diagnosed as amyloidosis, 10 were AA and 5 AL. All had been stained with H&E, PAS, and Masson's trichrome; amyloid was confirmed by Congo red with apple-green birefringence. Immunohistochemistry (IHC) was used for subtyping. Clinical information – age, gender, glomerular filtration rate (GFR), proteinuria, underlying conditions – was extracted from the referral forms and medical records. For statistical analysis, we used the Mann-Whitney U test for continuous and ordinal variables and Fisher's exact test for categorical data, with $p<0.05$ considered significant.

Results and their discussion. The AA group had a mean age of 58.0 years (60% female), the AL group 63.8 years (60% male). Neither age nor sex differences were statistically significant, but they aligned with expected epidemiology. The clinical data accompanying the biopsies revealed that AA cases had more advanced kidney disease at the time of biopsy. Four of the ten AA patients were already on dialysis or had a GFR <15 mL/min, compared to only one of the five AL patients. Median GFR was 30.0 mL/min in AA versus 50.0 mL/min in AL ($p=0.25$). Proteinuria was heavy in both groups (median 3.8 g/day AA, 3.0 g/day AL; $p=0.74$). Oedema was present in 70% of AA and 80% of AL; anaemia was more common in AA (70% vs 40%, $p=0.33$), which we attributed to underlying chronic inflammation.

Histologically, we noted that amyloid in glomeruli was present in 90% of AA biopsies and 40% of AL ($p=0.10$). Amyloid in tubular basement membranes showed a similar distribution: 90% AA versus 40% AL ($p=0.10$). Although not statistically significant, these trends suggested that glomerular and basement membrane involvement might be more frequent in AA in our series. The most striking difference came from the degree of chronic irreversible damage. The percentage of globally sclerotic glomeruli was significantly higher in AA (median 26.6% vs 17.0%, Mann-Whitney $U = 9.0$, $p = 0.03$). Interstitial fibrosis also tended to be more extensive in AA (median 20% vs 10%, $p = 0.07$). These findings made sense given the clinical histories: many AA patients had long-standing rheumatoid arthritis, psoriatic arthritis, or vasculitis, meaning their kidneys had likely been exposed to years of inflammatory stress before the amyloid became apparent. IHC helped confirm the subtypes. Among AL biopsies, two showed kappa light chain restriction, one lambda restriction, and two had both kappa and lambda positivity (mixed pattern). AA biopsies were either negative or showed weak, non-specific staining without restriction. Protein casts were nearly universal (90% AA, 100% AL), highlighting that tubular injury is common irrespective of subtype.

Conclusions. Our experience with these 15 biopsies reinforced that AA and AL amyloidosis, while both leading to amyloid deposition, often present with different degrees of chronic renal scarring. AA biopsies showed significantly more glomerulosclerosis ($p = 0.07$) and a trend toward more interstitial fibrosis ($p = 0.07$) – changes that likely reflect the prolonged inflammatory milieu in these patients.