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ПРОБЛЕМЫ ДИАГНОСТИКИ ПОЧЕЧНОГО АМИЛОИДОЗА

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CHALLENGES IN THE DIAGNOSTIC WORKUP OF RENAL AMYLOIDOSIS

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Резюме. Проанализированы 15 биопсий почек пациентов с амилоидозом (10 с амилоидозом АА, 5 - с АЛ). В биоптатах с АА амилоидозом выше были показатели гломерулосклероза (p=0,03) и фиброза стромы (p=0,07). АА амилоидоз приводит к более тяжелому повреждению почек, что важно для выбора терапии. Рекомендуется рутинное иммуногистохимическое типирование.

Ключевые слова: амилоидоз почек, АА, АЛ, гломерулосклероз

Resume. Our study included 15 renal biopsies (10 AA and 5 AL). AA amyloidosis showed higher rates of glomerulosclerosis (p=0.03) and interstitial fibrosis (p=0.07). AA is associated with chronic inflammation, while AL is linked to plasma cell dyscrasias. AA leads to more severe irreversible kidney damage, which is crucial for treatment decisions. Immunohistochemistry plays a very important role in subtyping amyloid.

Keywords: renal amyloidosis, AA, AL, glomerulosclerosis

Relevance. When a patient presents with unexplained proteinuria and declining kidney function, renal amyloidosis is one of the possibilities that crosses our mind. But confirming amyloid is only half the battle – we also need to figure out whether it is AA or AL, because the two demand completely different treatments. AA usually arises from chronic inflammation, so we treat the underlying inflammatory disease. AL comes from a plasma cell problem, so we use chemotherapy. Get it wrong, and the patient suffers [2,5]. In this study we looked back at 15 of our own biopsy cases to see what clinical and histological clues could help us tell them apart.

Aim: our goal was simple: to compare the AA and AL cases in our series and highlight the features that actually helped us distinguish one from the other.

Objectives.

1. Review the demographic and clinical data (age, sex, GFR, proteinuria, anaemia, oedema) in both groups.
2. Compare the key microscopic findings – where the amyloid sits, how much glomerular scarring there is, and how much fibrosis has developed.
3. Show how immunohistochemistry helps us nail down the subtype by looking at light chain restriction.

Material and methods. We went through 15 renal biopsies that had been diagnosed as amyloidosis in our department. All of them had been stained with the usual panel – H&E, PAS, Masson's trichrome – and amyloid was confirmed with Congo red, which gave us that characteristic apple-green glow under polarized light [4]. Subtyping was done using immunohistochemistry (IHC) for AA and for kappa/lambda light chains. We also pulled clinical information from the referral forms and medical records – age, sex, creatinine, glomerular filtration rate (GFR), proteinuria, haemoglobin, oedema, and whatever underlying diseases were mentioned**.**

For statistics, we used the Mann-Whitney U test for things like percentages and grades (because our numbers were small and the data weren't perfectly normal), and Fisher's exact test for yes/no categories. We considered a p-value less than 0.05 as significant.

Results and their discussion. Out of the 15 biopsies, 10 turned out to be AA and 5 AL. The AA patients had a mean age of 58 years, the AL patients 63.8 years – not a big difference (p=0.46). On the sex side, AA had more women (60% female), while AL had more men (60% male) (Fig.1). That difference wasn't significant either (p=0.60), but it matches what we've read in the literature [3,6]**.**

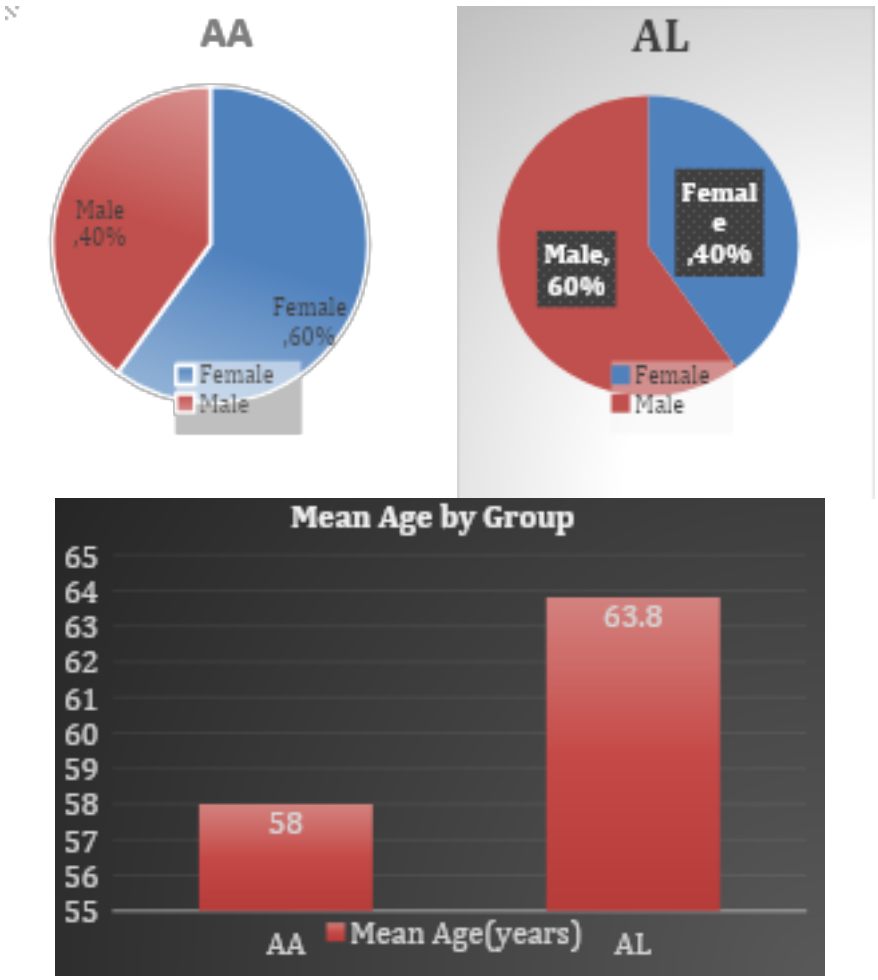

Fig. 1 – Distribution of cases by sex and age

When we looked at how advanced their kidney disease was, a clear pattern emerged. Four out of ten AA patients (40%) were already on dialysis or had a GFR below 15 mL/min at the time of biopsy. Only one of the five AL patients (20%) was that far gone. The numbers

are small, so the p-value is 0.60, but the trend is hard to ignore. Median GFR told the same story: 30 mL/min in AA versus 50 mL/min in AL (p=0.25). Proteinuria, on the other hand, was heavy in both groups – around 3.8 grams per day in AA and 3.0 in AL – so that didn't help us differentiate (p=0.74). Oedema was common everywhere (70-80%), but anaemia was more frequent in AA (70% vs 40%, p=0.33), which we suspect reflects the long-standing inflammation these patients carry**.**

What did we see under the microscope?

Amyloid in the glomeruli was present with apple-green birefringence under polarized light in 90% of AA biopsies but only 40% of AL (p=0.10). Tubular basement membrane amyloid showed exactly the same numbers – 90% vs 40%, p=0.10 (Fig. 2). Neither reached statistical significance, but the pattern is consistent: AA seems to involve both compartments more often.

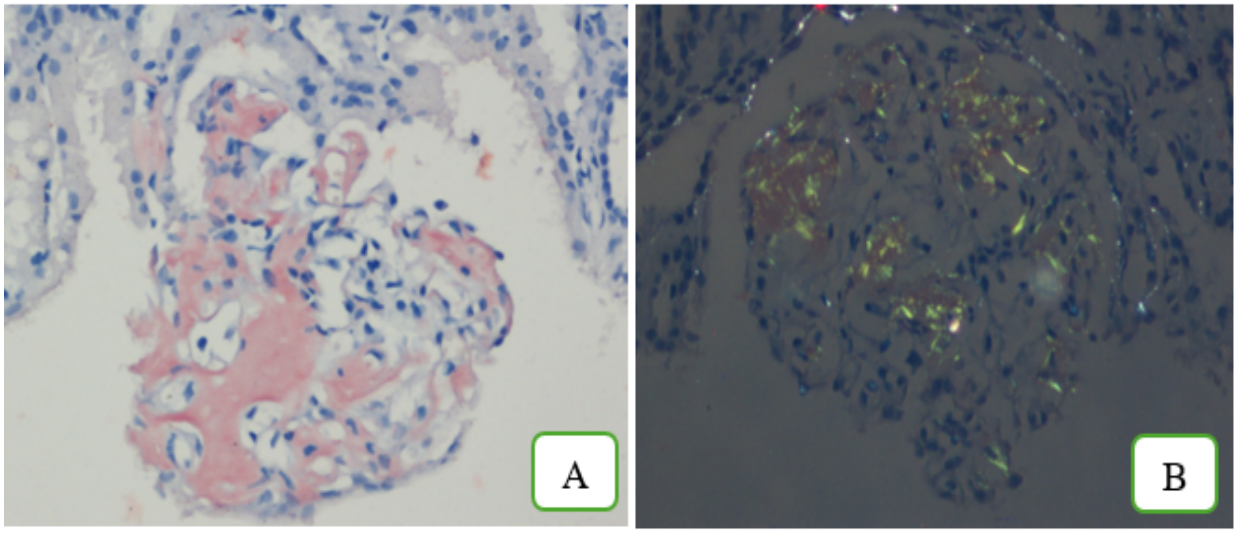

Fig. 2 – A: Amyloid deposits in the glomerulus (Congo red stain x200), B: Apple-green birefringence under polarized light (x200)

The real difference came when we looked at scarring. The percentage of globally sclerotic glomeruli was significantly higher in AA – a median of 26.6% compared to 17.0% in AL. The Mann-Whitney U test gave us U = 9.0 and a p-value of 0.03. That's statistically significant. Interstitial fibrosis also tended to be higher in AA (20% vs 10%, p=0.07) – not quite significant, but a strong trend.

These numbers make sense when you remember the clinical histories. Many of the AA patients had rheumatoid arthritis, psoriatic arthritis, or vasculitis – diseases that simmer for years. By the time the amyloid shows up on a biopsy, the kidney has already been through a lot of wear and tear (Fig. 3). That's probably why we saw so much more irreversible damage in the AA group.

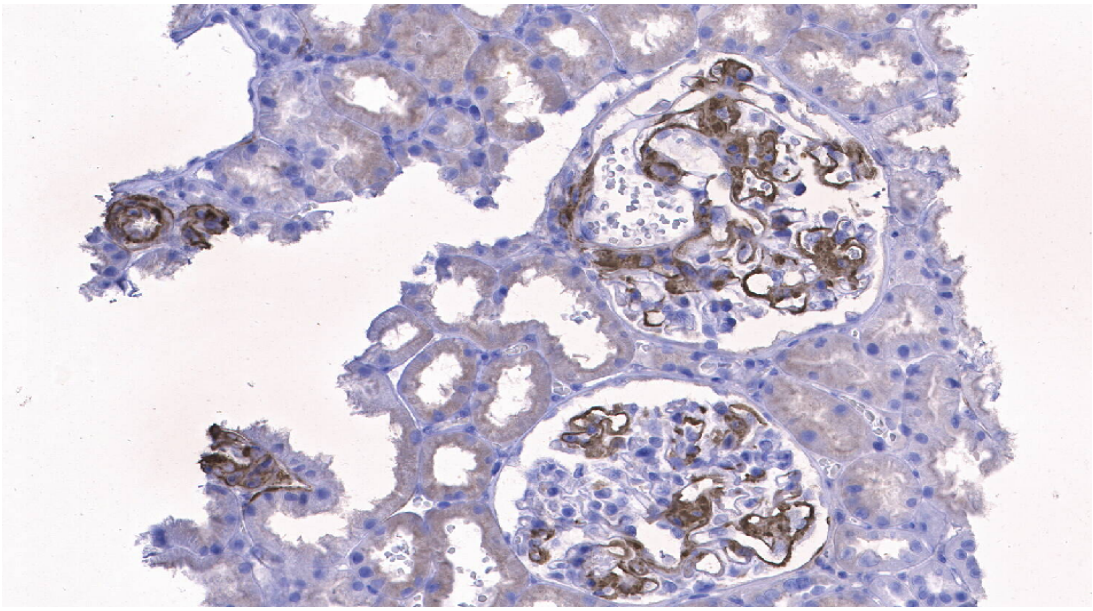

Fig. 3 – AA amyloid in the glomeruli and vascular walls (IHC AA amyloid x100)

IHC gave us the final answer. Among the AL cases, two showed kappa light chain restriction, one showed lambda restriction (Fig. 4), and two had a mixed pattern (both kappa and lambda). The AA cases were either completely negative or showed only weak, non-specific staining – no restriction. Protein casts in the tubules were seen in almost every case (90% of AA, 100% of AL), which reminds us that tubular injury is common no matter the subtype.

The clinical histories matched the IHC findings perfectly. The AA patients had chronic inflammatory conditions – three with rheumatoid arthritis, two with psoriatic arthritis, one with vasculitis. The AL patients had plasma cell disorders – two with multiple myeloma, one with monoclonal gammopathy.

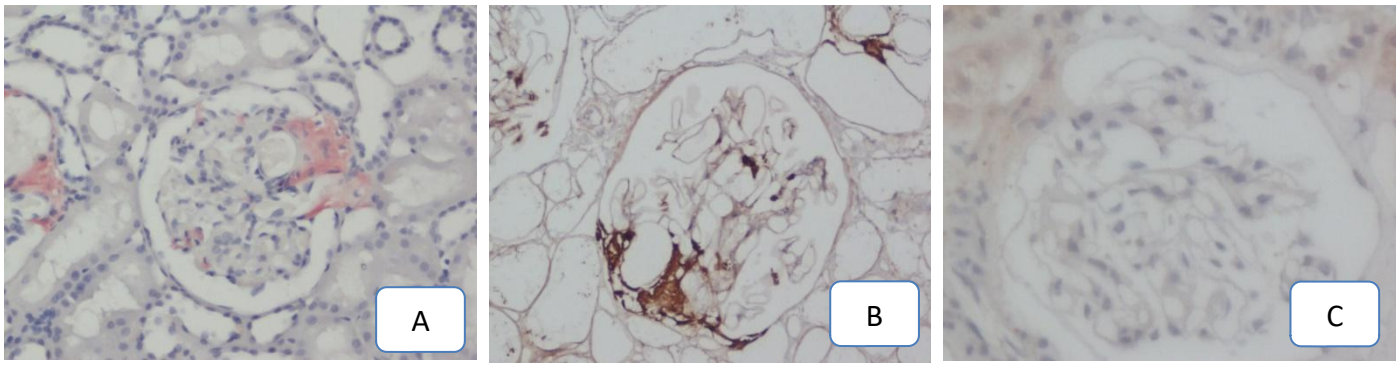

Fig. 4 – AL amyloidosis: A - Amyloid deposits in the glomerulus (Congo red stain x200), B - lambda expression (restriction) in the glomerular compartments (x300), C – negative kappa in the glomerulus (x400)

Conclusions:

1. Immunohistochemistry reliably separated the two groups, with AL showing light chain restriction (kappa, lambda, or mixed). The AA patients had a mean age of 58 years, the AL patients 63.8 years (p=0.46). On the sex side, AA had more women (60%), while AL had more men (60%).

2. AA amyloidosis in our series came with significantly more global glomerulosclerosis (p=0.03) and a clear trend toward more interstitial fibrosis (p=0.07) compared to AL. AA patients presented with worse kidney function – lower GFR and more often already on dialysis – even though proteinuria was just as heavy as in AL.

3. The bottom line: to subtype renal amyloidosis correctly, you need to look at the tissue, use IHC, and pay attention to the patient's clinical background – because the underlying disease dictates the treatment.

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