PATHOLOGICAL DIAGNOSIS OF RENAL AMYLOIDOSIS IN UKRAINE: A SINGLE-CENTRE 10-YEAR DATA

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Introduction and Aim

Accurate typing of amyloid is critical for prognosis, treatment, and proper management of kidney amyloidosis. However, determining the correct type of amyloidosis is sometimes difficult because histopathologic findings may be confused with another related form. In the present study, 10-year pathology data on amyloidosis in adult kidney patients from a single center in Ukraine were analyzed.

Materials and Methods

Histopathologic findings of 231 amyloid-positive biopsies from buccal mucosa, gums, abdominal fat (**Fig. 1**) and kidney tissue (**Fig. 2**) collected between 2013 and 2022 were analyzed by amyloid type. Non-kidney biopsies were studied by bright light (alkaline Congo Red (also polarized microscopy), alkaline Sirius Red) and fluorescence (Thioflavin T, Congo Red), and immunofluorescence (κLC, λLC and AA). Kidney biopsies were assessed by light microscopy (H&E, PAS, PAMS, Trichrome, Picro-Sirius, alkaline Congo Red), immunofluorescence (IgA, IgG, IgM, κLC, λLC, C1q, C3c, fibrinogen, and AA) and electron microscopy (semithin and ultrathin (in part) sections). Data were expressed as means and standard deviations or as median and ranges and compared with ANOVA or Kruskal-Wallis tests. Categorical variables were expressed as proportions and compared using the chi-square (χ^2) test.

Table. The patients' clinical data and histopathological findings according to amyloidosis

	AA AMYLOIDOSIS	AL AMYLOIDOSIS	UNCLASSIFICATED TYPE (NON-AA AMYLOIDOSIS)	p-value
THE TOTAL NUMBER OF PATIENTS WITH BIOPSY-PROVEN AMYLOIDOSIS, n (%)	37 (16.0)	142 (61.5)	52 (22.5)	
KIDNEY BIOPSY, n (%)	18 (21)	50 (60)	16 (19)	
Age, years [median (range)]	45 (17-82)	58 (23-75)	55 (37-72)	**0.01**
Sex, male/female ratio	3.5:1	1:1.5	1.1:1	**0.02**
Hypertension, n (%)	3 (17)	8 (16)	4 (25)	0.71
Renal insufficiency, n (%)	8 (44)	15 (30)	8 (50)	0.27
Proteinuria, g/day [median (range)]	7.6 (3.5-20)	7.1 (1.2-22.4)	6.5 (1.9-23.7)	0.72
Serum Cr, μmol/L [median (range)]	119 (57-769)	98 (56-350)	119 (76-619)	0.08
eGFR, mL/min/1.73 m2 [median (range)]	56.5 (9-116)	60.5 (14-122)	48 (4-160)	0.13
Amyloid distribution, %				
glomerular compartment	100%	100%	100%	-
interstitial compartment	67%	68%	69%	0.99
tubular basement membrane	28%	10%	38%	**0.03**
vascular compartment	94%	86%	69%	0.12
Class (Sen&Sarcic, 2010), %				
I-III	39%	30%	31%	
IV	56%	70%	63%	
V-VI	6%	0	6%	0.44
Grade (Sen&Sarcic, 2010), %				
I	11%	18%	13%	
II	56%	64%	56%	
III	33%	18%	31%	0.64
Glomerular area Congo-positive, % [mean (SD)]	24.6 (15.7)	21.8 (9.6)	29.6 (10.2)	0.11
Cortical interstitial fibrosis area, % (Picro-Sirius method) [mean (SD)]	22.5 (10.1)	19.7 (5.6)	25.0 (8.6)	0,07
PAMS-positive amyloid, %	6%	30%	19%	0.11
Immunofluorescence (scale 0, trace (0.5+), 1-4+, frozen), positive cases, % (mean intensity):				
IgA	72% (1.2)	64% (0.9)	75% (0.9)	0.65
IgG	78% (1.3)	58% (0.9)	81% (1.0)	0.12
IgM	83% (1.2)	70% (1.0)	63% (0.9)	0.41
kappa {AL k}	100% (1.6)	62% (1.4) {100% (3.1) **AL k-12%**}	81% (1.1)	0.17
lambda {AL λ}	100% (2.0)	92% (3.1) {100% (3.6) **AL λ-88%**}	81% (1.2)	0.13
C1q	61% (0.8)	52% (0.8)	56% (0.6)	0.80
C3	67% (1.0)	66% (0.9)	75% (0.8)	0.79
fibrinogen	67% (0.8)	68% (0.7)	75% (0,7)	0.85
NON-KIDNEY BIOPSY, n (%)	19 (12.9)	92 (62.6)	36 (24.5)	
Age, years [median (range)]	48 (26-76)	61 (36-77)	56 (47-81)	**0.02**
Sex, male/female ratio	1:1	1:1	1:2.3	0.11
Amyloid distribution, %				
stromal compartment	79%	91%	81%	0.17
vascular compartment	43%	55%	34%	0.09
Immunofluorescence (scale 0-3+, paraffin), positive cases, % (mean intensity):				
kappa	32% (0.9)	46% (1.5) **{AL k-14%}**	53% (0,9)	0.33
lambda	37% (0.9)	90% (2.7) **{AL λ-86%}**	47% (0,8)	<0.001

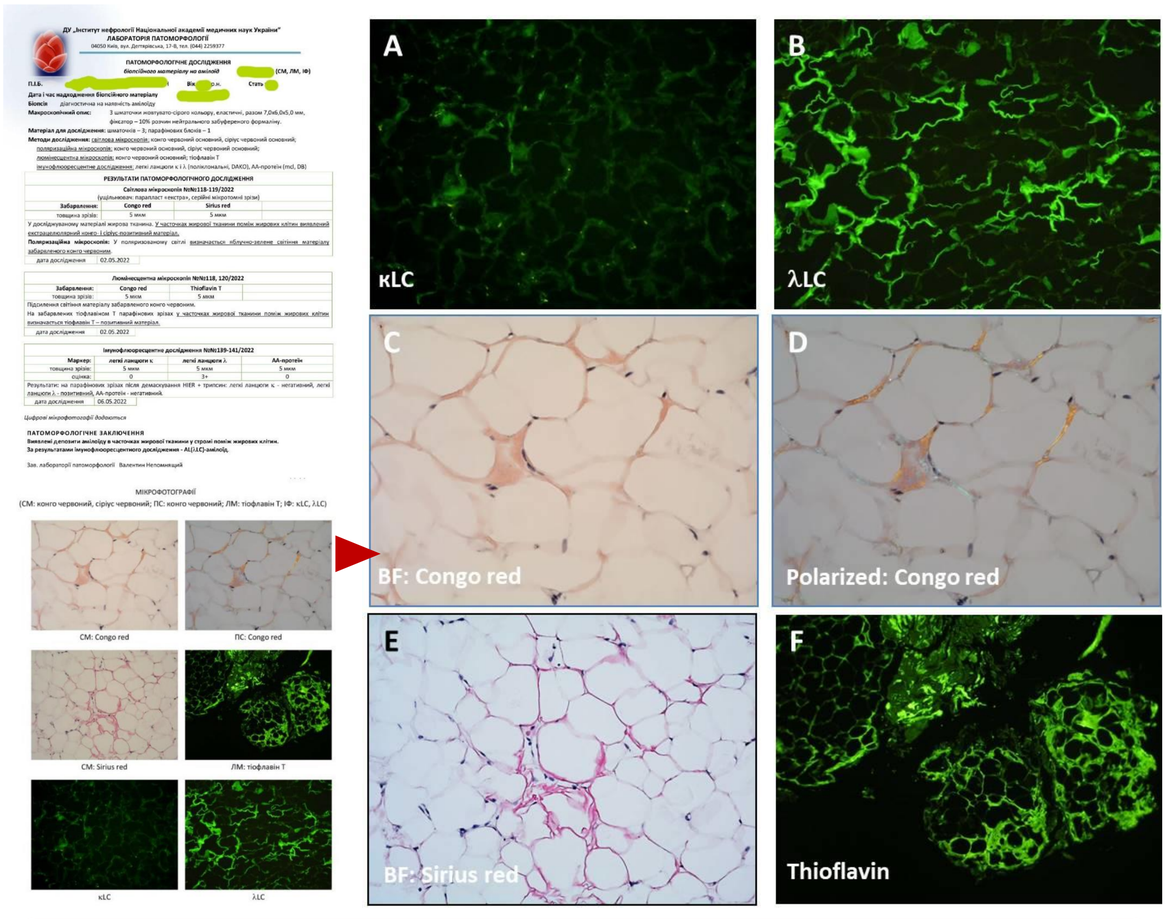

Fig. 1. The abdominal fat biopsy pathology report.
A, B – Immunofluorescence for κ and λ light chains, x200. C, D – Congo Red (bright and polarized field), x400. E – Sirius red, x200 . F – Thioflavin T, x 100.

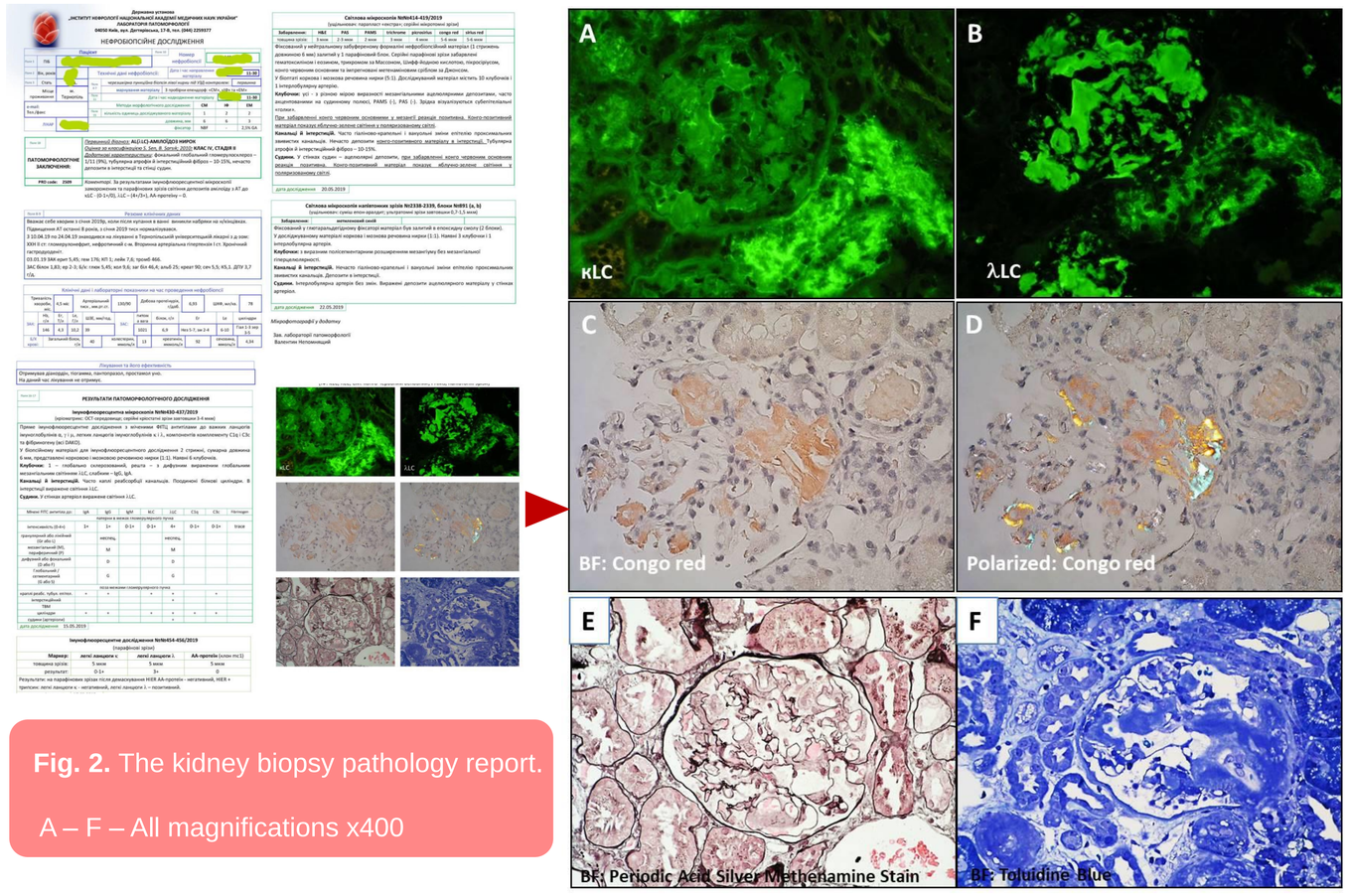

Fig. 2. The kidney biopsy pathology report.

A – F – All magnifications x400

Results

Of the 13477 primary nephrology patients, 1217 (9.1%) were indicated for kidney biopsy, and 424 (3.1%) patients with suspected systemic amyloidosis underwent non-kidney biopsy. Amyloidosis was detected by kidney biopsy in 84 (6.9%)/1217 patients and by non-kidney biopsy in 147 (35%)/424 patients. Among the patients with amyloidosis detected by nephrobiopsy, 79/84 (94%) had nephrotic syndrome and 26 (31%) had kidney failure; in 69/84 (82%) cases, the diagnosis was incidental. The patients' clinical data, typing results, and tissue distribution of amyloid are shown in Table.

Conclusions

Our 10-year data show a relatively higher prevalence of amyloidosis in Ukrainian kidney patients compared with global data. Although amyloid typing remained unreliable in 22.5% of our patients, AL amyloidosis was the main form of kidney amyloidosis (61.5%). Improvement of amyloidosis diagnosis in Ukraine, especially differentiation between amyloid types, requires the introduction of modern proteomic analysis and genetic testing.