Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Renal involvement in AA amyloidosis: A single-center experience with clinical and histopathological data

Meric Oruc[a,*], Sukran Sarikaya Kayipmaz[b]

[a] *Kartal Dr.Lutfi Kirdar City Hospital, Department of Nephrology, Istanbul, Türkiye*
[b] *Kartal Dr.Lutfi Kirdar City Hospital, Department of Pathology, Istanbul, Türkiye*

ARTICLE INFO

Keywords:
Renal biopsy
AA amyloidosis
End-stage renal disease

Received: Apr 11, 2022
Accepted: Sep 08, 2022
Available Online: 22.10.2022

DOI:
10.5455/annalsmedres.2022.04.127

Abstract

Aim: We aimed to evaluate clinicopathological features in patients with renal amyloid A (AA) amyloidosis to analyze the impact of renal biopsy on renal and patient outcomes.

Materials and Methods: We retrospectively collected data regarding baseline and follow-up clinical and laboratory features. The same pathologist scored each kidney biopsy specimen according to amyloid distrubition and amount with tubulointerstitial findings. We added all scores and obtained renal amyloid prognostic score (RAPS) and then divided patients into three RAPS grades (RAPS grade I, II, III).

Results: Eighteen patients (male, 72.2%) with a median age of 51.5 (IQR, 45-58.3) years were included in the study. The most common disease related to AA amyloidosis was previous tuberculosis (33.3%). Median serum creatinine of patients at renal biopsy time was 1.61 (IQR, 0.91-2.89) mg/dL with a median 24-h protein excretion, 6.8 [IQR, 4.6-8.9] g/day. 100%, 94.4%, 55.6% of patients' renal biopsies had vascular, glomerular (mostly diffuse mesangiocapillary) and interstitial amyloid depositions. RAPS grade I, II and III were detected in 5.6%, 27.8% and 66.7% of the patients, respectively. Ten patients (55.5%) reached end-stage renal disease (ESRD) at a median time of 15 (IQR, 2.3-32.3) months post-biopsy. ESRD was correlated with interstitial fibrosis/tubular atrophy (r=0.608, P=0.01). Death-censored renal survival rates at 1,3 and 5 years were 83.3%, 58.7% and 43.5%, respectively. Six patients (33.3%) died. Patient survival rates at 1,3 and 5 years were 88.9%, 69.6 and 55.7%, respectively.

Conclusion: Early diagnosis of AA amyloidosis with renal biopsy and scoring biopsy specimen according to amyloid distribution with other histopathological findings may be useful to manage the disease and predict the prognosis.

Copyright © 2022 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Introduction

Amyloidosis is a rare entity characterized by extracellular deposition of amyloid fibrils in various organs [1]. Overproduction of serum amyloid A (SAA) by liver under inflammatory conditions is the main mechanism of deposition of insoluble AA fibrils [2-6].

Renal involvement of AA amyloidosis includes proteinuria and/or renal insufficiency, progressing to endstage renal disease (ESRD) in most of patients [7]. According to the Registry Reports of the Turkish Society of Nephrology, the prevalence of AA amyloidosis as the cause of dialysis was 1.7% in 2019 [8].

Characteristics of amyloid deposition with other histopathological findings in AA amyloidosis including may be valuable to predict renal and patient outcome. Few authors have studied histopathological distribution of amyloid deposition in kidneys related to baseline clinical characteristis and clinical outcomes [9-14].

The aim of the study was to evaluate the relationship between histopathological renal findings and clinical characteristics in patients with AA amyloidosis and moreover to analyze the impact of renal biopsy on renal and patient outcomes.

Materials and Methods

We retrospectively screened all of the patients' renal biopsies with AA amyloidosis aged ≥ 18 years and followed-up in our nephrology outpatient clinics in the period May 2010 through May 2021. Patients followed-up less than 3 months were excluded. Patients without adequate renal biopsy specimens were also excluded.

We obtained data regarding baseline and follow-up clinical and laboratory findings from electronical medical

*Corresponding author:
Email address: mericozd@yahoo.com (Meric Oruc)

records. At admission age, gender, presence of pretibial edema, comorbid diseases and aetiology of amyloidosis were recorded. The laboratory data included serum creatinine (SCr), uric acid, albumin, total cholesterol (TC), HDL (high-density lipoprotein) cholesterol, LDL (low-density lipoprotein) cholesterol, triglycerides, C-reactive protein (CRP), urinalysis, and proteinuria. We calculated estimated glomerular filtration rate (eGFR) by using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [15]. Decreased eGFR was defined as less than 60 ml/min/1.73 m^2. Time from renal biopsy to the last visit or death was defined as follow-up period.At the last visit SCr, serum albumin and 24-h proteinuria were also recorded for patients without ESRD. Medications related to AA amyloidosis were also recorded. Renal survival was defined as time from biopsy to initiation of renal replacement treatment. ESRD was defined as an eGFR $<$ 15 ml/min/1.73m^2 or need for renal replacement therapy. We confirmed the patients' current status at the end of the study by a telephone call.

Renal biopsy evaluation

Renal biopsy specimens were revised by the same pathologist. Hematoxylin and eosin, periodic acid–Schif, Masson's trichrome, Jones methamine silver, crystal violet and Congo red stains were applied for light microscopy (LM). For immunofluorescence microscopy, kappa, lambda, IgG, IgM, IgA, fibrinogen, C3c and C1q antibodies were used for immunofluorescence examination (1/20 dilution, DAKO, Glostrup, Denmark). Renal amyloidosis diagnosis was confirmed showing the apple-green birefringence under polarized light with Congo red stain and positive immunohistochemical staining with amyloid A antibodies was used to specify amyloidosis. Pathologist scored each specimen's amyloid distribution according to the classification previously described by Sen and Sarsik (Table 1) [16]. Finally, renal amyloid prognostic score (RAPS) was obtained by adding all scores and RAPS was divided into three RAPS grades (grade I: early renal amyloidosis, RAPS 1–7; grade II: late renal amyloidosis, RAPS 8–15; grade III: advanced renal amyloidosis, RAPS 16 or higher).Limited and extensive involvements ($\leq$50% or$>$50%) were defined according to glomerular amyloid deposition, interstitial fibrosis and tubular atrophy, interstitial infammatory infltration and glomerular sclerosis [13].

Ethics

All the biopsies and blood samples included in this study were performed according to our clinical follow-up and biopsy protocol. No additional biopsy or blood samples were taken for the purpose of this retrospective study. Local ethics committee approval of Kartal City Hospital was obtained (date: 28.04.2021 number: 2021/514/200/18).

Statistical analysis

Categorical variables (gender, etiology of renal amyloidosis, lower leg edema, microscopic hematuria, glycosuria, histological findings, treatments, ESRD, survival rates) were presented as percentages and continuous variables (age, laboratory values such as SCr, eGFR, albumin, uric acid, proteinuria, urinalysis pH. . . etc, follow-up time, survival time) were presented as medians and interquartile ranges. Spearman's correlation analysis was used to assess the correlations between ESRD and various clinical factors and renal histopathological findings. For evaluation of death-censored renal survival and patient survival, Kaplan–Meier analysis was used. P value $<$ 0.05 was considered to be statistically significant. Data were analyzed with Statistical Package of Social Science (SPSS) softwareversion 17.0 (SPSS Inc., Chicago, IL, USA).

Results

613 patients with native kidney biopsies were secreened and a total of 26 patients (4.2%) were diagnosed as AA amyloidosis. We evaluated 18 patients (2.9%) in this study. Patients were generally male (72.2%) and the median age was 51.5 (IQR, 45-58.3) years. Three patients had diabetes mellitus, 4 patients had hypertension, and 1 patient had atherosclerotic heart disease. Previous tuberculosis was the most common underlying disease (33.3%). Familial Mediterranean fever (FMF) and rheumatoid arthritis were also detected in five (27.8%) and three patients (16.7%), respectively. One patient had both rheumatoid arthritis and FMF, one patient had both rheumatoid arthritis and tuberculosis. Two patients had spondyloarthropathies, one with FMF and the other with tuberculosis. In one patient, systemic lupus erythematosus was detected. In three cases, underlying diseases were not defined.

The patients mainly presented with lower leg edema (46.7%). At the time of renal biopsy median SCr of was 1.61 (IQR, 0.91-2.89) mg/dL, median eGFR of 47.4 (IQR, 22.3-95.7) ml/min/1.73m^2 and median serum uric acid was 4.6 (IQR, 4.2-6.6) mg/dL. All patients presented with proteinuria (median 24-h protein excretion, 6.8 [IQR, 4.6-8.9] g/day) with decreased serum albumin levels (2.5 [IQR, 2.1-2.9] (Table 2).

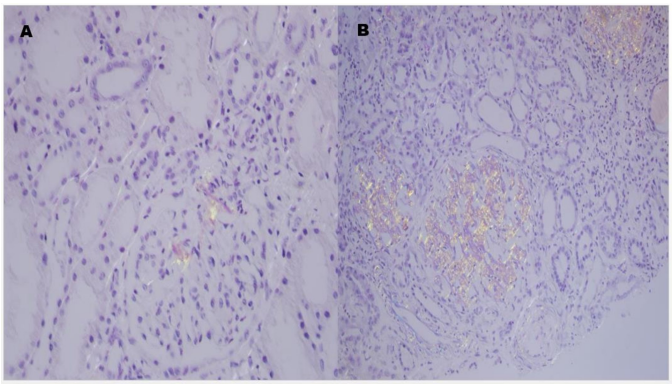

Figure 1. A: Glomerular amyloid distribution in renal biopsy specimens: early type (Congo red–stained sections showing apple green birefringence under polarized light, x 400). B: Glomerular amyloid distribution in renal biopsy specimens:late type (Congo red–stained sections showing apple green birefringence under polarized light, x 400).

Table 1. Scoring of histopathological findings in renal biopsies.

	Definition	Score
Glomerular amyloid deposition (GAP)	0: absent, 1: hilar, 2: minimal mesangial, 3: focal mesangial, 4: mesangiocapillar, 5: membranous, 6: global sclerotic	0-6
Glomerular amyloid deposition (GA%)	0: absent, 1: 1–10%, 2: 11–25%, 3: 26–50%, 4: 51–75%, 5: 76–100%	0-5
Vascular amyloid deposition (VA)	0: absent, 1: minimal, 2: focal, 3: moderate, 4: severe	0-4
Interstitial amyloid deposition (IA)	0: absent, 1: minimal, 2: focal, 3: moderate, 4: severe	0-4
Interstitial fibrosis and tubular atrophy (Ifb)	0: absent, 1: 1–10%, 2: 11–25%, 3: 26–50%, 4: 51–100%	0-4
Interstitial infammatory infiltration (Iinf)	0: absent, 1: 1–10%, 2: 11–25%, 3: 26–50%, 4: 51–100%	0-4
Glomerular sclerosis (GS)	0: absent, 1: 1–10%, 2: 11–25%, 3: 26–50%, 4: 51–100%	0-4

Table 2. Characteristics of patients with renal AA amyloidosis at the time of renal biopsy.

Variables	Patients (n=18)
Age (years)	51.5 (45-58.3)
Gender (male,%)	72.2
Urea (mg/dL)	43.5 (33.8-67.8)
SCr (mg/dL)	1.61 (0.91-2.89)
eGFR (ml/min/1.73m^2)	47.4 (22.3-95.7)
Decreased eGFR (%)	66.7
Albumin (g/L)	2.45 (2.03-2.93)
Total cholesterol (mg/dL)*	248 (214.3-370.8)
HDL cholesterol (mg/dL)**	49 (37-59)
LDL cholesterol (mg/dL)**	174 (141-261.5)
Triglycerides (mg/dL)*	168.2 (130.5-270.8)
CRP (mg/L)**	14.1 (5.7-58.2)
Uric acid (mg/dL)**	4.6 (4.2-6.6)
Albuminuria (g/day)***	1.1 (0.8-2.6)
Proteinuria (g/day)	6.8 (4.6-8.9)

Data are expressed as median (IQR) unless otherwise indicated. CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SCr: serum creatinine. *Data were available for 16 patients. **Data were available for 15 patients. ***Data were available for 14 patients.

Table 3. Baseline urinalysis data in patients with AA amyloidosis.

Variables	Patients (n=18)
pH, median (IQR)	6 (5.5-6)
Specific gravity, median	(IQR) 1015 (1010.8-1019.8)
Protein, %	
1+	6.3
2+~3+	93.7
Blood, %	
0, negative or trace	25
1+	25
2+~3+	50
Glucosuria, % *	35.7
Urine microscopy automated, %	
White blood cells $\geq$ 5/hpf	15.4
Red blood cells $\geq$ 3/hpf	53.8

Data are expressed as median (IQR) unless otherwise indicated. *Data were available for 13 patients. hpf: high power field.

Baseline urinalysis data of study patients is shown in Table 3. The median pH value was 6 (IQR, 5.5-6) and the median urine-specific gravity was 1015 (IQR, 1010.8-1019.8). Glycosuria was found in 35.7% patients and median blood glucose level at the time of urinalysis of these patients was 77 (IQR, 74.5-99.5). 53.8% of 13 patients presented with microscopic hematuria.

Glomerular involvement was found in all patients except one. Glomerular amyloid depositions were found as mostly diffuse mesangiocapillary (38.9%), focal mesangial (27.8%) and minimal mesangial (22.2%). All of the patients had vascular amyloid deposition and 55.6% of the patients had interstitial amyloid deposition. Interstitial fibrosis/tubular atrophy and interstitial infammatory infiltration were observed in 88.9% and 94.4% of the biopsies. Extensive involvements of glomerular amyloid deposition, interstitial fibrosis and tubular atrophy, interstitial infammatory infltration and glomerular sclerosis were detected in 83.3%,5.6%,5.6% and 5.6% of biopsies, respectively. RAPS grade was I in 5.6%, II in 27.8% and III in 66.7% of the biopsies.

Baseline median eGFR, serum albumin, proteinuria in RAPS grade II and III were 48.8 (IQR, 17.7-79.8) vs. 50.5 (IQR, 23.5-111.3) ml/min/1.73m^2, 2.2 (IQR, 2.1-3.1) vs. 2.5 (1.8-2.9) g/dl, Land 5.6 (IQR, 4.1-13.7) vs. 6.9 (IQR, 5.1-10.7) g/day, respectively.

Median follow-up time was 37.5 (IQR, 12.3-59.3) months. Sixteen (88.9%) patients were treated with colchicine and six (33.3%) patients were treated with methylprednisolone/prednisolone. One patient with FMF received canakinumab for three months and because of severe pneu-

Table 4. The correlations between end-stage renal disease (ESRD) and renal histopathological findings in patients with AA amyloidosis.

Variables	Spearman's rho	P
Glomerular amyloid deposition (GAP)	0.361	0.14
Glomerular amyloid deposition (GA%)	0.199	0.43
Vascular amyloid deposition (VA)	0.162	0.52
Interstitial amyloid deposition (IA)	0.230	0.36
Interstitial fibrosis and tubular atrophy (Ifb)	0.608	0.01
Interstitial infammatory infltration (Iinf)	0.420	0.08
Glomerular sclerosis (GS)	0.144	0.57
Renal amyloid prognostic score (RAPS)	0.339	0.17

Table 5. Clinical characteristics and kidney biopsy findings of the study patients.

No	Sex	Age (year)	Underlying Disease	At The Time of Renal Biopsy				Kidney Biopsy Findings								Treatment	Follow-up					
				SCr (mg/dL)	eGFR (mL/min/ 1.73m^2	Albumin (g/dL)	Proteinuria (g/day)	GAP	GA%	VA	IA	Ifib	Iinf	GS	RAPS		Time (mo)	SCr (mg/dL)	eGFR (mL/min/ 1.73m^2)	ΔeGFR (mL/min/ 1.73m^2	Albumin (g/dL)	Proteinuria (g/day	Mortality
1	M	50	Empyema	0.4	144.6	2.5	6.5	4	5	3	0	2	2	2	3	Colchicine, ACEinh/ARB	32			ESRD			Yes
2	F	56	RA, FMF	1.6	35.7	2.8	2.5	3	5	3	0	0	2	3	3	Pred, HCQ, Colchicine, ACEin/ARB	112	1.4	39.3	3,6	4	0.7	No
3	M	55	Unknown	1.1	75.4	2.11	7.1	3	5	3	1	3	3	3	3	Pred, Colchicine	131	1.86	36.9	-38.5	3.9	NA	No
4	M	52	FMF	1.5	55	3	6.4	3	5	2	2	3	3	2	3	Colchicine, canakinumab, ACEinh/ARB	43			ESRD			No
5	F	58	Tuberculosis	1.1	54	2.2	3.7	2	1	2	2	3	3	1	2	ACEinh/ARB	34			ESRD			No
6	F	32	Tuberculosis	4.2	13.1	3.7	4.5	2	2	2	0	2	3	0	2	Colchicine	15	1.1	68.9	55.8	4.1	0.5	No
7	M	54	Bronchiectasis	1.7	46.1	1.6	8.1	4	5	2	2	3	3	1	3	Colchicine	23			ESRD			Yes
8	M	45	AS, Tuberculosis	**3.2**	22.1	1.8	12.9	4	5	4	3	3	2	1	3	Colchicine	3						Yes
9	M	23	AS, FMF	0.7	137.3	1.5	11.6	3	5	2	0	2	3	1	3	Colchicine, canakinumab, ACEinh/ARB	58			ESRD			No
10	M	73	Unknown	2.9	21	1.8	13.9	4	5	3	2	3	2	2	3	Colchicine	4			ESRD			No
11	M	45	Tuberculosis	2.7	27.6	2.5	6.9	6	5	4	2	4	4	4	3	Colchicine	69			ESRD			No
12	M	42	FMF	1	92.4	2.6	4.6	4	5	3	3	2	2	0	3	Colchicine, ACEinh/ARB	60	1.2	69.5	-22.9	4.1	NA	Yes
13	M	59	RA	2.9	22.3	2.4	19.9	2	5	3	0	1	1	0	2	Pred, Colchicine	1			ESRD			Yes
14	M	62	RA, Tuberculosis	0.6	106	2.1	5.6	2	5	2	0	1	1	3	2	Pred, Colchicine Tocilizumab, ACEInh/ARB	42	1.5	49	-57	3.2	6.1	No
15	M	51	FMF	1.6	48.8	2.1	7.4	3	5	2	0	1	1	0	2	Colchicine, ACEinh/ARB	59	0.7	107.4	58.6	2.9	NA	No
16	F	46	Tuberculosis	4.8	10.1	2.9	7.6	4	5	4	4	2	2	2	3	Pred	3	1.9	30.2	20.1	NA	NA	No
17	F	47	Unknown	0.5	117.6	3.4	2.3	4	5	4	2	3	3	0	3	Colchicine	15			ESRD			Yes
18	M	60	SLE	1.8	39.8	3.7	6.6	0	0	2	0	0	0	3	1	Pred, HCQ, Colchicine, AZA, ACEinh/ARB	41	2.02	34.1	-5.7	4.1	2.1	No

ACEinh/ARB: angiotensin converting enzyme inhibitors/ angiotensin receptor blockers; AS: ankylosing spondilitis; AZA: azathioprine; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease F: female; FMF: familial mediterranean fever; GAP: class of glomerular amyloid deposition; GA%: percentage of glomerular amyloid deposition; GS: glomerular sclerosis; HCQ: hydroxychloroquine; IA: interstitial amyloid deposition; Ifb: interstitial fibrosis and tubular atrophy; Iinf: interstitial infammatory infltration; M: male; Pred: methylprednisolone/prednisolone; RA: rheumatoid arthritis; RAPS: renal amyloid prognostic score; SCr: serum creatinine; SLE: systemic lupus erythematosus; VA: vascular amyloid deposition.

monia canakinumab was stopped. The other patient with FMF also received canakinumab for forty-two months, however due to Covid-19 disease it was stopped. And one patient with rheumatoid arthritis and previous tuberculosis was still on treatment with tocilizumab.

Ten patients (55.5%) reached ESRD at a median time of 15 (IQR, 2.3-32.3) months. There was a significant negative correlation between ESRD and steroid treatment (r=-0.553, P= 0.02). There were no significant correlations between other studied variables and ESRD (Data not shown). In Table 4, the correlations between ESRD and renal histopathological findings in patients with AA amyloidosis are shown. ESRD was correlated with interstitial fibrosis/tubular atrophy (r=0.608, P= 0.01). In overall group, death-censored renal survival rates at 1,3 and 5 years were 83.3%, 58.7% and 43.5%, respectively. Excluding ESRD patients, the median of SCr at follow-up was 1.5 (IQR, 1.1-1.9) mg/dL, the median eGFR was 44 (IQR, 37.5-69.4) ml/min/1.73m^2. Only one patient had transient hemodialysis.

Six patients (33.3%) died. The median survival time of patients was 38.5 (IQR, 16.5-62.3) months. Patient survival rates at 1, 3 and5 were 88.9%, 69.6 and 55.7%, respectively. Table 5 shows clinical and histopathological findings of study patients.

Discussion

In this study, we reported eighteen patients presenting with AA amyloidosis with different clinical and morphological lesions. Previously larger studies of renal amyloidosis including all types of amyloidosis have reported the prevalence as approximately 0.7–5.5 % [17]. The prevalance of AA amyloidosis was found 4.2% of all renal biopsies in our series. This finding was lower than other series reported from Turkey [13].

In our study the patients were generally male and middle-aged like usual in AA amyloidosis [10,11,13,18]. In other studies, female predominance was shown due to rheumatic diseases affecting women more commonly [19-23]. Chronic infammatory arthritis was mostly diagnosed as an underlying disease in developed countries [11,18-21]. We found previous tuberculosis as a leading cause of amyloidosis. This finding was higher than other reports from Turkey. FMF was mostly found as a leading cause of AA amyloidosisin other studies reported from Turkey [12,13,24-27].

Different studies described histopathological classifications according to the distribution such as glomerular, vascular or interstitial type [9,11,16,22]. In our study, most of the patients had predominantly glomeruler amiloid deposits as mesengiocapillary [10-13,28]. Mesangium is known as the earliest site of amyloid deposition in the glomerulus, this finding is in accordance with the literature [11]. Although, amyloidosis is known as a diffuse disease [22], and our study also showed that amyloid deposition could be focal in manner.

Most of our patients had more extensive glomerular amyloid involvement contrary to studies reported from developed countries [10,22,23]. Said et al also observed glomerular amyloid deposition in in 100% of biopsy specimens of AA amyloidosis patients [29].

Vascular involvement from amyloid differed between 67% and 79% [12]. We found vascular amyloid deposition in all patients similar to other studies [12,29]. Verine reported vascular amyloid deposition, mostly juxtaglomerular arterioles, in 65 renal biopsies (95.6%) [10]. In one study reported by Uda H et al defined amyloid deposits only

around blood vessels not glomeruls in 28.9% of patients [30]. In our study, we detected amyloid deposits around vessels without glomerul deposition in only one patient (5.6%).

Percentage of interstitial amyloid deposition in this study (55.6%) was lower than reported studies [12,13,29] and similar to the study reported by Verine et al [10]. Interstitial inflammation was present in all patients except one. Verine et al reported an inflammation with amyloid deposits in thirty biopsises (44.1%) of the patients [10]. Kendicelebi et al found interstitial inflammation in 28 patients (78%) [12].

In previous studies associations between amyloid depositions with other histopathological parameters and renal manifestations were shown [11,20-22,28]. Verine et al. reported that the glomerular amyloid distribution and inflammation were independently associated with proteinuria level [10]. In a previous study, Celtik et al found that advanced renal amyloidosis had signifcantly lower eGFR than patients with early and late amyloidosis classified according to RAPS score system and percentage of glomerular amyloid deposition was an independent variable related to proteinuria [13]. In contrast; Min et al. and Kuroda et al reported the independent associations between increased amount of glomerular amyloid deposits and decreased renal functions, but not with proteinuria [21,22]. However, we failed to show any correlations between the histologic lesions and baseline clinical data.

In our center percentage of patients progressed to ESRD were higher than other reports [10,13,18,19,23,24]. The median renal survival was reported between 18 and 64 months in the literature. Our study showed a relatively lower renal survival time of months than reported studies [12,20]. In our study, interstitial fibrosis and tubular atrophy was shown as a significant risk factor for ESRD. Celtik et al. showed that ESRD was independently associted to extensive glomerular amyloid deposition, baseline eGFR and proteinuria [13]. Bohle et al found the worst prognosis of AA amyloidosis in patients with both acute renal failure and interstitial fibrosis at the time of the biopsy [19]. Verine et al. also found interstitial fibrosis and tubular atrophy as an independent predictor of ESRD instead of pattern and abundance of glomerular amyloid deposits in Cox regression analysis in patients with AA amyloidosis [10]. Development of ESRD was found to be associated with glomerular enlargement, global involvement of the glomerulus, tubular atrophy, and interstitial inflammationin correlation analysis in a study reported by Kendicelebi et al. However, multivariate analysis showed the global glomerular amyloid load as the only variable related to ESRD [12].

There were several limitations in our study. The most important limitation was it's design was retrospectiveand our series had a small number of patients.The changes of CRP and SAA levels were not analyzed due to lack of data.Another limitation of our study is the advanced renal disease, therefore we observed many chronic changes in renal tissue samples. Biopsy specimens of patients with early stage kidney disease may be more accurate in predicting prognosis.

Conclusion

In conclusion most of the patients with AA amyloidosis (55.6%)in our study had poor prognosis finalized as ESRD. Classical prognostic histopathological findings as seen in primary glomerular diseases, such as tubular atrophy and interstitial fibrosis, suggests that this feature could be used as a marker of progression of renal damage in AA amyloidosis.

We expected to find AA amyloidosis more frequent in our renal biopsy specimens due to higher prevalence of tuberculosis and FMF in Turkey. Also we found advanced renal amyloid depositions in our series. This might be explained by late referral to nephrology departments from other clinics and minimal depositions might be overlooked by pathologists. In patients with a history of inflammatory diseases who had proteinuria and/or unexplained renal insufficiency, kidney biopsy should be performed as soon as possible to prevent irreversible organ damage and to increase survival in AA amyloidosis patients. AA amyloidosis scoring and grading system according to histopathological findings may also be useful to predict and improve the prognosis of patients.

Ethics approval

Local ethics committee approval of Kartal City-Hospital was obtained (date: 28.04.2021 number: 2021/514/200/18).

References

1. Sunde M, Blake C. The structure of amyloid fbrils by electron microscopy and X-ray difraction. Adv Protein Chem. 1997;50:123–59.
2. Merlini G, Bellotti V. Molecular mechanisms of amyloidosis. N Engl J Med. 2003;349:583–96.
3. Uversky VN, Fink AL. Conformational constraints for amyloid fibrillation: the importance of being unfolded. Biochim Biophys Acta. 2004;1698:131–53.
4. Gillmore JD, Lovat L, Persey MR, Pepys MB, Hawkins PN.Amyloid load and clinical outcome in AA amyloidosis in relation to circulating concentration of serum amyloid protein. Lancet. 2001;358:24–9.
5. Husby G, Husebekk A, Skogen B,et al. Serum amyloid A (SAA)-the precursor of protein AA in secondary amyloidosis. Adv Exp Med Biol. 1988;243:185–92.
6. Dember LM. Amyloidosis-associated kidney disease. J Am Soc Nephrol. 2006;17:3458–71.
7. Obici L, Merlini G. AA amyloidosis: basic knowledge, unmet needs and future treatments. Swiss Med Wkly. 2012;142: w13580.
8. National Nephrology. Dialysis and Transplantation Registry Report of Turkey; 2019.
9. Shiiki H, Shimokama T, Yoshikawa Y, Toyoshima H, Kitamoto T, Watanabe T. Renal amyloidosis. Correlations between morphology, chemical types of amyloid protein and clinical features. Virchows Arch A Pathol Anat Histopathol 1988; 412: 197–204.
10. Verine J, Mourad N, Desseaux K, et al. Clinical and histological characteristics of renal AA amyloidosis: a retrospective study of 68 cases with a special interest to amyloid-associated inflammatory response. Hum Pathol 2007; 38: 1798–1809.
11. Hopfer H, Wiech T, Mihatsch MJ. Renal amyloidosis revisited: amyloid distribution, dynamics and biochemical type. Nephrol Dial Transplant. 2011; 26: 2877–84.
12. Kendi Celebi Z, Kiremitci S, Ozturk B, et al. Kidney biopsy in AA amyloidosis: impact of histopathology on prognosis. Amyloid. 2017;24:176-82.
13. Celtik A, Sen S, Keklik F, et al. A histopathological scoring and grading system to predict outcome for patients with AA amyloidosis. Int Urol Nephrol. 2020;52:1297-1304.

14. Fonseca EO, Caldas MLR, Soares Filho PJ, Almeida JR. Correlation between amyloid deposits affecting renal compartments and glomerular filtration rate during renal biopsy in a renal amyloidosis case series. Braz J Med Biol Res. 2020;53:e8625.
15. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009; 150: 604-12.
16. Sen S, Sarsik B. A proposed histopathologic classifcation, scoring, and grading system for renal amyloidosis: standardization of renal amyloid biopsy report. Arch Pathol Lab Med. 2010;134:532–44.
17. Nishi S, Muso E, Shimizu A, et al. A clinical evaluation of renal amyloidosis in the Japan renal biopsy registry: a cross-sectional study. Clin Exp Nephrol. 2017;2:624-32.
18. Lachmann HJ, Goodman HJ, Gilbertson JA, et al. Natural history and outcome in systemic AA amyloidosis. N Engl J Med. 2007;356:2361–71.
19. Bohle A, Wehrmann M, Eissele R, von Gise H, Mackensen-Haen S, Müller C. The long-term prognosis of AA and AL renal amyloidosis and the pathogenesis of chronic renal failure in renal amyloidosis. Pathol Res Pract. 1993;189:316-31.
20. Bergesio F, Ciciani AM, Santostefano M,et al.Immunopathology Group, Italian Society of Nephrology. Renal involvement in systemic amyloidosis--an Italian retrospective study on epidemiological and clinical data at diagnosis. Nephrol Dial Transplant. 2007;22:1608-18.
21. Min KW, Na W, Jang SM, Park MH.Prognostic associations of clinical and histopathological features in renal amyloidosis. Postgrad Med J. 2011;87:529-34.
22. Kuroda T, Ito Y, Imai N, et al. Significant association between renal function and area of amyloid deposition in kidney biopsy specimens from patients with AA amyloidosis associated with rheumatoid arthritis and AL amyloidosis. Amyloid. 2019;26(sup1):125-6.
23. Ozawa M, Komatsuda A, Ohtani H, et al. Long-term prognosis of AL and AA renal amyloidosis: a Japanese single-center experience. Clin Exp Nephrol. 2017;21:212.
24. Erdogmus S, Kendi Celebi Z, Akturk S, et al. Profile of renal AA amyloidosis in older and younger individuals: a single-centre experience. Amyloid. 2018;25:115-9.
25. Tuglular S, Yalcinkaya F, Paydas S,et al. A retrospective analysis for aetiology and clinical findings of 287 secondary amyloidosis cases in Turkey. Nephrol Dial Transplant. 2002;17:2003–05.
26. Ensari C, Ensari A, Tumer N,Ertug E.Clinicopathological and epidemiological analysis of amyloidosis in Turkish patients. Nephrol Dial Transplant. 2005;20:1721–25.
27. Yilmaz M, Unsal A, Sokmen M, et al. Renal involvement in AA amyloidosis: clinical outcomes and survival. Kidney Blood Press Res. 2013;37:33–42.
28. Castano E, Palmer MB, Vigneault C, Luciano R, Wong S, Moeckel G. Comparison of amyloid deposition in human kidney biopsies as predictor of poor patient outcome. BMC Nephrol. 2015;16:64.
29. Said SM, Sethi S, Valeri AM,et al. Renal amyloidosis: origin and clinicopathologic correlations of 474 recent cases. Clin J Am Soc Nephrol. 2013;8:1515–23.
30. Uda H, Yokota A, Kobayashi K, et al. Two distinct clinical courses of renal involvement in rheumatoid patients with AA amyloidosis. J Rheumatol. 2006;33:1482-7.