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RESEARCH

Adult primary glomerular diseases due to podocytopathies: a single center experience on patient characteristics, treatment and outcomes

Podositopatilere bağlı erişkin primer glomerüler hastalıklar: hasta özellikleri, tedavileri ve sonuçlarına ilişkin tek merkez deneyimi

İsmail Bulgur[1], Sait Şen[2], Banu Sarsık Kumbaracı[2], Meltem Seziş Demirci[3], Mümtaz Yılmaz[3], Gülay Aşçı[3]

[1]SBU Bursa City Hospital, Bursa, Turkey
[2]Ege University, İzmir, Turkey

Abstract

Purpose: This study aims to evaluate the demographic, clinical, and pathologic characteristics and response to immunosuppressive therapy, particularly corticosteroids, in adult patients with primary focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD), which are classified as podocytopathies.

Materials and Methods: Between January 1998 and December 2014, this study included 44 patients (27 with primary FSGS and 17 with MCD) aged older than 18 years with a histopathologic diagnosis, symptoms of nephrotic syndrome, and a minimum follow-up of six months. Patients were divided into two groups according to the treatment they received and three groups according to their response to treatment. Patients diagnosed with primary FSGS and MCD were evaluated based on clinical, demographic, and laboratory findings, as well as response to treatment, and a comparison was conducted between the two groups.

Results: 59.1% of the patients were male with a mean age of 44.8±17.7 years. At the time of diagnosis, there were no statistically significant differences in clinical and demographic characteristics between MCD and primary FSGS patients. However, in patients with MCD, the mean creatinine clearance (118.0±46.7 ml/min) was higher and the rate of microscopic hematuria (11.8%) was lower at the time of diagnosis. There was an increased need for alternative immunosuppressive treatments besides corticosteroids in patients with primary FSGS to achieve partial or complete remission. At both the third and sixth-month follow-ups, MCD patients achieved a higher rate of complete remission (proteinuria <0.3 g/day) than FSGS patients.

Öz

Amaç: Bu çalışma podositopatiler çatısı altında değerlendirilen primer fokal segmental glomerüloskleroz (FSGS) ve minimal değişiklik hastalığı (MDH) tanılı erişkin hastaların demografik, klinik, patolojik özelliklerini ve başta kortikosteroidler olmak üzere uygulanan immunsupresif tedaviye yanıtlarını değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Çalışmaya Ocak 1998 ve Aralık 2014 tarihleri arasında, en az 6 ay takip edilen, nefrotik sendrom bulguları gösteren, histopatolojik olarak MDH ve primer FSGS tanısı almış, 18 yaş üstü 44 hasta (27 primer FSGS ve 17 MDH) dahil edildi. Hastalar uygulanan tedavi açısından 2 gruba, tedaviye cevap durumuna göre ise 3 gruba ayrıldı. Primer FSGS ve MDH tanılı hastalar klinik, demografik, laboratuvar bulgularının yanı sıra tedaviye yanıt açısından değerlendirilmiş ve iki grup arasında karşılaştırma yapılmıştır.

Bulgular: Hastaların %59.1'i erkek olup, yaş ortalaması 44.8±17.7 yıldı. Klinik ve demografik özellikler açısından tanı anında MDH ve primer FSGS hastaları arasında istatistiksel olarak anlamlı fark saptanmadı. Fakat, MDH'da tanı anında kreatinin klirensi ortalamasının (118.0±46.7 ml/dk) daha yüksek olduğu saptanmış, mikroskobik hematüri oranı (%11.8) ise daha düşük bulunmuştur. Primer FSGS hastalarında parsiyel veya tam remisyon elde edebilmek amacıyla kortikosteroid dışında diğer immunsupresif tedavilere daha fazla ihtiyaç duyulmuştur. 3. ve 6. ay takiplerinde, tam remisyona (proteinüri <0,3 g/gün) girme oranının MDH hastalarında FSGS hastalarından daha yüksek olduğu saptanmıştır.

Sonuç: Primer FSGS'nin MDH'a kıyasla daha çok progresyon gösterme eğiliminde olduğu, parsiyel veya tam remisyon elde edebilmek amacıyla kortikosteroid dışında

Address for Correspondence: İsmail Bulgur, SBU Bursa City Hospital, Bursa, Turkey
E-mail: smilebulgur@hotmail.com
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Conclusion: Compared to MCD, primary FSGS is more likely to progress, requires more immunosuppressive therapy beyond corticosteroids to achieve partial or complete remission, and has a lower treatment response rate.

Keywords:. Podocytopathy, primary focal segmental glomerulosclerosis, minimal change disease, proteinuria, prognosis

diğer immunsupresif tedavilere daha fazla ihtiyaç duyulduğu ve tedaviye yanıtının da daha düşük olduğu saptanmıştır.

Anahtar kelimeler: Podositopati, primer fokal segmental glomerüloskleroz, minimal değişiklik hastalığı, proteinüri, prognoz

INTRODUCTION

Minimal change disease (MCD) and primary focal segmental glomerulosclerosis (FSGS) are primary glomerular diseases characterized by manifestations of nephrotic syndrome, including proteinuria, edema, and hypoalbuminemia [1]. These conditions are diagnosed by renal biopsy[1]. They are classified as podocytopathies, with glomerular epithelial damage serving as the basis[2,3]. Since both diseases share clinical findings and similar treatment approaches involving corticosteroids, alkylating agents, and calcineurin antagonists, some experts suggest that they may represent two subtypes of a single disease or different manifestations of the same condition[3,4]. Despite the suggested several causes, including genetics, immunology, hemodynamics, circulating permeability factors, and lymphokines, the exact etiopathogenesis of MCD and FSGS remains unclear[5,6].

The incidence of adult MCD is 10-25% of all nephrotic syndromes[7]. In rare cases, hypertension (HT), hematuria (10-30%), and reduced renal function (20-25%) may occur[8,9]. In adult studies, more than 80% of patients achieved complete remission with corticosteroids[7,9]. However, although 50-75% of adults who respond to corticosteroids experience relapses, a subgroup of 10-25% fall under the frequent relapse category. End-stage renal disease (ESRD) is rare in MCD patients and has mostly been reported in steroid-resistant patients[10].

Primary FSGS is reported in 20-30% of adult nephrotic syndrome patients[11]. Microscopic hematuria, hypertension, and renal failure are common and occur in 30-45% of patients at presentation[12]. Most patients with untreated or unresponsive primary FSGS experience an increase in proteinuria and progression to renal failure. More than 50% of patients with nephrotic-level proteinuria develop ESRD within 5-10 years[12]. Compared to MCD, FSGS patients exhibit a greater tendency for progression and lower response rates to treatment[3,4]. Based on the hypothesis that MCD and primary FSGS may represent early and late stages of the same disease[2], we considered that these patients may show differences in prognosis, treatment management, and response. This study aimed to objectively evaluate the demographic, clinical, and pathological features of adult patients diagnosed with primary FSGS and MCD by renal biopsy and their response to immunosuppressive therapy, particularly corticosteroids. However, few studies in the literature have evaluated podocytopathies among primary glomerular diseases in the adult population as a whole. Therefore, we believe that evaluating and comparing these diseases can contribute valuable knowledge to the literature, particularly regarding prognosis and disease management.

MATERIALS AND METHODS

The study was conducted at the Ege University Faculty of Medicine with the approval of the Clinical Research Ethics Committee (approval number: 16-5.2/9, date: 24.05.2016). The Ege University Faculty of Medicine was established in Izmir in 1955. It is a reference tertiary health institution serving in the Aegean region. This institution provides healthcare, trains research assistants and medical students, and conducts scientific research simultaneously. Academic activities are planned and conducted under the supervision of faculty members. Renal biopsy samples are discussed weekly in the Clinical Pathology Council, which is jointly chaired by the faculty members of the Division of Nephrology and the expert nephropathologists of the Department of Medical Pathology. In this way, medical decisions in diagnosis and treatment are taken in a multidisciplinary manner. This study was conducted based on the principles of the Declaration of Helsinki.

Study population

This study was conducted by retrospectively examining the files of 201 patients with a diagnosis of

FSGS or MCD by renal biopsy at Ege University, Division of Nephrology, between January 1998 and December 2014. The study included 44 patients (27 with primary FSGS and 17 with MCD) aged older than 18 years with symptoms of nephrotic syndrome and a minimum follow-up of six months. It excluded patients who did not attend regular follow-ups, had missing data, or had histopathologic or clinical evidence of secondary FSGS (such as systemic diseases, connective tissue diseases, systemic vasculitis, sequelae of other glomerulonephritis, or HBV).

Procedure

The analyzed data included age, gender, date of diagnosis/biopsy, presence of peripheral edema, body weight at the time of diagnosis, diastolic and systolic blood pressure, presence of comorbidities and frequency of antihypertensive drug use at the time of diagnosis, serum creatinine level and basal creatinine clearance, rate of reduced creatinine clearance (≤90 ml/min), presence of hematuria and microscopic hematuria rate, 24-hour urinary protein excretion, serum albumin, hypoalbuminemia rate, globulin, urea, total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), hemoglobin, fasting blood glucose values, immunosuppressive therapy received, response status, and follow-up periods. All renal biopsy samples were routinely examined using light and immunofluorescence microscopy. The expert nephropathologists of the Ege University Faculty of Medicine, Department of Medical Pathology evaluated and reported the results. We recorded the number of glomeruli, presence of interstitial fibrosis, tubular atrophy, segmental glomerulosclerosis, and global glomerulosclerosis from biopsy pathology reports.Serum creatinine levels, basal creatinine clearance, 24-hour urinary protein excretion, and serum albumin levels were used to evaluate patient response to treatment and disease follow-up.

Definitions

Complete remission (response) was defined as a reduction in proteinuria below 300 mg/day; *partial remission (response)* was defined as a 50% reduction in proteinuria between 0.3 and 3.5 g/day; and *relapse* was defined as the recurrence of proteinuria of 3.5 g/day after a previous complete or partial response [7]. The persistence of proteinuria greater than 3.5 g/day despite at least 3 months of treatment was defined as clinical failure to achieve remission. Outpatient follow-up data were analyzed at three-month intervals, with a minimum of two intervals (six months) and a maximum of four intervals (12 months). The laboratory parameters relevant to treatment response were appropriately recorded. The patients were also followed for at least one follow-up period (three months) after relapse to assess their response to the therapy.

Identification of treatment

Our treatment regimen for MCD in our department is oral methylprednisolone 1 mg/kg (up to 60 mg/day) for a minimum of one month and a maximum of three months. After remission is achieved, the corticosteroid is tapered over three months. In primary FSGS patients, the first-line treatment is oral methylprednisolone 1 mg/kg (up to 60 mg/day) for a minimum of two months and a maximum of three months. After remission is achieved, corticosteroids are tapered over six months. In MCD/primary FSGS patients who fail to achieve clinical remission, oral cyclosporine or oral/intravenous cyclophosphamide regimens are used in combination with low-dose corticosteroids as second-line therapy. Furthermore, angiotensin converting enzyme inhibitor/angiotensin receptor antagonist (ACEi/ARB) therapy has not been routinely added to the standard clinical protocol for patients with MCD and primary FSGS receiving immunosuppressive therapy.

Statistical analysis

All data were analyzed using the SPSS 22.0 statistical software (IBM Corporation, Armonk, New York, United States). The descriptive statistics were first evaluated without distinguishing between the diseases. Then, two groups were defined as primary FSGS and MCD and the results were reevaluated by performing comparative group statistics. Descriptors for the parameters were expressed as percentages (%) and means. Frequencies were expressed as percentages (%), while the means were expressed ± standard deviation (sd). For descriptive analyses, percentages, frequencies, means ± standard deviations, and medians (min; max) were calculated. Categorical variables were shown as the number of patients (n) with percentages (%), while quantitative variables were shown as means, standard deviation (sd), min–max, and medians. Pearson's chi-square test and Fisher's exact test were used for analyzing the

categorical data, while the Shapiro–Wilk test was used to assess the data's conformity to a normal distribution. For statistical analysis of quantitative data in independent groups, the Mann-Whitney U test was used for non-normally distributed data, while the independent sample t-test was used for normally distributed data. A p value ≤0.05 indicated statistical significance.

RESULTS

Of the 44 patients with a mean age of 44.8±17.7 years (median: 40.5, min–max: 20-87), 18 (40.9%) were female and 26 (59.1%) were male. The incidence of both diabetes and cardiovascular disease was 11.4%. The rate of antihypertensive medication use was 15.9%, and 31.8% of patients had a blood pressure ≥140/90 mmHg at diagnosis. All patients presented with peripheral edema. Furthermore, there was no significant difference in clinical and demographic characteristics between MCD and primary FSGS patients at the time of diagnosis (p>0.050). Patients with MCD had longer follow-up, although the difference between the two groups was not significant (p=0.097) (Table 1).

Table 1. Clinical and demographic characteristics in primary FSGS and MCD.

Variables		All patients (n:44)		Primary FSGS(n:27)		MCD(n:17)		p
		n	%*	n	%*	n	%*	
Gender	Male	26	59.1	18	66.7	8	47.1	0,198*
	Female	18	40.9	9	33.3	9	52.9	
Diabetes mellitus	Yes	5	11.4	2	7.4	3	17.6	0,359**
Cardiovascular disease	Yes	5	11.4	4	14.8	1	5.9	0,634**
Hypertension frequency (≥140/90)	Yes	14	31.8	10	37.0	4	23.5	0,349*
Antihypertensive drug use	Yes	7	15.9	5	18.5	2	11.8	0,689**
Variables		Mean/sd	Median	Mean/sd	Median	Mean/sd	Median	p***
Age (years)		44.8±17.7	40.5	45.4±19.2	39.0	43.9±15.6	44.0	0,894***
Systolic blood pressure (mm/hg)		122.6±13.5	120.0	122.5±12.3	120.0	122.6±10.4	125.0	0,874***
Diastolic blood pressure (mm/hg)		78.9±9.3	80.0	78.1±10.6	80.0	80.1±6.8	80.0	0,504****
Weight (kg)		73.9±15.9	73.0	72.6±14.7	70.0	76.2±18.1	76.5	0,589****
Follow-up period (years)		3.9±3.0	3.0	3.3±2.6	2.0	4.9±3.4	4.0	0,097***

%Column percentage is used. *Pearson Chi-Square, **Fisher's Exact Test, ***Mann Whitney U test, **** Independent samples t test, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease, sd: standard deviation

Table 2 shows the biochemical parameters of the patients at the time of diagnosis. The serum albumin concentration, creatinine level, mean creatinine clearance, and urinary protein levels were not different between the two groups (p>0.050). Although there was no significant difference between the two groups, the mean creatinine clearance at diagnosis was greater in the MCD group (p=0.080). Additionally, MCD patients had significantly greater HDL levels and lower rates of microscopic hematuria (p<0.050) (Table 2).

Table 2. Biochemical parameters in primary FSGS and MCD.

Biochemical variables	All patients (n:44)		Primary FSGS(n:27)		MCD(n:17)		p
	Mean/sd	Median	Mean/sd	Median	Mean/sd	Median	
Urea (mg/dL)	47.7±37.8	38.0	54.9±44.4	40.0	36.3±20.5	30.0	0,101*
Creatinine (mg/dL)	1.1±0.8	0.8	1.3±0.9	0.9	0.8±0.4	0.8	0,072*
Creatinine clearance (ml/min)	102.5±46.5	102.5	92.7±44.6	92.0	118.0±46.7	116.0	0,080**
Globulin (g/dL)	2.6±0.4	2.5	2.6±0.4	2.5	2.5±0.3	2.5	0,856*
Albumin (g/dL)	2.4±0.9	2.2	2.5±0.8	2.3	2.3±0.9	2.1	0,266*
Triglyceride (mg/dL)	259.8±173.2	270.5	243.1±105.1	271.0	286.4±248.0	253.0	0,904*
Total cholesterol (mg/dL)	362.0±127.7	361.0	334.2±114.4	358.0	406.1±138.4	371.0	0,068**
HDL (mg/dL)	62.5±25.3	56.0	55.3±19.4	51.0	73.9±29.6	61.0	0,026*
LDL (mg/dL)	243.0±116.1	237.5	227.4±97.3	230.0	267.8±144.0	245.0	0,265**
Haemoglobin (g/dL)	13.6±2.0	13.5	13.2±1.9	12.9	14.2±1.9	14.7	0,074**
Fasting blood glucose (mg/dL)	95.6±14.8	96.0	92.9±14.3	90.0	100.0±14.8	98.0	0,119**
Proteinuria (g/day)	8.0±3.6	7.3	8.5±4.0	7.5	7.2±2.7	7.1	0,317*
Haematuria (erythrocyte count)	2.1±2.3	2.0	2.5±2.7	2.0	1.3±0.9	1.0	0,237*
	n	%	n	%	n	%	p
Albumin ≤ 3.5 g/dL	38	86.4	22	81.5	16	94.1	0,380***
Creatinine clearance ≤ 90 ml/min	20	45.5	14	51.9	6	35.3	0,283****
Microscopic haematuria (≥3 erythrocytes)	13	29.5	11	40.7	2	11.8	0,040****

% Column percentage is used. * Mann Whitney U test, ** Independent samples t test, ***Fisher's Exact Test, **** Pearson Chi-Square, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease, HDL: High density lipoprotein, LDL: Low density lipoprotein, sd: standard deviation

Table 3 shows the histopathologic features of renal biopsies from patients with primary FSGS and MCD. Tubular atrophy and segmental glomerulosclerosis were not detected in the MCD biopsies. The rate of global glomerulosclerosis was 11.4% in primary FSGS patients and 1.4% in MCD patients. Compared to those in patients with primary FSGS, the count and rate of global glomerulosclerosis were lower in those with MCD (p<0.050) (Table 3).

Table 3. Histopathologic features of renal biopsies in primary FSGS and MCD

Variables	Primary FSGS(n:27)		MCD(n:17)		p*
	Mean/sd	Median	Mean/sd	Median	
Glomerulus number	35.2±20.7	30.0	23.8±13.5	20.0	0,034
Segmental sclerosis count	1.8±3.8	1.0	0.0±0.0	0.0	<0,001
Global sclerosis count	3.5±3.9	2.0	0.4±0.6	0.0	0,003
Variables	n	%	n	%	p
İnterstitial fibrosis	11	40.7	3	17.6	0,109**
Tubular atrophy	12	44.4	0	0.0	0,001***

% Column percentage is used. * Mann Whitney U test, ** Pearson Chi-Square, *** Fisher's Exact Test, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease, sd: standard deviation

Patients were evaluated in two treatment groups: the corticosteroid group (CS) and the immunosuppressive group (IS). The IS group included administration of other immunosuppressive treatments (cyclosporine and cyclophosphamide) in combination with corticosteroids. The demographic, laboratory, and clinical characteristics of the CS and IS groups were compared, showing no significant difference between the groups (p>0.050). Microscopic hematuria was slightly greater in the IS treatment group (p>0.050) (Table 4). Only 2 patients in the MCD group (11.7%) were treated with oral cyclosporine as a second-line treatment. However, 13 patients (48.1%) in the FSGS group received immunosuppressive treatment (oral cyclosporine in eight patients and oral/intravenous cyclophosphamide in five patients) (p=0.013).

Table 4. Evaluation of treatment groups in primary FSGS and MCD with clinical, demographic and laboratory characteristics

		CS (n:29)		IS(n:15)		p
		n	%	n	%	
Disease	Primary FSGS	14	48.3	13	86.7	0,013*
	MCD	15	51.7	2	13.3	
Gender	Male	17	58.6	9	60.0	0,930*
	Female	12	41.4	6	40.0	
Diabetes mellitus		5	17.2	0	0.0	0,149**
Cardiovascular disease		4	13.8	1	6.7	0,647**
Microscopic haematuria (≥3 erythrocytes)		7	24.1	6	40.0	0,313**
Variables		Mean/sd	Median	Mean/sd	Median	p
Age (years)		46.7±18.1	44.0	41.2±16.8	34.0	0,353***
Systolic blood pressure (mm/hg)		122.8±13.1	120.0	122.0±14.6	120.0	0,843****
Diastolic blood pressure (mm/hg)		78.9±8.2	80.0	78.7±11.3	80.0	0,849***
Creatinine (mg/dL)		1.1±0.9	0.9	1.2±0.8	0.7	0,629***
Creatinine clearance (ml/min)		99.0±45.9	92.0	109.2±48.6	116.0	0,496*****
Albumin (g/dL)		2.2±0.6	2.1	2.8±1.1	2.7	0,078***
Proteinuria (g/day)		8.1±3.6	7.4	7.8±3.6	7.0	0,638***
Urine erythrocyte count		1.7±1.4	2.0	2.8±3.4	2.0	0,676***

% Column percentage is used. * Pearson Chi-Square, ** Fisher's Exact Test, ***Mann Whitney U test, **** Independent samples t test, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease, CS: corticosteroid group, IS: immunosuppressive group, sd: standard deviation

Patients' response to treatment was evaluated based on the degree of reduction in proteinuria[7]. The response status of treated patients at the three-month nephrology outpatient clinic follow-up was analyzed and categorized into three groups: no remission (for which remission could not be achieved), partial remission and complete remission. Table 5 presents the three-month follow-up data of patients with primary FSGS and MCD for a total of 12 months. This includes the numbers and percentages for each disease separately and in comparison. At the third and sixth-month follow-ups, patients with MCD had higher complete remission rates than did those with primary FSGS (p<0.050) (Table 5).

The number of relapses and the percentage of relapsed primary FSGS and MCD patients were obtained. One primary FSGS patient (3.7%) relapsed during the 6th-9th month follow-up period, while three patients (11.1%) relapsed during the 9th-12th month and after the 12th month follow-up periods, respectively. One patient (5.8%), two patients (11.7%), and six patients (35.2%) with MCD relapsed during the 6th-9th, 9th-12th, and after the 12th months of follow-up periods, respectively. The relapse frequency during the 6th-9th month and 9th-12th month follow-up periods did not significantly differ between primary FSGS patients and MCD patients (p>0.050). However, the frequency of relapse after the 12th month was significantly greater in patients with MCD (p=0.050).

The laboratory follow-up parameters were compared between primary FSGS patients and MCD patients at the end of the first year. The mean creatinine level was 1.4±2.1 mg/dl, the mean creatinine clearance

was 95.8±53.9 ml/min, the mean albumin level was 3.9±1.0 g/dl, and the mean proteinuria level was 1.2±1.6 g/day at the end of the first year in patients with primary FSGS. The mean creatinine level was 0.8±0.3 mg/dl, the mean creatinine clearance was 114.3±32.3 ml/min, the mean albumin level was 4.4±0.8 g/dl, and the mean proteinuria level was 1.5±2.8 g/day at the end of the first year in patients with MCD. The mean laboratory results at the end of the first year were not significantly different between the two groups (p>0.050).

Two patients (7.4%) with primary FSGS eventually progressed to ESRD and required hemodialysis during the follow-up period. One patient underwent a living donor renal transplant. ESRD was not observed during the follow-up period in patients with MCD.

Table 5. Response status to treatment in primary FSGS and MCD patients at periodic follow-up.

Follow-up		Remission status						p
		No		Partial		Complete		
		n	%	n	%	n	%	
3rd month	Primary FSGS	11	40.7	5	18.5	11	40.7	0,010*
	MCD	4	23.5	0	0.0	13	76.5	
	All patients	15	34.1	5	11.3	24	54.5	
6th month	Primary FSGS	11	40.7	3	11.1	13	48.1	0,020*
	MCD	2	11.7	0	0.0	15	88.2	
	All patients	13	29.5	3	6.8	28	63.6	
9th month	Primary FSGS	9	33.3	3	11.1	15	55.5	0,081*
	MCD	3	17.6	0	0.0	14	82.3	
	All patients	12	27.2	3	6.8	29	65.9	
12th month	Primary FSGS	4	14.8	4	14.8	19	70.3	0,067*
	MCD	1	5.8	0	0.0	16	94.1	
	All patients	5	11.3	4	9.1	35	79.5	

%Row percentage is used. * Fisher's exact test, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease

DISCUSSION

Of the 17 patients diagnosed with MCD, eight were male and nine were female (M: F, 1:1.1). The age at diagnosis ranged from 23 to 68 years. Although MCD is reported more common among boys during childhood, there are no significant gender differences in adults[13]. Hypertension was detected in 23.5% of patients, while 11.8% had signs of microscopic hematuria. Although hematuria and hypertension are rare in childhood, they may be present in adult-onset MCD[8]. MCD studies in adults with a similar mean age revealed a greater incidence of hypertension[8,14]. The rate of microscopic hematuria in our study group was similar to that in previous studies (10-30%)[9]. The mean proteinuria and renal function values of MCD patients at the time of diagnosis were better than those reported in previous studies[8,14-16]. The presence of hypertension at the time of diagnosis is correlated with acute kidney injury[8,9,14] as well as elevated levels of serum creatinine and urea[17]. In addition, studies have shown that the degree of proteinuria is greater in patients with acute kidney injury[8,9,14] and that proteinuria is negatively correlated with creatinine clearance[17]. Therefore, the better renal function at diagnosis in our study group may be associated with the lower mean proteinuria and frequency of HT at diagnosis. Severe and irreversible histopathological findings may also contribute to renal function deterioration.

Of the 27 patients diagnosed with primary FSGS, 18 were male and 9 were female (M: F, 2:1). The age at diagnosis ranged from 20 to 87 years. Consistent with the findings of previous studies, the current study found significant male dominance[11,18-20]. One retrospective study by Stirling et al., using patient data from five different UK centers, showed that the mean age was similar to that in our study[20]. Hypertension, microscopic hematuria, and renal failure are common in adult patients with primary FSGS and occur in 30-45% of patients at initial presentation[12]. There may also be varying degrees of proteinuria, but more than 70% of cases manifest with nephrotic-range proteinuria[12]. In our study, the mean proteinuria level was found to be in the nephrotic range, at 8.5±4.0 g/day. The rates of hypertension (37%)[12,18] and microscopic hematuria (40.7%)[12] were similar to those in previous studies. In

previous studies, 25-50% of FSGS patients had elevated serum creatinine levels at diagnosis[21]. Among our patients, 51.9% had a creatinine clearance rate less than 90 mL/min at diagnosis.

Renal biopsy of primary FSGS patients revealed 11.4% global glomerulosclerosis, 40.7% interstitial fibrosis, and 44.4% tubular atrophy. In the study by Ren et al., the rate of glomerulosclerosis and the severity of tubulointerstitial lesions, including tubular atrophy and interstitial fibrosis, were used to assess the extent of renal damage and its risk factor for loss of renal function[19]. Creatinine levels and the degree of proteinuria at diagnosis, as well as the glomerular sclerosis rate and severity of interstitial fibrosis, are known predictors of renal survival[11]. Clinical and histologic features that predict progression to ESRD include a serum creatinine concentration greater than 1.3 mg/dl and interstitial fibrosis greater than 20% at the time of diagnosis[12,22].

According to the Kidney Disease Improving Global Outcomes (KDIGO) recommendations, patients with MCD and primary FSGS can be treated with corticosteroids daily or every other day, and if there are no contraindications, corticosteroids are recommended as first-line therapy[7,23]. All patients were initially treated with corticosteroids based on the clinical protocol. To achieve complete or partial remission in primary FSGS patients, immunosuppressive treatments other than corticosteroids were more needed and these findings were significant (p=0.013). This could be attributed to the fact that podocyte injury in primary FSGS patients is more severe and often irreversible than in MCD patients, resulting in greater corticosteroid resistance and a greater need for second-line therapies. Primary FSGS patients generally exhibit more disease progression than MCD patients and treatment response rates tend to be lower[3,4].

In our study, 15 of the 17 MCD patients (88.2%) achieved complete remission at the end of the sixth month of corticosteroid treatment, while two patients (11.7%) did not achieve clinical remission (no remission). There were no patients with MCD in partial remission. The complete remission rates observed with corticosteroid therapy (80-97%) were similar to those reported in other studies[10,13,17]. Relapse rates are high among adult MCD patients. In studies, 56%-76% of patients experienced at least one relapse after corticosteroid remission[9]. Asian studies have reported lower relapse rates (31-44%)[15]. In the study by Mak et al., half of the patients (17/34) who achieved remission with corticosteroids relapsed by the end of the first year[17]. In our study, the relapse rate in MCD patients was 17.6% in the first year and 35.2% after the first year.

Among the primary FSGS patients, 14 were in the CS group and 13 were in the IS group. At the end of the first year, 19 of 27 primary FSGS patients (70.3%) achieved complete remission, four (14.8%) achieved partial remission, and four (14.8%) did not achieve clinical remission (no remission). The relapse rate in primary FSGS patients was 14.8% in the first year and 11.1% after the first year. In the study by Bagchi et al., 43.1% (50/116) of the patients achieved complete remission, 31% (36/116) achieved partial remission, and 25.9% (30/116) did not achieve remission[11]. In previous studies, response rates ranged from 32% to 47% for complete remission and 19% to 29% for partial remission. 25% to 36% of patients relapsed after complete remission and more than 50% of patients relapsed after partial remission[12]. The relapse rate in primary FSGS patients ranged from 19% to 46.4% in the study by Ren et al.[19]. Although our study group included a small number of patients, the complete remission rate was greater, and the relapse rate was lower. Patients with relatively preserved renal function and low levels of proteinuria had a better prognosis than did other patients[12,24]. Early diagnosis, treatment and management of proteinuria are essential for delaying the progression of FSGS patients to ESRD and improving their long-term prognosis[19]. Responding to corticosteroids reduces the risk of chronic kidney disease by 83%, while achieving complete remission reduces this risk by 89%[13].

The study has several limitations. It was a retrospective study, with a limited the number of patients, short follow-up period, and involving a single center. In addition, electron microscopy was not used in the diagnostic process. However, these limitations are not considered to affect the reliability of the results. Patients with secondary FSGS were excluded based on laboratory and clinical data.

In conclusion, both MCD and primary FSGS are categorized as podocytopathies and have similar clinical manifestations and treatment approaches. As with other forms of glomerulonephritis, renal biopsy is the gold standard for diagnosis. The present study revealed that the response to treatment, the presence of irreversible histopathologic features and renal survival differed between the two diseases. Primary FSGS tends to be more progressive than MCD, has a

reduced response to treatment, and requires additional immunosuppressive therapies beyond corticosteroids. The podocytopathies treatment aims to achieve regression of nephrotic syndrome and to prevent renal failure. Achieving a reduction in proteinuria with treatment is associated with a reduced risk of renal failure. Therefore, appropriate treatment and follow-up for podocytopathies, as with other glomerulonephritides, can affect the disease mortality and the clinical course. There are a limited number of studies in the literature evaluating podocytopathies collectively in adults. Therefore, larger, multicenter, prospective, controlled studies are needed to evaluate the prognosis and treatment options for podocytopathies.

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