CLINICAL CHARACTERISTICS OF BIOPSY-PROVEN RENAL SARCOIDOSIS IN JAPAN

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ABSTRACT. *Background:* Although some articles have described renal sarcoidosis, the incidence among biopsy cases remains unclear. Here, we defined the incidence of renal sarcoidosis among renal biopsy cases and analyzed the clinical course. *Methods:* We performed an epidemiological study examining renal biopsy cases treated at 5 centers between January 2000 and September 2015 and identified 16 cases (7 men, 9 women; mean (±SD) age, 59.4±18.6 years) out of a total of 14191 renal biopsy cases. Renal involvement of sarcoidosis was defined as granulomatous tubulointerstitial nephritis, tubulointerstitial nephritis without granulomatous lesions, and renal calcinosis. Fifteen of the cases were treated with steroid therapy. One case initially received steroid pulse therapy. The outcome was evaluated based on the estimated glomerular filtration rate (eGFR), CKD stage, and the change in eGFR (ΔeGFR) after treatment. A favorable response was defined as ΔeGFR ≥25%. *Results:* The incidence of renal sarcoidosis was 0.11%. The mean eGFR was 28.2±16.1 mL/min/1.73 m². At the last observation, the mean eGFR was 43.7±19.7 mL/min/1.73 m². Although a favorable response to steroid therapy was found in the majority of cases (10/15, 67%), 12 of the 15 cases (80%) had residual renal dysfunction at the last observation and 8 cases (53%) had moderate to severe renal dysfunction. *Conclusion:* Renal sarcoidosis is extremely rare among renal biopsy cases. Among cases with an unfavorable response to steroid therapy, pathogenetic mechanisms other than sarcoidosis and severe nephron damage were observed. *(Sarcoidosis Vasc Diffuse Lung Dis 2018; 35: 252-260)*

KEY WORDS: renal biopsy, renal sarcoidosis, tubulointerstitial nephritis, epidemiological study

INTRODUCTION

Sarcoidosis is a systemic inflammatory disease characterized by granulomatous lesions of unknown pathogenesis. The most commonly affected organs are the lungs and peripheral lymph nodes, followed by the eyes, liver, and muscles, etc. The incidence of renal sarcoidosis is lower than that of other organs. Post-mortem studies have reported incidences of renal sarcoidosis of 3%-19% among autopsy cases (1, 2). A diagnosis of the renal involvement of sarcoidosis is usually confirmed by a renal biopsy. In some case series of renal sarcoidosis, the initial number of renal biopsies was not described, and the incidence of renal sarcoidosis among renal biopsies remains unclear. Here, we reviewed renal biopsy cases and se-

lected individuals with renal sarcoidosis based on defined criteria to investigate the epidemiology of this disease. Most of the cases had moderate to severe renal dysfunction even after treatment. We examined the correlations between treatment outcome, clinical characteristics, and pathology, especially among refractory cases, and compared the results with those of other reports.

Reserch design and methods

Diagnosis of renal sarcoidosis

Renal biopsies performed between January 2000 and September 2015 were reviewed. The cases diagnosed as renal sarcoidosis were selected from among 5 medical departments and affiliated hospitals (Tohoku University, JCHO Sendai Hospital, Nihon Medical University, Yamagata University, and Kitamurayama Hospital). We first examined whether these cases actually fulfilled the criteria for sarcoidosis based on the 2014 WASOG Statement (3).

Renal involvement of sarcoidosis was defined according to the presence of the following criteria:
1. Granulomatous tubulointerstitial nephritis
2. Tubulointerstitial nephritis without granulomatous lesions
3. Renal calcinosis

When a renal sarcoidosis candidate did not exhibit any granulomatous lesions in a renal biopsy, we also examined whether granulomatous lesions were present in other organs; cases without granulomatous lesions in any organ were excluded. Other diagnoses resulting in exclusion from the study were as follows: infectious diseases, connective tissue diseases, malignancy, and drug allergies. These diagnoses were made based on a clinical chart review, and 16 cases were finally enrolled in the study.

Renal pathology

The renal biopsies of each department were examined by a pathologist, and all the samples were reviewed by one specialized pathologist (J.K.). The biopsy specimens were fixed in formalin-alcohol, embedded in paraffin, and sectioned. Thin-slice sections were stained with hematoxylin-eosin, periodic acid-Schiff, Masson trichrome, and periodic acid-

methenamine-silver. Immunostaining for IgG, IgA, IgM, C3, and C4 was performed using thin sections from frozen specimens or formalin-alcohol embedded specimens. The grades of tubulointerstitial fibrosis were defined according to the Banff classification (4), as follows: 0%-5% was defined as F0, 6%-25% was defined as F1 (mild), 26%-50% was defined as F2 (moderate), and >50% was defined as F3 (severe).

Clinical data at time of renal biopsy

Proteinuria was defined as a daily urinary protein level ≥300 mg/day or a urinary protein-urinary creatinine ratio ≥0.3 g/g·Cr, hematuria was defined as a red blood cell count of ≥5 per high-power field, and leukocyturia was defined as a white blood cell count of ≥5 per high-power field. The serum creatinine level was measured using an enzymatic method in each department, and the eGFR was calculated based on the serum creatinine level and patient age according to the "Revised equations for estimated GFR from serum creatinine in Japan" (5). The eGFR values were then graded according to the KDIGO 2012 Guidelines (6). We analyzed the relations between the eGFR at each time point and the grade of interstitial fibrosis. Hypercalcemia was defined as a corrected total plasma calcium level ≥10.5 mg/dL. The levels of serum angiotensin-converting enzyme and the blood cell counts were recorded. Anemia was defined as a hemoglobin level <13 g/dL for men and <11 g/dL for women.

Follow-up and Response to Therapy

We evaluated the outcomes and the responses to therapy based on the eGFR. The response to therapy was evaluated by the ΔeGFR at the final observation compared with the eGFR at the start of therapy. A favorable response was defined as ΔeGFR ≥25%. The CKD stage was also used to predict the patient outcome.

Statistics

We used SPSS Ver. 19 (IBM Corporation) and Statview Ver. 5 (SAS Institute) for the statistical analysis. Clinical data were described as the mean±standard deviation. The correlations among the variables were analyzed using the Spearman rank

correlation coefficient. The differences in measurements between the groups were analyzed using the Mann-Whitney test. The distribution of elements among the groups was analyzed using the chi-square test.

Results

Case profiles at the time of renal biopsy

Table 1 shows the case profiles, as follows: reason for biopsy, eGFR at the time of biopsy and the initiation of therapy, extrarenal lesions, and medication. The average patient age was 59.4±18.6 years (18.5-78.8 years). The mean observation period was 5.2±4.6 years. At the time of the renal biopsy, the mean eGFR was 28.2±16.1 mL/min/1.73 m² (range, 7.1-58.7 mL/min/1.73 m²). At the initiation of therapy, the mean eGFR was 28.1±15.0 mL/min/1.73 m² (range, 6.1-51.0 mL/min/1.73 m²).

Clinical and laboratory findings and chest X-ray stage at the time of renal biopsy

Table 2 shows the clinical, laboratory, chest X-ray findings and extrarenal lesions at the time of renal biopsy. One case initially received temporary hemodialysis on two occasions because of severe renal dysfunction. After steroid therapy, hemodialysis was no longer required.

Pathology

Among the main clinical findings leading to a renal biopsy, renal dysfunction was the most common finding (15 cases, 94%), and progressive renal dysfunction was the reason for the renal biopsy in 10 of these cases. In one case, persistent microhematuria and proteinuria were the main symptoms leading to the renal biopsy (Case 2).

The pathological findings were as follows: granulomatous tubulointerstitial nephritis was found in

Table 1. Case profiles

ID	Age	Sex	Reason for renal biopsy	Observation period	eGFR at renal biopsy (Creatinine)	eGFR at the initiation of therapy(Creatinine)	Extrarenal lesion	Medication
1	18.5	M	Progressive renal dysfunction and massive proteinuria	6.42	39.4(2.0)	39.4(2.0)	Lung, Eye, Heart, Lymph node	Carvedilol, Cilnidipine, Temocapril, Magnesium Oxide, Lansoprazole, Risedronate, Telmisartan
2	41.8	M	Microhematuria, proteinuria, urinary cast and chronic kidney disease	15.16	58.7(1.12)	-	Lung	Losartan, Allopurinol, Amlodipine, Diltiazem
3	69.9	F	Progressive renal dysfunction and Suspicion of RPGN or ATN	12.74	10.6(3.55)	10.7(3.52)	Lung, Eye	Nifedipine, Fluvastatin, Alfacalcidol, Calcium aspartate
4	19.2	M	Renal dysfunction	0.35	40.2(1.94)	43.9(1.79)	Lung, Eye, Heart	None
5	77.9	F	Progressive renal dysfunction Suspicion of ATN	2.56	11.5(3.19)	7.9(4.53)	Lung, Eye, Heart	Ursodeoxycholic acid, Pitavastatin
6	46.6	M	Progressive renal dysfunction	10.65	27.2(2.20)	41.3(1.50)	Lung, Heart, Skin, Muscle	None
7	65.1	F	Progressive renal dysfunction	1.04	15.8(2.51)	14.6(2.70)	Lung, Eye	Magnesium oxide, Dimethicone, Sennoside, Omeprazole
8	67.9	F	Microhematuria and proteinuria	9.76	51.0(0.85)	51.0(0.85)	Lung, Eye	Magnesium oxide
9	73.4	M	Progressive renal dysfunction	6.18	7.1(6.7)	6.1(7.7)	Lung	Nifedipine, Polystyrene Sulfonate
10	62.6	F	Progressive renal dysfunction	2.32	17.8(2.28)	27.7(1.52)	Lung, Eye, Skin, Lymph node	None
11	70.0	M	Renal dysfunction and hypercalcemia	3.86	50.1(1.13)	47.8(1.18)	Lung, Eye, Skin	Potassium citrate/sodium citrate hydrate, Allopurinol
12	60.0	F	Renal dysfunction and hypercalcemia	4.85	27.0(1.57)	30.1(1.42)	Lung	None
13	61.0	F	Progressive renal dysfunction	3.39	26.3(1.60)	26.3(1.60)	Lung, Eye	Etizolam, Sulpiride, Zolpidem tartrate, Tofisopam
14	78.8	M	Progressive renal dysfunction	0.04	9.5(5.01)	11.6(4.17)	Lung, Eye	None
15	71.8	F	Renal dysfunction and hypercalcemia	1.84	31.8(1.29)	34.1(1.21)	Lung, Eye, Heart	Candesartan cilexetil
16	65.9	F	Slowly progressive renal dysfunction	2.16	27.3(1.52)	28.7(1.45)	Lung, Eye, Skin, Lymph node Nerve	Buformine hydrochloride, Losartan, Dipyridamole

Table 2. Clinical and laboratory findings, extrarenal involvement of sarcoidosis and renal pathology at presentations. Elevated interstitial marker means urinary level of α1-MG or β2-MG was above normal limit

	Number	%			Number	%
Clinical symptoms			**Extrarenal lesion**			
Weight loss>5kg	5	31		Lung	16	100
General lassitude	3	19		Eye	12	75
Fever	2	13		Heart	5	31
Appetite loss	6	38		Skin	4	25
Laboratory Findings				Neuromusclar lesion	2	13
Hypercalcemia	5	31	**Renal pathology**			
Anemia	11	69	Granulomatous tubulointerstitial nephritis		13	81
Increased ACE	9	56				
Detected autoantibody	3	19	Tubulointerstitial nephritis without granulomatous lesion		3	19
Urinalysis						
Microhematuria	5	31				
Leukocyturia	5	31	Calcification (concomitant of granulomatous lesion)		2	13
Proteinuria	10	63				
Nephrotic level	1	6				
Elevated interstitial marker	16	100	Glomerular lesion (concomitant of granulomatous lesion)		2	13
ChestX-P stage						
Stage0	3	19	**Others**			
Stage I	6	38	Hemodialysis		1	6
Stage II	5	31	Prior known sarcoidosis before renal biopsy		10	63
Stage III	2	13				
Stage IV	0	0				

13 cases (81%), tubulointerstitial nephritis without granuloma was observed in 3 cases (19%), renal calcinosis was observed in 2 cases (13%), and glomerular lesions were observed in 2 cases (13%). Glomerular lesions were observed in two cases (Case 1 and Case 2) with concomitant tubulointerstitial nephritis. Case 1 had focal segmental glomerulonephrosclerosis. After the initiation of treatment with an antihypertensive agent and subsequent steroid therapy, the renal function improved and the proteinuria decreased. Case 2 had hypertensive nephrosclerosis.

The degree of tubulointerstitial fibrosis was as follows: 10 cases (63%) were classified as F3, and the mean eGFR was 22.1 ± 14.7 mL/min/1.73 m² at the time of biopsy. The eGFR values of the cases classified as F3 were significantly lower than those of the 6 cases classified as F1 or F2 (mean eGFR, 38.4 ± 13.7 mL/min/1.73 m²).

Treatment and Outcome

The mean daily loading dose of prednisolone (PSL) was 27.0 mg/day (0.5 mg/kg). One month after the initiation of treatment, the mean PSL dose was 19.7 mg (0.4 mg/kg). At 1 year after the initiation of treatment, the dose was 7.1 mg (0.2 mg/kg) in 11 cases, while one case (case 15) received 5 mg of PSL every other day. Among the cases with favorable responses, the mean daily loading dose of PSL was 29.5 mg/day (0.6 mg/kg) and the mean daily dose of PSL at 1 month after the initiation of treatment was 23.5 mg/day (0.5 mg/kg). Among the cases with unfavorable responses, the mean daily loading dose was 22.0 mg/day (0.4 mg/kg), and the mean daily dose of PSL at 1 month after the initiation of treatment was 12.0 mg/day (0.2 mg/kg). The period of steroid tapering was as follows: tapering was performed after 1 month in 10 cases, after less than 3 weeks in 4

cases, and after 6 weeks in 1 case. The mean duration of PSL treatment was 3.49 years.

The mean eGFR changed from 28.1±15.0 mL/min/1.73 m² at the initiation of therapy to 43.5±20.4 mL/min/1.73 m² at the final observation, and both eGFRs were significantly correlated with each other (r = 0.693, P = 0.004). Case 2 did not receive steroid therapy because nephrosclerosis was determined to be the main cause of renal injury. Case 8 received methotrexate because of PSL sparing. Oral PSL treatment was discontinued in 6 cases (Cases 6, 9, 12, 13, 15, and 16) because of the stabilization of renal function in 2 cases (Cases 6 and 9) and the lack of a response to treatment in 4 cases (Cases 12, 13, 15, and 16). The mean period until the discontinuation of treatment was 2.26 years. Recurrence was observed in one case (Case 11). Case 11 had received oral PSL, 30 mg/day, as an initial therapy. The eGFR increased from 47.8 mL/min/1.73 m² to 64.3 mL/min/1.73 m² at 1 month after the start of steroid therapy. At 1.5 years after steroid initiation, the eGFR had decreased from 54.1 to 42.3 mL/min/1.73 m² during the 3-month period during which the oral PSL dose was tapered to 1 mg/day. Then, the oral PSL dose was increased to 15 mg/day, and the eGFR recovered to 56.4 mL/min/1.73 m². Eight months later, the PSL dose was tapered. Two months after the temporary suspension, the eGFR decreased from 48.3 to 40.6 mL/min/1.73 m². PSL at 10 mg/day was restarted, and maintenance therapy at 5 mg/day of PSL was continued until the final observation period. Immunosuppressants were not administered in this case.

We evaluated the response to steroid therapy based on the ΔeGFR. A favorable response was observed in 60% of the cases that received steroid therapy (Table 3a). The distribution of cases with severe tubulointerstitial fibrosis did not differ according to the degree of the response to steroid therapy when examined using a chi-square test.

Table 3b shows the number of cases with each CKD stage at the start and end of steroid therapy. At steroid initiation, most of the cases had severe renal dysfunction (Stage 4/5 CKD). The number of cases with severe renal dysfunction decreased over time after steroid therapy.

The eGFR values at the final observation were significantly correlated with the eGFRs at steroid initiation and at 1 month and 1 year after initiation (Table 4). Among the 13 cases with observation pe-

Table 3a. Change in eGFR (ΔeGFR) at the final observation, compared with the eGFR at the start of steroid therapy among the cases that received the steroid therapy

|	Number (%)
Favorable response (ΔeGFR ≧ 25%)	10 (67)
Unfavorable response (ΔeGFR < 25%)	5 (33)
Deterioration (ΔeGFR < 0%)	1 (7)
Total Number	15 (100)

Table 3b. Chronic kidney disease (CKD) stage at steroid initiation and end of observation

CKD stage	Steroid initiation		End of observation	
	Number	%	Number	%
stage1/2	0	0	3	20
stage3a	2	13	4	27
stage3b	5	33	3	20
stage4	3	20	5	33
stage5	5	33	0	0
Total	15	100	15	100

Table 4. Correlations in eGFR between each time point and at the final observation. Data were analyzed by determining the Spearman Rank-order correlations coefficients.

			eGFR at the final observation
eGFR at each point	Initiation	r	0.693
		p value	0.004
		N	15
	1month	r	0.846
		p value	0.000
		N	15
	1year	r	0.895
		p value	0.000
		N	12

riods of over 1 year, we analyzed the time courses of eGFR after the steroid initiation. The eGFR values improved significantly after the steroid initiation, and this improvement was maintained until the final observations (Figure 1).
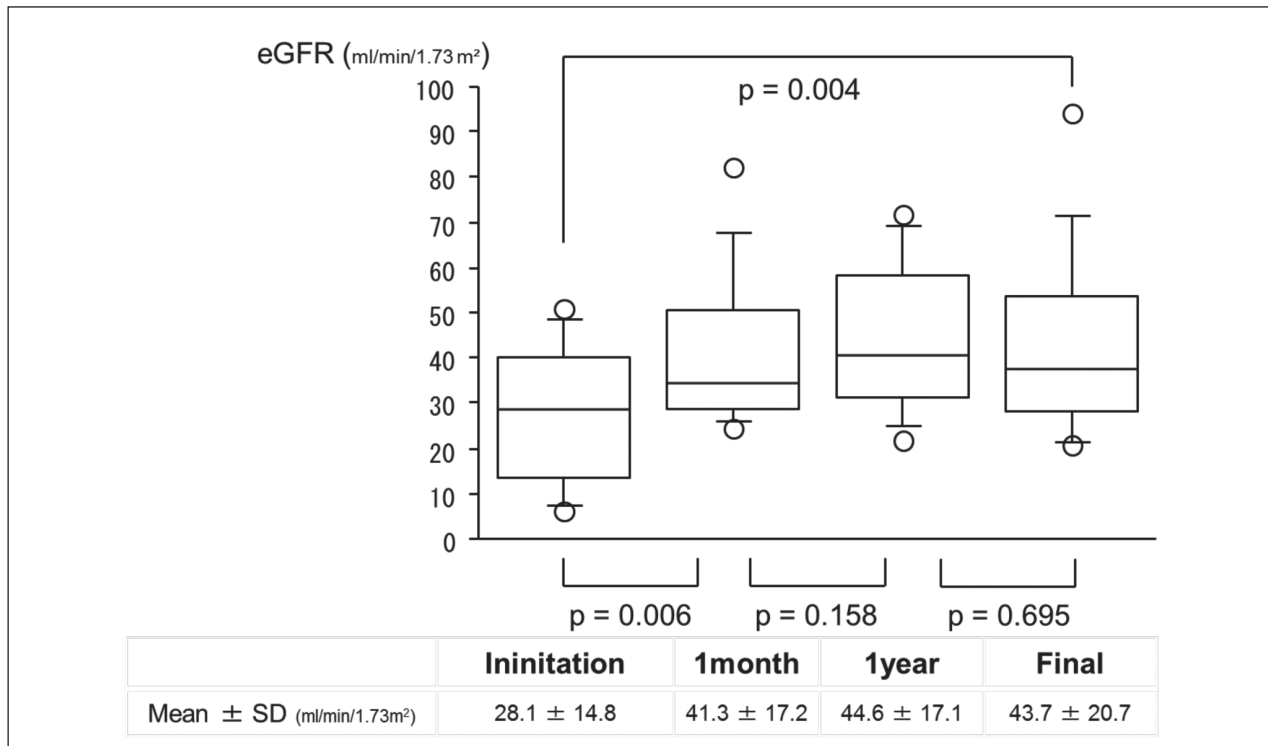
Fig. 1. Time course of estimated glomerular filtration rate (eGFR) values after steroid initiation among cases observed for over 1 year. Each value are analyzed using the Mann-Whitney test

The presence of hypercalcemia, hypertension, and diabetes mellitus did not have a significant impact on the steroid response. Furthermore, cases without renal granulomatous lesions did not respond to steroid therapy.

Discussion

Epidemiology

Most reports on renal sarcoidosis in which the diagnosis was based on a renal biopsy are case reports or case series. However, these reports did not describe the total number of renal biopsies performed during the study periods, and the incidence of renal sarcoidosis among renal biopsies has been unclear. Reports on the incidence of granulomatous tubulointerstitial nephritis may provide a clue to this issue (7, 8, 10). In these previous studies, the reported incidences of renal sarcoidosis were 0.11% (11 cases out of 9779 renal biopsy cases in the USA

between 1987-2004), 0.18% (19 cases out of 10023 renal biopsy cases in the USA between 2000-2011), and 0.64% (20 cases out of 3132 renal biopsy cases in France between 1991-2004), which are all extremely low. The incidence of renal sarcoidosis was similar in these countries even though the annual incidences of sarcoidosis varied (Table 5). However, these studies did not include tubulointerstitial nephritis without granuloma or renal calcinosis lesion with renal involvement. In contrast, the present study also included interstitial nephritis cases without granulomatous lesions and cases with renal calcinosis lesions. Although the renal biopsies included in the present study were aggregated from multiple institutions in eastern Japan, the data likely reflect the actual condition of renal sarcoidosis in Japan because the rate of tubulointerstitial nephritis among the renal biopsies in the present study was 3.3%, which was equal to data from the Japan Renal Biopsy Registry (15). The correct diagnosis of renal involvement requires a renal biopsy. However, a biopsy is not always performed because of variations in the indications for

Table 5. Comparison of present study results and those of biopsy based studies examing granulomatous tubulointerstitial nephritis

Study	Country	Number of biopsies	Number of biopsies with renal sarcoidosis	Criteria for renal sarcoidosis	Renal biopsy proven	Annual Incidence of sarcoidosis per 100,000 of the population in the relevant country
Bijol et al.(7)	USA	9779	11	Clinical and previous diagnosis as sarcoidosis or granulomatous inflammation of extrarenal biopsy	+ (by only granulomatous lesion)	Henke CE et al(9) : 6.1 Ungprasert et al(10) :10
Bagnasco (8)	USA	10023	19	Granulomatous tubulointerstitial nephritis and systemic sarcoidosis	+ (by only granulomatous lesion)	
Javaud et al(11).	France	3132	20	Previous diagnosis as sarcoidosis or renal biopsy-proven cases with other clinical and radiological localization	+ (by only granulomatous lesion)	Nunes H et al(12) : 9-10
present study	Japan	14191	16	According to 2014 WASOG Statement	+ (by Granulomatous lesion, tubulointerstitial nephritis and renal calcinosis)	Morimoto T et al(13) : 1.01 Yamaguchi M et al(14) : male 1.2 female 1.4

performing a biopsy among institutions (16). Furthermore, the preferred indications for performing renal biopsy differ among countries (17). Therefore, the actual incidence of renal involvement is difficult to determine. In any case, renal sarcoidosis seems to be relatively rare among renal biopsy cases.

Clinical course

The majority of cases with renal sarcoidosis responded to steroid therapy. However, the renal outcomes were not ideal, since 12 cases (80%) exhibited residual renal dysfunction and 8 cases (53%) had moderate to severe renal dysfunction (Stage 3b/4). Most of the cases already had severe renal damage at the time of the renal biopsy. Ten cases (67%) had severe fibrosis (F3), and the mean eGFR of these cases was 22.1±14.7 mL/min/1.73 m^2 before treatment. Furthermore, 8 cases (50%) were classified as Stage 4/5 CKD. Recovery to an eGFR above 60 mL/min/1.73 m^2 only occurred in 3 cases, similar to the results reported by Singer (18). These results suggest

that renal sarcoidosis was not detected at an early stage. In patients with renal sarcoidosis, especially tubulointerstitial nephritis, the predominant urinalysis findings are non-nephritic proteinuria or microhematuria. These findings might not be sufficient for physicians to perform a renal biopsy. Consequently, the onset of renal failure might be the predominant indication for renal biopsy, enabling treatment to only begin after the renal injury has already progressed.

The characteristics of the cases with unfavorable responses were as follows. Case 13 showed renal deterioration after treatment. This case had severe tubulointerstitial fibrosis and severe tubulointerstitial infiltration. Cases 15 and 16 had diffuse glomerular sclerosis (global sclerosis/total glomeruli: Case 15 = 85/92, Case 16 = 28/38). In Case 15, the renal pathology results showed severe tubulointerstitial fibrosis and severe inflammatory cell infiltration. In Case 16, the renal pathology results showed that renal ischemia was the main type of pathogenesis. Case 12 responded to steroid therapy at first, and the PSL dose was tapered. The eGFR had decreased slightly

at the final observation (ΔGFR, 24%). Case 11 experienced a recurrence and showed an unfavorable response at the final observation, but the patient's renal function remained within the category of mild dysfunction. Case 11 showed an improvement in renal function at 1 month after steroid initiation. Rajakariar reported that continuous low-dose steroid treatment can preserve renal function (19). The continuance of low-dose steroid treatment might enable a better outcome in this case.

Steroid therapy is effective for suppressing active inflammation, but other drugs that suppress subsequent fibrosis may be needed to further improve the renal prognosis. An anti-fibrotic agent that has been used for the treatment of interstitial pneumonia is one possible candidate for such treatment (20).

A differential diagnosis of granulomatous nephritis should include drug interactions, infectious diseases, connective tissue diseases, and malignancy (21). In the present study, all the registered cases had lung involvement and/or other organ involvement, and these systemic findings could not be explained by drug effects alone. A culture test, the biopsy specimens, and the course after treatment did not provide any evidence of bacterial infection in any of the cases. In 3 cases, autoantibodies (Case 3, anti-GBM antibody; Case 7, anti SS-A and SS-B antibodies; and Case16, anti-nuclear antibody) were detected, but symptoms typical of autoimmune diseases were not found. Case 9 had previously undergone a total gastrectomy for the treatment of gastric cancer, and a whole-body CT did not show the recurrence of gastric cancer.

In the present study, the renal granulomas were located in the tubulointerstitum, and not the glomerulus. Some cases with glomerular nephritis concomitant with sarcoidosis have been reported (22), but granulomatous lesions of the glomerulus have never been reported.

Comparison with other studies

In the present study, over 60% of the cases showed a favorable response, similar to the results reported by Löffler (23). The mean eGFRs before and after treatment in each study were as follows: Rajakariar (19), 26.8±14 and 47.9±6.8 mL/min/1.73 m²; Mahévas (24): 20±19 and 49.13±25 mL/min/1.73 m²; Löffler: 38±21 and 57±26 mL/min/1.73 m²; pre-sent study: 28.1±15.0 and 43.3±20.6 mL/min/1.73 m². In Rajariar's and Mahévas's reports, the renal functions of most of the cases were severely impaired at the time of presentation. In Rajariar's case series, the indication for biopsy was progressive renal impairment. In Mahévas's and Löffler's reports, the indications for biopsy were unclear. Therefore, we could not adequately explain what caused these variations in renal function at the time of presentation and at the final observation. A considerable number of cases seemed to have severe renal dysfunction at the time of the renal biopsy, similar to the present study. Among the above-mentioned reports (19, 23, 24), one case required maintenance dialysis.

Conclusion

Although previously unclear, the incidence of renal sarcoidosis among the renal biopsy cases in the present series was extremely low. Among cases with an unfavorable response to steroid therapy, the existence of another form of pathogenesis other than sarcoidosis and the presence of tubulointerstitial nephritis without granulomatous lesions were observed. The initial number of renal biopsies was thought to be large enough to define the incidence of renal sarcoidosis based on renal biopsy cases, and the present study is also the first epidemiological study to focus on renal biopsy cases of renal sarcoidosis in Asia.

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