Characteristics of Minimal Change Nephrotic Syndrome in the Elderly Patients

Motoaki Miyazono[1*], Tomoya Kishi[1], Tsuyoshi Takashima[2], Makoto Fukuda[1], Keiichiro Matsumoto[2], Masatora Yamasaki[1], Mai Sanematsu[1], Yasunori Nonaka[1], Yuki Awanami[1], and Yuji Ikeda[1]

[1]Department of Nephrology, Saga University Faculty of Medicine, 5-1-1 Nabeshima, Saga-shi, Saga, 849-8501, Japan

2Department of Nephrology, Ureshino Medical center, 2436 Ureshino Machi shimogyo kihei, Ureshino-shi, Saga, 843-0393, Japan

*Corresponding author: Motoaki Miyazono, MD, PhD, Department of Nephrology, Saga University Faculty of Medicine, 5-1-1 Nabeshima, Saga-shi, Saga, 849-8501, Japan, Tel: +81-952-34-2370; Fax: +81-952-34-2017; E-mail: miyazono@cc.saga-u.ac.jp

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Abstract

Background and Aim of Study

We examined the differences in clinical characteristics of minimal change nephrotic syndrome (MCNS) in elderly and young patients.

Patients and Methods

Patients with MCNS diagnosed by renal biopsy were divided into the elderly (65 years or older) and young (18–64 years old) groups and were evaluated for the results of basic statistical analysis, clinical items, and treatment.

Results

A total of 18 patients were evaluated: 8 in the elderly group and 10 in the young group, with a mean age of 70.4 ± 5.1 and 35.2 ± 15.5 years, respectively. The follow-up periods were 88.5 ± 50.0 months in the elderly group and 59.9 ± 37.3 months in the young group. The urine protein-to-creatinine ratios at baseline in the elderly and young groups were comparable at 7.9 ± 2.9 and 8.8 ± 3.7 g/g Cre, respectively, whereas the selectivity index was favorable in both groups at 0.131 ± 0.05 and 0.143 ± 0.05, respectively. All patients in the young group started treatment with prednisolone (PSL) and achieved complete remission (CR). In the elderly group, 7 patients received treatment with PSL in combination with cyclosporine or cyclophosphamide (CPA), whereas only 1 patient started treatment with PSL alone. Only 1 patient who received the combination of PSL and CPA had incomplete remission type I; excluding this one patient, the time to remission in patients with CR was 153 ± 178.6 days in the elderly group and 35 ± 59.8 days in the young group, showing a longer trend in the elderly. Recurrences occurred in 4 of 7 elderly patients and 8 of 10 young patients, and the numbers of recurrences were 1.3 ± 1.6 and 3.0 ± 2.4, respectively, showing a higher trend in young patients for both the frequency and number of recurrences. In renal function, however, no deterioration in creatinine level was observed in either group during the follow-up period. Concerning complications during the treatment period, 2 elderly patients had Pneumocystis pneumonia.

Conclusion

Whereas there was no difference in the remission induction rate between elderly and young patients, the time to remission induction was longer in the elderly. Accordingly, as the risk of complications such as infection may be high in elderly patients, it considered necessary to continuously evaluate the treatment up to remission induction in the future.

Keywords: Minimal change nephrotic syndrome; Elderly

Abbreviations: MCNS: Minimal Change Nephrotic Syndrome; PSL: Prednisolone ; CR: Complete Remission; CyA: Cyclosporine; CPA: Cyclophosphamide

Introduction

According to the renal biopsy registry reported in 2012, primary nephrotic syndrome accounts for 61.9% of nephrotic syndrome cases in patients 65 years or older in Japan. In the pathological diagnosis, membranous nephropathy has the highest incidence at 31.5%, followed by minimal change nephrotic syndrome (MCNS) at 12.6% [1]. Nair et al. [2] reported that when histological diagnosis was conducted in nephropathy patients by renal biopsy, the percentage of membranous nephropathy was less in patients 80 years or older than in younger adult patients, and the percentage of MCNS is large.

MCNS is a steroid-responsive disease that shows the following characteristics: a frequent recurrence type with repeating recurrence and remission; a type showing steroid dependency or steroid resistance; a type resulting in complications such as acute renal failure or thromboembolism; and the risk of infection, osteoporosis, diabetes, or hypertension due to adverse reactions to steroid. However, few reports have examined whether the frequencies of occurrences of such characteristics are different between elderly patients and young patients, and the grouping of elderly patients varies across reports. Therefore, we studied the clinical characteristics of MCNS in the elderly (65 years or older, the World Health Organization's definition of "elderly").

Patients and Methods

The study was approved by the Ethics Committee of the Saga University Hospital (Permit Number: 2013-06-06) and conducted in compliance with our institutional guidelines. We examined the clinical records of patients who were followed in the Department of Nephrology at Saga University Hospital between 2000 and 2011, and analyzed those who had been given a diagnosis of MCNS in the pathological assessment. We excluded patients who had nephrotic syndrome resulting from a secondary cause or had other concomitant diseases in the pathological examination of the kidney, those who were younger than 18 years at the time of MCNS diagnosis, or who were followed for <12 months. We evaluated urine protein, urinary occult blood, serum total protein, serum albumin, serum creatinine, total cholesterol, and selectivity index as basic data for statistical analysis.

According to age at diagnosis, patients were divided into 2 groups: the elderly group (≥65 years) and the young group (18-64 years). The elderly and young groups were compared for clinical items, including the timing of onset and remission, recurrence or non-recurrence and the number of recurrences, timing of initial recurrence, presence or absence of frequent recurrences, use or nonuse of steroids, use or nonuse of secondary drugs, presence of complications, and increase in serum creatinine.

Renal Biopsy

The histological criteria for diagnosing MCNS included: presence of foot process effacement of podocytes on electron microscopy and absence of electron dense deposits, basement membrane thickening, segmental sclerosis and immunofluorescence.

Patients showing steroid resistance who had concurrent renal disease in the subsequent renal biopsy were excluded.

Treatment

All patients in the young group started treatment with PSL (0.8 mg/kg/day); in the elderly group, PSL alone (0.8 mg/kg/day) was administered to 1 patient, PSL (20mg) in combination with cyclosporine (CyA:150mg) in 1 patient, CyA (150mg) alone in 2 patients, cyclophosphamide (CPA: 450mg-500mg) in 3 patients, and PSL (20mg) in combination with CPA (50mg) in 1 patient. Prednisolone (PSL) dose was reduced according to the clinical course, and tapered when complete remission (CR) was achieved within at least 3 months. Concerning adverse reactions resulting from high-dose and long-term PSL administration, use of secondary drugs was considered in patients for the elderly group.

Definitions

The results of urinary occult blood and urinary qualitative tests of negative, ±, 1+ 2+, 3+, and 4+ were scored as 0, 0.5, 1, 2, 3, and 4, respectively.

CR was defined as urine protein <0.3 g/day, or "±" to"-" in the qualitative test.

Recurrence was defined as urine protein >3 g/day, or "3+" to "4+" in the qualitative test.

Frequent recurrence was defined as 2 or more recurrences within 6 months or 4 or more recurrences within a year.

Early recurrence was defined as recurrence within 6 months after CR.

Steroid dependence was defined as recurrence at the time of steroid tapering or within 4 weeks after steroid discontinuation, requiring long-term steroid use.

Statistical Analysis

Along with SPSS Statistics 19 software, the Mann-Whitney test and Fisher's exact probability test were used depending on data. Continuous variables were presented as mean ± SD or median values. Statistically significant difference was set at P <0.05.

Results

The subjects consisted of 8 patients (3 men, 5 women) in the elderly group and 10 patients (3 men, 7 women) in the young group. The mean age was 70.4 ± 5.1 years in the elderly group and 35.2 ± 15.5 years in the young group. The follow-up period was 88.5 ± 50.0 months in the elderly group and 59.9 ± 37.3 months in the young group (Table 1).

Urinary occult blood by the test strip method was 2.06 ± 1.08 in the elderly group and 1.15 ± 1.23 in the young group, showing a higher positive rate in the elderly. Pretreatment urine protein by the urinary protein-to-creatinine ratio was comparable, at 7.9 ± 2.9 g/gCre in the elderly group and 8.8 ± 3.7 g/gCre in the young group. The selectivity index was favorable in both groups, at 0.131 ± 0.05 in the elderly group and 0.143 ± 0.05 in the young group (Table 1).

Table. 1 Base line demographic charactaristics of patients with MCNS

	elderly group (n=8)	young group (n=10)	P-value
Duration of follow-up (month)	88.5±50.0	59.9±37.3	0.168
age	70.4±5.1	35.2±15.5	<0.01*
Male:female ratio	3:5	3:7	1.000
Urine occult blood	2.06±1.08	1.15±1.23	0.075
Urine protein (g/day)	5.4±2.3	8.8±6.7	0.131
Urine protein:urine creatinine ratio (g/gCre)	7.9±2.9	8.8±3.7	0.722
Selectivity index	0.131±0.05	0.143±0.05	0.531
Serum total protein (g/dl)	4.50±1.07	4.26±0.53	0.929
Serum albumin (g/dl)	1.91±0.40	1.66±0.50	0.418
Serum cholesterol (mg/dl)	417±128	440±92	0.859
Pre-serum creatinine (mg/dl)	1.08±0.53	0.89±0.40	0.373

The data are expressed as either the number of patients or the means ± SD.

All patients in the young group achieved CR, whereas only 1 patient to whom PSL in combination with CPA was administered had incomplete remission in the elderly group. Excluding this one patient, the time to remission was 153 ± 178.6 days in the elderly group and 35 ± 59.8 days in the young group, showing a shorter trend in the young group (Table 2).

In patients who achieved CR, recurrence was observed in 4 of 7 elderly patients and 8 of 10 young patients, whereas the number of recurrences among these patients was 1.3 ± 1.6 in the elderly group and 3.0 ± 2.4 in the young group, showing that both frequency and the number of recurrences were higher in the young group. Whereas early recurrence occurred in 1 patient in the elderly group, it occurred in 4 patients in the young group; in addition, frequent recurrences were observed in 4 patients, but in none of the patients in the elderly group, showing that early recurrences as well as frequent recurrences were more common in young patients. The time to initial recurrence in patients with recurrence was shorter in the young group: 20.6 ± 19.2 months in the elderly group and 16.5 ± 15.6 months in the young group (Table 2).

Table .2 The end of follow-up demographic data of patients with MCNS

	elderly group	young group	P-value
Number of complete remisson	7(87.5%)	10(100%)	0.444
Duration until complete remission (month)	153±178.6	35±59.8	0.057
Duration of first relapse (month)	20.6±19.2	16.5±15.6	0.259
Number of relapsed patients	4(57.1%)	8(80%)	0.593
The recurrent number of times	1.3±1.6	3.0±2.4	0.149
Number of early Relapsed patients	1(14.2%)	4(40%)	0.338
Number of frequet relapsed patients	0(0%)	4(40%)	0.092
Presence of acure renal failure during treatment of immunosuppressive agent	2(25%)	3(30%)	1.000
Presence of pneumocystis pneumonia during treatment of immunosuppressive agent	2(25%)	0(0%)	0.183
Post-serum creatinine (mg/dl)	1.04±0.41	0.70±0.12	0.041*

The data are expressed as either the number of patients or the means ± SD.

The creatinine levels at the start of steroid treatment and at the end of the follow-up period were higher in the elderly group: 1.08 ± 0.5 and 1.04 ± 0.4, respectively, in the elderly group and 0.89 ± 0.4 and 0.7 ± 0.12, respectively, in the young group. However, no exacerbation of kidney function was observed during the follow-up period in either group (Table 1,2).

Complications during the treatment period included acute renal failure in 2 elderly patients and 3young patients, and Pneumocystis pneumonia in 2 elderly patients.

Discussion

The results of this study showed a high incidence of urinary occult blood by the test strip method in the elderly group. Although we were unable to perform a urinary sediment test, in cases of elderly patients with nephrosis, it was considered necessary to keep in mind that urinary occult blood could also be observed in patients with MCNS.

Urine protein and the selectivity index were comparable between the elderly and young groups, showing no difference.

Concerning adverse reactions resulting from high-dose and long-term PSL administration, there is a risk of concomitant Pneumocystis pneumonia induced by other immunosuppressants [3,4]; however, PSL is reported to be particularly associated with concurrent Pneumocystis pneumonia [5,6]. In addition, as advanced age itself could be a risk for Pneumocystis pneumonia [7], many patients in the elderly group concomitantly used immunosuppressants or cytotoxic agents from the initial treatment. Although a simple comparison is difficult, the rate of remission of nephrotic conditions was high in both the elderly and the young group; all patients excluding 1 patient in the elderly group achieved CR. However, the time to remission was long in the elderly group, which might have adversely led to the long-term use of the therapeutic drug, affecting the frequency of Pneumocystis pneumonia. A previous report stated that Asian people may be more responsive to steroid treatment [8]; therefore, it is considered necessary to use a high-dose steroid as the first-line therapy in the elderly, similarly to young patients, while paying attention to adverse reactions.

Concerning recurrences, some reports state that recurrence is strongly correlated with age and young patients are more prone to recurrence, whereas other reports state that patients 40 years or older are more prone to have recurrence [9]; yet, other reports claim that there is no correlation between recurrence and age [10]. In this study, the recurrence rate was higher, the time to the initial recurrence was shorter, and the frequency of recurrences was higher in young patients.

Concerning complications, concurrent acute renal failure was observed in both young and elderly patients; however, no change was observed in the creatinine levels at the start of steroid treatment and at the end of the follow-up period, suggesting some effect on kidney prognosis, albeit only a temporary effect on renal function.

Conclusion

As few reports have examined whether there is any difference in MCNS between elderly and young patients, we examined Japanese elderly patients with nephrotic syndrome in this study. Although there was no difference in the remission induction rate between the elderly and young patients, the time to remission induction was longer in elderly patients, which resulted in a high risk of complications such as infection in these patients. Therefore, we believe it is necessary to continuously evaluate the treatment up to remission induction in the future. In addition, as this study was conducted in the limited number of patients, a study of a larger sample size will be required for a more detailed comparison between elderly and young patients.

Conflict of Interests

The authors have no conflict of interests.

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