Mortality and Morbidity in Peripheral Neuropathy Associated Churg-Strauss Syndrome and Microscopic Polyangiitis

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ABSTRACT. ***Objective.*** Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA) are commonly characterized by systemic necrotizing vasculitis and frequent occurrence of axonal neuropathy. We investigated whether the neuropathy in these 2 diseases reveals differences in clinicopathologic features and predicts survival and functional outcome.

Methods. We compared 30 patients with CSS associated neuropathy with 26 patients with MPA associated neuropathy in terms of clinical, laboratory, electrophysiologic, and outcome data.

Results. MPA cases showed a significantly higher age at onset, a higher male/female ratio, and more extensive systemic organ involvement than CSS. Inflammatory markers including antimyeloperoxidase antibody titers were also significantly higher in MPA. Both CSS and MPA showed similar neuropathic symptoms, electrophysiologic findings, and sural nerve biopsy findings representing acute axonal changes. Functional disability assessed by modified Rankin score, muscle strength, and nerve conduction variables were similar in CSS and MPA, both in the acute peak phase and during longterm followup. However, survival was significantly worse in MPA than CSS.

Conclusion. Neuropathy associated CSS and MPA shared common neuropathic features throughout the course, but systemic organ involvement, inflammatory marker concentrations, and relapse rates were significantly higher in MPA, which showed a poorer survival rate. (J Rheumatol 2002;29:1408–14)

Key Indexing Terms:
CHURG-STRAUSS SYNDROME
MICROSCOPIC POLYANGIITIS
NEUROPATHY
PROGNOSIS

Microscopic polyangiitis (MPA) is a systemic necrotizing vasculitis involving small-size arteries[1,2], while classic polyarteritis nodosa (PAN) shows medium-size arteritis[3-7]. Churg-Strauss syndrome (CSS) is characterized by eosinophilia, bronchial asthma, and granuloma formation; however, this disease also has features of systemic necrotizing vasculitis[8-11]. MPA and CSS present with similar arteritis features affecting vessels of similar diameter (about 80 to 320 μm). Arteritis features also include transmural arterial necrosis, including hyaline change and infiltration by a mixture of lymphocytes and polymorphonuclear leukocytes[12-14]. Moreover MPA and CSS both frequently are associated with peripheral ischemic neuropathy that presents as mononeuritis multiplex[12,15-20]. Acute axonal dysfunction resulting from axonal lesions in both myelinated and unmyelinated nerve fibers caused by necrotizing arteritis is a common feature of these neuropathies[21,22].

Some authors have reported that prognosis in CSS is better than in "PAN"[23], which may include PAN and MPA, while other investigators have concluded that "PAN" and CSS show a similar survival rate[24,25]. These divergent results may reflect study of extremely heterogeneous groups of patients with a wide variety of systemic involvement as well as neuropathic features. Inclusion criteria for "PAN" (including both MPA and PAN) could have been divergent among the reports. Further, numbers of patients with CSS that were studied have been considerably smaller than numbers of patients with "PAN"[23-25]. MPA has been clearly distinguished from PAN[7,26,27] based on the spectrum of the diseased vessel size and the titer of antimyeloperoxidase antibody (MPO-ANCA). The clinical and pathologic features, therapeutic response, functional prognosis, and survival rate in neuropathy between CSS and MPA thus remain unclear. We sought to resolve these questions by studying adequate numbers of patients with neuropathy associated with CSS and MPA.

MATERIALS AND METHODS

Patients. We assessed 30 patients with CSS including neuropathy and 26 patients with MPA associated with neuropathy who had been referred to the hospital at Nagoya University School of Medicine and affiliated hospitals

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between 1989 and 1998. Diagnoses all were made using criteria for MPA and CSS adopted by the Chapel Hill Consensus Conference[27] in 1994. Neuropathic symptoms preceded visceral involvement in all patients with CSS and MPA, except for bronchial asthma and eosinophilia in CSS. Other patients whose visceral involvement preceded peripheral neuropathy were not included.

Clinical assessment. Patients without a nerve biopsy were excluded from the study, even if they showed features of peripheral neuropathy. Muscle strength was evaluated using the UK Medical Research Council scale. For quantitative assessment, the biceps and thenar muscles were included for the upper limbs, and the iliopsoas and tibialis anterior were included for the lower limbs. Functional state was estimated according to modified Rankin score[28]: 0, no symptoms; 1, nondisabling symptoms not interfering with lifestyle; 2, mildly disabling symptoms leading to some restriction of activity but not interfering with patients' capacity to look after themselves; 3, moderately disabling symptoms significantly interfering with lifestyle or with a totally independent existence; 4, moderately to severely disabling symptoms clearly precluding independent existence, but not requiring constant nursing attention; 5, severely disabling symptoms requiring around-the-clock nursing care; and 6, death. All patients underwent laboratory examinations including routine hematologic and serum biochemical tests, serologic studies, urinalysis, and cerebrospinal fluid (CSF) examination. We also assessed systemic visceral involvement, using radiographs, computed tomography (CT), magnetic resonance imaging (MRI), endoscopy, and other examinations as needed.

Since both CSS and MPA are systemic vasculitides, we used a systemic necrotizing vasculitis damage index (SNVDI) to evaluate systemic involvement including visceral organs, the musculoskeletal system, the nervous system, and the skin, according to Abu-Shakra, *et al*[23]. The SNVDI includes 12 scoring items: ocular involvement, 0 to 4; pulmonary, 0 to 3; cardiovascular, 0 to 5; peripheral vascular, 0 to 5; gastrointestinal (GI), 0 to 5; gonadal, 0 to 2; renal, 0 to 2; cutaneous, 0 to 1; nervous, 0 to 11; and musculoskeletal, 0 to 2. Malignant neoplasms (0 to 2) and diabetes mellitus (0 to 1) were also rated. The worst possible total score was 43 points.

Electrophysiologic and pathologic variables. Motor and sensory nerve conduction studies were performed for the median, ulnar, tibial, and sural nerves by standard methods[29]. Sural nerve biopsy was performed in all patients between 2 days and 5 weeks after onset according to described methods[11,30]. Most of the nerve biopsies were performed before the treatment started. A portion of the nerve specimen was fixed in either 2% glutaraldehyde in 0.025 M cacodylate buffer at pH 7.4 or 10% buffered formalin solution and processed for Epon-embedded sections or paraffin-embedded sections, respectively. Myelinated and unmyelinated fiber densities in sural nerve specimens were determined on Epon-embedded transverse sections by light and electron microscopy as described[11,30]. Frequency of axonal and demyelinating pathology was assessed in teased-fiber preparations as described[11,30]. Populations of infiltrating lymphocyte subclasses and macrophages were characterized by immunohistochemical staining of a portion of the sural nerve biopsy specimen quickly frozen in liquid nitrogen, using monoclonal antibodies against CD45RO, CD68, CD4, and CD8 (all from Dako, Glostrup, Denmark)[11]. Subpopulations among invading cells were assessed as the number of cells positive for each marker divided by the total number of invading cells in the vasculitic lesion. Diameters of arteries involved by vasculitis were measured using the residual internal elastic membrane seen in Gomori trichrome-stained sections as a landmark.

Treatment. All patients were treated with oral prednisone (initially 1 mg/kg). Doses of corticosteroids were tapered individually according to clinical symptoms and inflammatory markers. In 8 patients with CSS and 14 with MPA, methylprednisolone was administered intravenously at a dose of 1000 mg/day for 3 consecutive days before oral prednisone treatment was initiated. Cyclophosphamide was given to 2 patients with CSS and 6 with MPA. No significant difference was noted between the 2 groups as to duration of treatment with prednisone at the initial high dose (1 mg/kg). Patients eventually required cyclophosphamide treatment more frequently in the MPA group. Functional state at followup was assessed by neurological examination and by the estimated functional score (modified Rankin score) for each patient. Survival time was calculated from the date when neuropathic symptoms first occurred. Relapse was defined as an acute increase of body temperature, inflammatory markers, occurrence of neuropathic symptoms, or an increase in modified Rankin score of at least 1.

Statistical analysis. Statistical assessment was performed by the Mann-Whitney U test, Spearman's regression analysis, and chi-square analysis. Differences where the probability of a chance result (p) was < 0.05 were considered significant. Survival curves were analyzed using the Kaplan-Meier method with the log-rank test.

RESULTS

Clinical features are summarized in Table 1. Patients with CSS associated neuropathy included 23 women and 7 men with mean age at onset of 52 years (range 22 to 78). Patients with MPA associated neuropathy consisted of 19 men and 7 women (mean age at onset 67 years, range 44 to 79). Age at onset of MPA was significantly higher than that of CSS ($p < 0.0001$), and MPA showed a strong male preponderance, contrasting with a female preponderance in CSS ($p < 0.0001$). Weight loss and elevation of body temperature showed no significant difference between the 2 diseases. Initial symptoms of neuropathy were paresthesia, pain, and edema in the area initially involved, which were common to both diseases. Mononeuritis multiplex showing sensory involvement in all modalities and occurring most often in a lower limb was a common presenting pattern in both CSS and MPA (Table 1). Duration of followup was 6.3 ± 2.9 years for CSS and 4.5 ± 3.0 years for MPA, ranging from 2 to 12 years in both diseases. Over the followup period, almost all patients progressed to polyneuropathy with varying degrees of asymmetry in both CSS and MPA; in this respect the neuropathic features were not distinguishable by disease. Organ system involvement as indicated by the SNVDI was 4.1 ± 1.2 in CSS and significantly higher, 5.2 ± 1.4, in MPA ($p < 0.01$) especially in renal involvement presenting glomerulonephritis; however, pulmonary and GI involvement in CSS tended to be higher than corresponding scores in MPA. Otherwise, no significant differences in organ involvement distribution were noted between the 2 diseases.

Laboratory data are shown in Table 1. Leukocytosis was seen in both CSS and MPA, but was significantly greater in CSS ($p < 0.0001$), particularly with respect to eosinophilia ($p < 0.0001$). Serum lactate dehydrogenase (LDH) activity was elevated in both diseases, and was significantly greater in CSS than MPA ($p < 0.0001$). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) concentrations were significantly higher in MPA than in CSS (ESR, $p < 0.05$; CRP, $p < 0.05$). The platelet count and serum immunoglobulin G concentrations were similarly elevated in both diseases. Anti-MPO-ANCA exceeded 20 U/ml in 93% with MPA, but in only 27% with CSS ($p < 0.05$). The

Table 1. Clinical features and inflammatory markers in patients with neuropathy from Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA) at the initial peak phase of symptoms.

Features	CSS, n = 30	MPA, n = 26	p, CSS vs MPA
General			
Age, years, mean ± SD (range)	52.4 ± 12.8 (22–78)	67.4 ± 8.2 (44–79)	< 0.0001
Sex, M/F	7/23	19/7	< 0.0001
Weight loss, kg	9.5 ± 0.7	8.1 ± 4.2	NS
Temperature, ˚C	37.9 ± 0.8	38.0 ± 0.4	NS
Neuropathic			
Onset to peak involvement, days	23.4 ± 10.5	24.5 ± 11.9	NS
Initial symptoms*, %			
Paresthesia/pain	75	100	
Edema	43	42	
Distribution, %			
Mononeuritis multiplex	71	69	
Symmetric polyneuropathy	0	12	
Asymmetric polyneuropathy	29	19	
SNVDI score	4.1 ± 1.2	5.2 ± 1.4	< 0.01
Involvement of each organ**, %			
Lung	63	54	
Heart	10	23	
Gastrointestinal	37	27	
Renal (glomerulonephritis)	7	42	
Skin	23	35	
Inflammatory markers			
White blood cells, $mm^3 \times 10^3$	23.7 ± 14.7	11.0 ± 3.3	< 0.0001
Eosinophils, $mm^3 \times 10^3$	14.4 ± 13.8	0.4 ± 0.5	< 0.0001
Platelets, $mm^3 \times 10^3$	349 ± 160	337 ± 158	NS
Lactate dehydrogenase, IU/l	597 ± 273	264 ± 107	< 0.0001
ESR, mm/h	58.9 ± 39.8	88.7 ± 31.5	< 0.05
CRP, mg/dl	6.5 ± 6.3	10.9 ± 6.5	< 0.05
Immunoglobulin, mg/dl	1859 ± 624	1970 ± 650	NS
MPO-ANCA, IU/dl	39.9 ± 82.9	218.5 ± 189.8	< 0.01
Positive rate of MPO-ANCA, %	27	93	< 0.05

SNVDI: systemic necrotizing vasculitic index; MPO-ANCA, myeloperoxidase antineutrophil cytoplasmic antibody, NS: not significant. Normal range for white blood cell count 5 to 8 × 10^3, eosinophils, 100 to 700; platelet, 18 to 35 × 10^3; lactate dehydrogenase, 120 to 450 IU/l; ESR, < 10; CRP, < 0.6; immunoglobulin G, 800 to 1800; and MPO-ANCA, < 10. Units are as above. * Initial symptoms were assessed within 2 weeks** Involvement of each organ represents percentage of cases.

mean anti-MPO-ANCA concentration was significantly higher in MPA than in CSS ($p < 0.01$). Cell count and protein in CSF revealed normal findings in both groups.

Pathologic findings are shown in Table 2. In both CSS and MPA associated neuropathy, axonal degeneration was prominent. Myelinated fiber density was reduced to one-fourth to one-ninth of normal, with a slightly more severe reduction in MPA than in CSS ($p < 0.05$). Unmyelinated fiber density was severely and similarly reduced in CSS and MPA. Overall, reductions in myelinated and unmyelinated fiber density were proportional in both CSS and MPA. In teased-fiber preparations, axonal degeneration was similarly frequent in CSS and MPA. Necrotizing vasculitis was seen in 53% of CSS cases and 81% of MPA cases. Size of the involved arteries in sural nerve specimens ranged between 80 and 320 μm, and was indistinguishable between CSS and MPA. Intrafascicular edema was seen in all cases in both diseases. CD4 and CD8 positive T lymphocytes predominated in infiltrates in all layers of vessel walls and were distributed circumferentially. Frequencies of lymphocyte subpopulations and macrophages stained in sural nerve vasculitic lesion did not differ significantly between CSS and MPA. Infiltrating cells consisted mainly of T lymphocytes in both diseases. Eosinophil invasion was in higher frequency in CSS than MPA.

In nerve conduction studies (Table 3), findings of acute axonopathy were characteristic. Compound muscle action potentials (CMAP) and sensory nerve action potential (SNAP) frequently were not elicited, predominantly in the tibial and sural nerves; this feature was common in both CSS and MPA. In nerves where motor and sensory nerve conduction velocities (MCV and SCV) were measurable, no significant reduction of conduction velocity was evident in either CSS or MPA. However, the amplitude of CMAP and SNAP was significantly reduced, while no significant difference was observed between CSS and MPA. Amplitude reduction was more prominent in the tibial and sural nerves than the median nerve in both CSS and MPA. Neither

Table 2. Pathologic findings in sural nerve specimens in Churg-Strauss syndrome (CSS) and microscope polyangiitis (MPA).

Features	CSS, n = 30	MPA, n = 26	p, CSS vs MPA
Myelinated fiber density, No./mm^2	1430 ± 1330	889 ± 945	< 0.05
Unmyelinated fiber density, No./mm^2	6190 ± 5410	5240 ± 5520	NS
Myelinated:unmyelinated fiber density ratio	0.33± 0.34	0.18 ± 0.25	NS
(correlation coefficient)	(r = 0.696)	(r = 0.816)	NS
Teased-fiber preparation			
Axonal degeneration, %	80.1 ± 25.2	78.7 ± 31.4	NS
Segmental demyelination and remyelination, %	2.5 ± 3.1	2.5 ± 3.8	NS
Size of artery involved, mean diameter, μ m*	158 ± 58.2	205 ± 75.9	NS
Intrafascicular edema, % of fascicles	11.7 ± 6.1	10.0 ± 5.7	NS
Necrotizing vasculitis, % of cases	53	81	
Inflammatory cell markers, % positive **			
CD45RO	62	79	
CD68	56	42	
CD4	50	43	
CD8	50	57	
Eosinophil invasion	25	9	

* Size of artery was estimated using the residual elastica seen with Gomori trichrome staining as a landmark. ** For inflammatory cell markers, "% positive" represents the ratio of stained cells counted to total number of invading cells counted in the vasculitic lesion. NS: not significant; values are mean ± SD.

Table 3. Nerve conduction findings in initial and followup Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA).

Features	CSS	MPA	p, CSS vs MPA
The initial study	n = 30	n = 26	
Median nerve			
MCV (m/s)/CMAP (mV)	54.2 ± 4.8/4.7 ± 3.4	52.1 ± 7.6/5.0 ± 4.7	NS/NS
NE, %	10	4	
SCV (m/s)/SNAP (V)	47.8 ± 9.8/10.3 ± 16.0	51.2 ± 6.8/17.5 ± 20.1	NS/NS
NE, %	18	21	
Tibial nerve			
MCV (m/s)/CMAP (mV)	42.6 ± 6.3/2.1 ± 3.4	41.0 ± 6.1/3.3 ± 3.6	NS/NS
NE, %	45	26	
Sural nerve			
SCV (m/s)/SNAP (μV)	55.4 ± 14.5/1.8 ± 4.9	46.4 ± 7.9/4.6 ± 3.3	NS/NS
NE, %	74	67	
Followup study (2–9 years)	n = 11	n = 9	
Median nerve			
MCV (m/s)/CMAP (mV)	52.8 ± 6.9/6.8 ± 3.7	55.8 ± 7.6/5.8 ± 4.8	NS/NS
NE, %	0	0	
SCV (m/s)/SNAP (μV)	51.9 ± 8.3/2.5 ± 2.0	54.9 ± 4.6/7.5 ± 3.5	NS/NS
NE, %	0	10	
Tibial nerve			
MCV (m/s)/CMAP (mV)	36.1 ± 9.5/6.4 ± 8.7	36.3 ± 12.3/4.7 ± 6.4	NS/NS
NE, %	50	0	
Sural nerve			
SCV (m/s)/SNAP (μV)	38.9 ± 13.8/6.9 ± 7.6	48.2 ± 2.9/9.0 ± 7.9	NS/NS
NE, %	25	30	

MCV: motor conduction velocity; CMAP: compound muscle action potential; NE: not evoked; SCV: sensory conduction velocity, SNAP: sensory nerve action potential; NS: not significant (comparison of velocity/comparison of amplitude).

conduction block nor temporal dispersion in motor conduction was observed. Denervation potentials were observed frequently in involved muscles. Overall, electrophysiologic findings were quite similar in CSS and MPA.

Longterm followup results are presented in Table 4, except where noted. In the CSS group, all patients were alive one year after onset, and at 3 years only one patient had died. On the other hand, in the MPA group, 5 patients had died at one year ($p < 0.01$) and 11 patients had died by 5 years after onset ($p < 0.001$). Kaplan-Meier survival

Table 4. Longterm followup features of neuropathy in Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA).

Features	CSS, n = 30	MPA, n = 26	p, CSS vs MPA
Followup duration, yrs, range	2–12	2–12	
Mean ± SD	6.3 ± 2.9	4.5 ± 3.0	NS
Survival rate (%), 5 years	97	58	< 0.001
Modified Rankin score			
Initial peak phase	4.4 ± 0.6	4.0 ± 0.7	NS
Followup phase	2.4 ± 1.1	2.6 ± 1.3	NS
Cause of death			
CNS involvement			
Cerebral hemorrhage	0	0	
Cerebral infarction	0	0	
Status epilepticus	0	2	
Renal involvement			
Renal infarction	0	0	
Glomerulonephritis	0	3	
Interstitial pneumonia	1	3	
Heart failure	0	2	
Gastrointestinal bleeding	0	1	
No. of patients with systemic relapses (%)	2 (7)	10 (39)	< 0.05

Relapses were as described in the text.

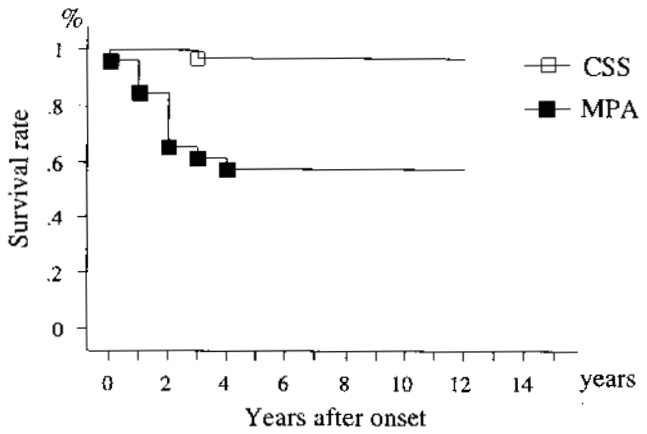

Figure 1. Kaplan-Meier survival curves of patients with neuropathy associated with Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA). CSS shows a significantly higher survival rate than MPA.

Table 5. Muscle strength of patients with Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA). Evaluation of muscle strength was performed by manual muscle testing using the scale of the UK Medical Research Council.

Muscles	CSS	MPA	p, CSS vs MPA
At initial peak	n = 30	n = 26	
Biceps	3.62 ± 1.82	3.77 ± 0.83	NS
Thenar	3.88 ± 1.05	3.23 ± 1.36	NS
Iliopsoas	3.45 ± 1.74	3.77 ± 1.01	NS
Tibialis anterior	2.28 ± 1.84	2.23 ± 1.88	NS
Followup (2–9yrs)	n = 21	n = 13	
Biceps	4.41 ± 0.73	4.23 ± 0.60	NS
Thenar	4.19 ± 0.93	3.77 ± 0.43	NS
Iliopsoas	4.32 ± 0.65	4.08 ± 0.49	NS
Tibialis anterior	3.48 ± 0.68	3.39 ± 0.65	NS

curves (Figure 1) revealed a significant difference between CSS and MPA (log-rank, $p < 0.0001$). Causes of death included interstitial pneumonia in one CSS patient, while in the MPA group 2 patients died of status epilepticus, 3 of renal failure due to glomerulonephritis, 3 of interstitial pneumonia and 2 of heart failure, and one of GI bleeding. No significant differences in muscle strength were noted between diseases at either the peak of neurological symptoms or at followup (Table 5). Modified Rankin score was exactly the same between CSS and MPA both in the initial peak and in the longterm followup phases. Followup nerve conduction studies revealed no significant differences between the 2 diseases in conduction velocities or action potential amplitudes, as was true for initial peak-phase studies (Table 3). Relapses of overall disease were apparent in 2 patients with CSS and in 10 patients with MPA, representing a significantly higher frequency for MPA ($p < 0.05$). Relapses of peripheral neuropathy were less prominent, but were more frequent in MPA patients. In MPA, patients with relapses tended to show less functional improvement than patients without relapses; CSS patients with relapses also had less functional improvement than patients without relapses.

DISCUSSION

This study revealed that neuropathic features at the initial

phase did not differ significantly between CSS and MPA associated neuropathy. Pathologic involvement of myelinated and unmyelinated sural nerve fibers also was similar between CSS and MPA. In addition, the histologic features of arteritis in the sural nerve specimen also were similar, except for more conspicuous eosinophils in CSS. These results, in agreement with our previous report[11], indicate that clinical and pathologic manifestations of peripheral neuropathy have shared characteristics in CSS and MPA, particularly in the initial phase.

The survival rate, however, was significantly better in CSS than in MPA according to Kaplan-Meier analysis. Our findings of better survival in CSS are in agreement with Abu-Shakra, *et al*[23]. In the initial phase, the SNVDI score was significantly higher in MPA than CSS, and each organ involvement including brain involvement was more intense in MPA than in CSS, except lung or GI. The anti-MPO-ANCA titer, considered to reflect the extent of vasculitic inflammation[31,32], was significantly higher in MPA than in CSS. Differences in mortality between CSS and MPA appear to reflect differences in the intensity of the generalized underlying vasculitic process at the initial phase[33,34], while the similarity in morbidity may reflect similar degrees of early neuropathic involvement.

Factors other than systemic involvement that appeared to affect mortality in CSS and MPA included differences in age, sex, and rate of relapse. The higher age at onset in MPA compared with CSS may have contributed to the higher mortality rate in MPA. Higher age at onset has been reported to predict significantly decreased survival in the necrotizing vasculitis in rheumatoid arthritis[35], Wegener's granulomatosis[36], systemic lupus erythematosus[37], and PAN[24], as well as MPA[34]. In CSS the age issue has not been assessed, but systemic organ failure may be more likely in older patients. The difference in sex preponderance between CSS and MPA also was significant. The mechanisms underlying any sex associated effect on the nature and behavior of vasculitic disease is obscure, but humoral or hormonal factors could be influential. A higher rate of relapse in MPA than in CSS may result in cumulative failure of visceral organs and thus lower the survival rate in MPA. Factors that might differentially influence MPA and CSS mortality rates should be assessed further in a large cohort study examining a large number of related variables[38].

Another important question is the effect of therapy on longterm prognosis in MPA and CSS groups. Even though the total amount of steroid administered was significantly higher in the MPA group, longterm morbidity was similar in both groups. Longterm functional prognosis in MPA and CSS has been evaluated in several studies, with varying conclusions[8,3-25,39,40]. One likely reason for disagreement is patient heterogeneity, particularly with respect to wide variation in systemic involvement as well as peripheral nerve involvement. The modified Rankin score was developed to evaluate chronic neurological disability, and has been validated in functional assessment of a wide variety of peripheral neuropathies[41] including vasculitic neuropathy[11]. Similar outcomes concerning neuropathy may reflect similar pathologic features of necrotizing vasculitis as seen in the sural nerve.

We observed that CSS and MPA share common features of peripheral nerve involvement in the initial and the longterm phase with respect to functional disability. However, the survival rate is significantly better in CSS, reflecting extent and severity of visceral involvement and the cumulative effect of relapses.

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