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Links

[Epidemiology of multiple sclerosis in Japanese: with special reference to opticopsinal multiple sclerosis]

[Article in Japanese]

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The fourth nationwide survey of multiple sclerosis (MS) disclosed that the estimated number of MS patients in Japan was 9,900, and the estimated prevalence rate of MS is 7.7 per 100,000, indicating that the number of MS patients has been rapidly increasing for the past 30 years. The demographic features of the present series were compared with those of the three past nationwide surveys. The ratio of female to male patients has increased from 1.3 to 2.9. As to distribution of age at onset, in 2004, the peak of the age at onset curve shifted from the 30s to 20s and the second peak at 50s seen in the 1989 survey disappeared this time. About 60% were conventional MS (CMS) while 20% were opticospinal MS (OSMS) plus optic-brainstem-spinal MS (OBSMS). The female to male ratio was significantly greater in OSMS than in CMS, and age at onset was also significantly higher in OSMS than in CMS in both male and female. By distribution of age at onset, CMS showed a single peak in the early 20s while OSMS showed the highest peak in the early 20s and a second peak in the 30s. Both visual impairment at onset and severe visual impairment during the course have decreased to about half of those found in the first survey, while frequencies of both quadriparesis and transverse myelitis considerably decreased in 2004 compared to 1989 in addition to a decrease of visual impairment. Disease progression was significantly faster with advancing age at onset. In respect to the McDonald criteria, dissemination in space was fulfilled in 45.5% in CMS while only in 8.2% in OSMS patients. Spinal cord

lesions were found in more than 90% of OSMS and 70% of CMS patients. Longitudinally extensive spinal cord lesions extending over 3 vertebral segments were detected in 41.2% of OSMS and 16.7% of CMS patients. In conclusion, the fourth nationwide survey disclosed significant changes in the prevalence and demographic features of MS in the Japanese population.

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Clinical and Laboratory Features of in-Patients with Multiple Sclerosis in a University Hospital in Tokyo from 1988–2002

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Abstract

Objective **The aim of this study was to analyze the clinical and laboratory features of each subtype of multiple sclerosis (MS) (relapsing-remitting, primary progressive, and secondary progressive) in the Tokyo metropolitan area.**

Methods and Patients **We retrospectively analyzed the medical records of 104 consecutive patients with a diagnosis of MS, who had been admitted to our university hospital from 1988 to 2002. They all met criteria for definite MS, by clinical or laboratory standards.**

Results **Eighty-four (80.8%) patients were classified as having relapsing-remitting MS, while 8 patients (7.7%) and 12 patients (11.5%) were classified as having primary progressive MS and secondary progressive MS, respectively. A significant female predominance existed in the relapse-remitting MS (female : male=2.4 : 1) cohort, but this ratio was 1 : 1 in both primary progressive and secondary progressive MS. The age at onset was older in the primary progressive MS (36.6±17.1 years of old) population than in either the relapsing-remitting MS (27.9±11.1) or the secondary progressive MS (27.8±11.5) subjects. Although the duration of illness was similar among the three types of MS, the number of exacerbations in the secondary progressive (5.9±4.6) cohort was significantly higher than that in the relapsing-remitting MS subjects (3.2±2.6). Patients with primary progressive MS showed a significantly higher rate of gait disturbance (87.5%) as the initial symptom than those with relapsing-remitting MS (23.8%), and this was thought to be due to the higher incidence of brainstem and spinal cord lesions. Visual disturbance as the initial symptom was frequently noted in those with secondary progressive MS (50.0%), while it was noted only in 29.8% and 12.5% in the relapsing-remitting and primary progressive patients, respectively. Primary progressive MS subjects had a higher propensity to be wheelchair-bound (75.0%) than those suffering from relapsing-remitting MS (1.2%). Increased total protein in the cerebrospinal fluid (CSF) of the secondary progressive cohort was statistically significant compared to the relapsing-remitting cohort. The frequency of oligoclonal IgG bands was rather low in each type of MS (17.1–33.3%). Gadolinium enhancement of plaques on MRI was more frequently present in secondary progressive MS (66.7%) than in either relapsing-remitting MS (32.1%) or primary progressive MS (50.0%). Of note, the opticospinal form was found in only 16.3% of the total MS patients, a proportion less than that in previous reports from southern Japan.**

Conclusion **The present study confirms that while the clinical and laboratory features of the MS patients in the Tokyo metropolitan area are similar to those in Western countries in most regards, features such as proportionally fewer primary and secondary progressive MS patients as well as less oligoclonal IgG bands on CSF analysis are different from those in Western countries.**
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Key words: multiple sclerosis, relapsing-remitting, primary progressive, secondary progressive, clinical features, laboratory features

Introduction

It has been well known that there are fewer cases of multiple sclerosis (MS) in Japan than in Western countries (1, 2). Previous studies have also emphasized some distinct clinical

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features of Japanese MS patients including a relatively higher rate of the opticospinal form of MS and a greater incidence of visual loss at the onset of illness (2–4). Recently, clinical and laboratory features have been reported for MS patients living in the northernmost part, Hokkaido (42–46 degrees north latitude) (5, 6), and the southernmost part, Kyushu (31–34 degrees north latitude) (7, 8), of mainland Japan. As is the case in the temperate zones of the USA and Australia, a small but statistically significant north-south gradient of MS prevalence rates exists in Japan with proportionally more opticospinal MS in the southern region of Japan (2). Our review of the literature revealed that to date there is no extensive study reporting on the MS patients in the Tokyo metropolitan area which is located at 36 degrees north latitude, and is in the central part of mainland Japan. In the present study, we retrospectively analyzed the clinical and laboratory features of 104 MS patients, who had been admitted to our university hospital located in the center of Tokyo metropolitan area between 1988 and 2002.

Materials and Methods

Patients

The medical records of the Department of Neurology of Keio University Hospital in Tokyo revealed a progressive increase in the number of patients who had been admitted to this department during the period of 1988–2002, and fulfilled the criteria developed by Poser et al of clinically definite or laboratory-supported definite MS (9), as shown in Fig. 1. This figure includes multiple admissions of some patients due to relapses or neurological deterioration among 104 consecutive and unrelated patients. Thus, we retrospectively reviewed the medical records of these 104 patients. One hundred patients (96.2%) were residents of the Tokyo metropolitan area. The other four patients lived in nearby suburbs. Seventy-one patients (68.3%) were born in Tokyo metropolitan area. During this period, the patients had neurological events for which neurological examination, CSF analysis, and brain and spinal cord MRI studies were performed at our center. The diagnosis of MS for these patients was also compatible with the diagnostic criteria of MS recently recommended by the International Panel on the Diagnosis of Multiple Sclerosis (10).

Based on the temporal clinical profiles and laboratory findings, the patients were also classified into relapsing-remitting, primary progressive, and secondary progressive types, as recommended by the International Panel. Secondary progression was defined as a period of deterioration, independent of relapses, sustained for at least 6 months, and that followed a relapsing-remitting phase (11).

Patients whose clinically localized primary lesions were thought to be confined to only the optic nerve and spinal cord without cerebellar or cerebral symptoms, were classified as having opticospinal MS (2). Those with minor brainstem signs, for example, nystagmus or transient double vision, in addition to optic-spinal involvement, were also included in the opticospinal form (2). The remainder of the patients, who showed involvement of multiple sites in the central nervous system (CNS), were classified as having the conventional form of MS (2, 7).

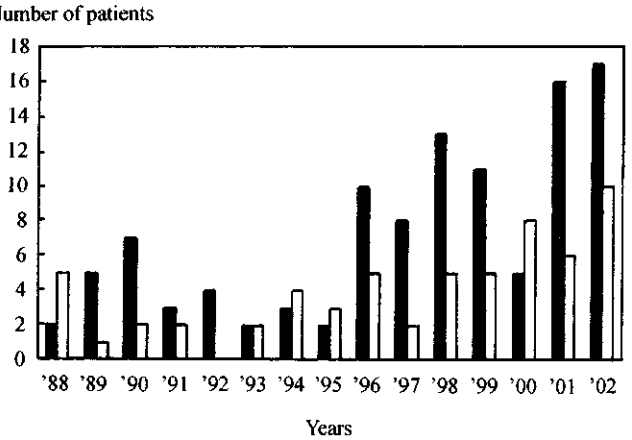

Figure 1. Changes in the number of patients with multiple sclerosis, who had been admitted to the Department of Neurology, Keio University Hospital during 1988–2002. This figure includes multiple admissions of some patients due to relapses or neurological deterioration among 104 consecutive and unrelated patients. Solid and open bars represent female and male patients, respectively. Note the recent increase in the admitted patients, especially female patients. X axis: years, Y axis: number of patients.

We reviewed the following items: 1) clinical manifestations; 2) spinal and brain MRI findings; 3) cerebrospinal fluid (CSF) findings (cell counts, total protein, IgG index, oligoclonal IgG bands). Only bands, which were detected in 30-fold concentrated cerebrospinal fluid by a standard agarose gel electrophoresis method and not detected in serum, were interpreted as oligoclonal IgG bands. When CSF studies were repeated in the same patient, only the study performed at the peak of exacerbation was considered.

MRI

In each patient, all of the MRI films taken between 1988 and 2002 were evaluated. All MRI studies for the brain were performed with 5 mm thick slices using a 1.5 Tesla superconducting scanner (Signa, GE Medical Systems, Milwaukee, WI, USA) or a 0.5 Tesla scanner (Signa, GE Medical Systems). The 1.5 Tesla scanner was used for the most recent MRI in every patient. Whole spinal cord was also examined by MRI in every patient. Any hyperintense areas in the brain and spinal cord on fast spin-echo T2-weighted images with a repetition time (TR) of 4,000 ms and an echo time (TE) of 80–100 ms were considered abnormal. A contrast-enhanced study was also done using the spin-echo T1-weighted sequences (TR=320–420 ms, TE=12–16 ms) with intravenous administration of gadolinium (0.1 mmol/kg). A blinded neuroradiologist and one neurologist among

Table 1. Clinical Features among Multiple Sclerosis Subtypes

	Relapsing-remitting (n=84)	Primary progressive (n=8)	Secondary progressive (n=12)
Female : male	59 : 25 (2.4 : 1.0)	4 : 4 (1.0 : 1.0)	6 : 6 (1.0 : 1.0)*
Age at onset (years)	27.9±11.1	36.6±17.1*	27.8±11.5
Patients with onset of symptoms at age >40 years	9/84 (10.7%)	3/8 (37.5%)*	2/12 (16.6%)
Age at last examination (years)	33.8±11.9	42.3±13.9*	35.3±11.9
No. of exacerbations	3.2±2.6	–	5.9±4.6^{b}
Duration of disease (years)	6.1±7.2	5.9±5.2	7.5±7.7
Relapse rate (/year)	0.79±0.52	–	–
Opticospinal form	15/84 (17.9%)	0/8 (0%)	2/12 (16.7%)
Initial symptoms			
Motor weakness	20/84 (23.8%)	4/8 (50.0%)*	5/12 (41.7%)
Sensory disturbance	32/84 (38.1%)	0/8 (0%)^{a}	2/12 (16.7%)
Visual disturbance	25/84 (29.8%)	1/8 (12.5%)	6/12 (50.0%)*
Brainstem/cerebellum	11/84 (13.1%)	2/8 (25.0%)	3/12 (25.0%)
Gait disturbance	20/84 (23.8%)	7/8 (87.5%)^{b}	5/12 (41.7%)
Sphincter disturbance	1/84 (1.2%)	1/8 (12.5%)	0/12 (0%)
Depressive state	2/84 (2.4%)	1/8 (12.5%)	0/12 (0%)
Motor disability at the last examination			
wheelchair-dependent	1/84 (1.2%)	6/8 (75.0%)^{b}	7/12 (58.3%)^{b}

^{b}p<0.01 vs. relapsing-remitting MS, ^{a}p<0.05 vs. relapsing-remitting MS, *p<0.1 vs. relapsing-remitting MS.

the authors evaluated the scans.

Statistical analysis

All of the data are shown as mean ± standard deviation. The Mann-Whitney *U* test, the χ^2 test and Fisher's exact probability test were used to compare the clinical and MRI data between MS subtypes.

Results

In the present study, 84 (80.8%) out of 104 patients were classified as having relapsing-remitting type of MS, while 8 patients (7.7%) and 12 patients (11.5%) were classified as having primary progressive and secondary progressive MS, respectively.

Clinical features

Clinical features are summarized in Table 1. A significant female predominance existed in the relapse-remitting cohort (female : male=2.4 : 1), but this ratio was 1 : 1 in both the primary progressive and secondary progressive groups. Distribution of total MS patients by age at onset of their initial symptoms is shown in Fig. 2, which clearly demonstrates that the onset of MS was noted mostly in young people between 20 and 34 years of age. As shown in Table 1, the age at onset was older in those with primary progressive MS (36.6±17.1 years) as compared to the other types of MS (relapsing-remitting MS: 27.9±11.1, secondary progressive MS: 27.8±11.5). A total of 37.5% of patients with primary progressive MS developed symptoms after 40 years of age, and this rate tended to be higher than that in patients with relapsing-remitting MS, 10.7%. The number of exacerbations

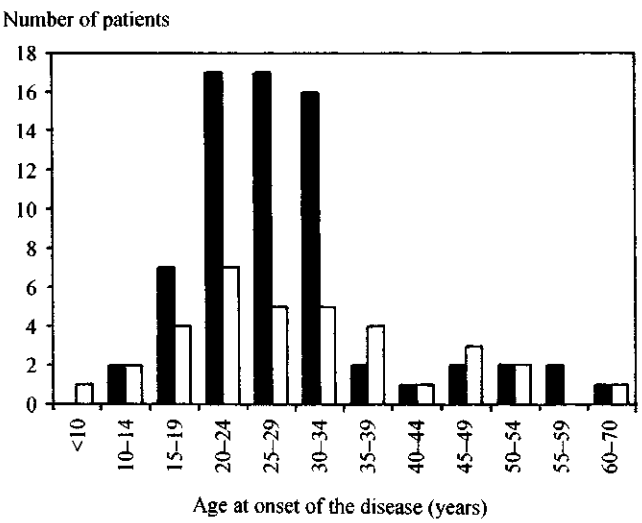

Figure 2. Distribution of total MS patients by age at onset of their initial symptoms. Solid and open bars represent female and male patients, respectively. Note a clear peak between 20 and 34 years of age. X axis: years of age, Y axis: number of patients.

Table 2. Findings of Cerebrospinal Fluid and Magnetic Resonance Imaging among Multiple Sclerosis Subtypes

	Relapsing-remitting (n=84)	Primary progressive (n=8)	Secondary progressive (n=12)
Cerebrospinal fluid			
Total protein (mg/dl)	35.8±19.4	46.6±30.5	56.6±47.9[b]
IgG index	0.74±0.31	0.86±0.51	0.74±0.29
Oligoclonal IgG bands	14/84 (17.1%)	2/8 (25.0%)	4/12 (33.3%)
Cell counts (/μl)	4.9±11.7	5.5±9.3	3.3±3.3
MRI (Brain and spinal cord)			
Gd-enhanced lesions	27/84 (32.1%)	4/8 (50.0%)	8/12 (66.7%)[b]
High intensity lesions (T2-weighted image)			
Optic nerve	6/84 (7.1%)	0/8 (0%)	2/12 (16.7%)
Cerebral white matter	66/84 (78.6%)	8/8 (100.0%)	12/12 (100%)
Cerebral deep gray matter	14/84 (16.7%)	3/8 (37.5%)	6/12 (50.0%)
Cerebellum	17/84 (20.2%)	2/8 (25.0%)	4/12 (33.3%)
Brainstem	39/84 (46.4%)	8/8 (100%)	12/12 (100%)
Spinal cord	53/84 (63.1%)	6/8 (75.0%)	11/12 (91.7%)

[b]$p<0.05$ vs. relapsing-remitting MS, *$p<0.1$ vs. relapsing-remitting MS, Gd: gadolinium.

found in secondary progressive MS (5.9±4.6) was significantly higher than that in relapsing-remitting MS (3.2±2.6) ($p<0.01$). The duration of illness was similar among the three types of MS, although secondary progressive MS patients had a slightly longer duration (7.5±7.7 years) than the other types of MS. In the secondary progressive MS patients, the period before the onset of the progressive phase was 6.4±7.2 years. Opticospinal MS was found in 17.9% and 16.7% of the relapsing-remitting and secondary progressive MS patients, respectively, whereas none of the patients with primary progressive MS had this form.

Review of the patient's initial symptoms found that the primary progressive group experienced motor weakness more frequently (50.0%) than those with the other types of MS (relapsing-remitting MS: 23.8%; secondary progressive MS: 41.7%). In contrast, none of the primary progressive cohort experienced sensory disturbance, whereas 38.1% and 16.7% of the relapsing-remitting and secondary progressive cohorts did. Visual disturbance was recognized as the initial symptoms in 50.0% of patients with secondary progressive MS, and this rate was relatively higher ($p<0.1$) than that in either the relapsing-remitting (29.8%) or the primary progressive (12.5%) types. Symptoms referable to the brainstem or cerebellum, such as diplopia, vertigo, and incoordination, were experienced similarly by all types of MS patients in this study. Patients with primary progressive MS showed a significantly higher rate of gait disturbance (87.5%) as the initial symptom than those with relapsing-remitting MS (23.8%) ($p<0.01$), whereas patients with secondary progressive MS showed an intermediate rate (41.7%). Although sphincter disturbance was rarely or never recognized in patients with relapsing-remitting or secondary progressive MS, 12.5% of patients with primary progressive MS experienced it as the initial symptom. Depressive state proved to be the initial symptom in only 2.4% of our relapsing-remitting patients, whereas 1 out of 8 patients (12.5%) with primary progressive MS had this as their first symptom. Patients were found to be wheelchair-bound in 75.0% and 58.3% of cases in primary progressive and secondary progressive MS, respectively at their most recent examinations. Only 1.2% of patients with relapsing-remitting MS ($p<0.01$) were found to be in a similar condition.

Cerebrospinal fluid findings

Total protein in the cerebrospinal fluid of patients with secondary progressive MS was statistically higher than that in those with relapsing-remitting MS ($p<0.05$) (Table 2). The mean IgG index was more than 0.7 in each type of MS, although patients with primary progressive MS showed higher IgG index values as compared to other types of MS. The frequency of oligoclonal IgG bands was rather low in each type of MS (relapsing-remitting MS: 17.1%; primary progressive MS: 25.0%; secondary progressive MS: 33.3%), as will be discussed later. There were no differences in cell counts.

MRI findings

Gadolinium enhancement in the brain and spinal cord was more frequently detected in patients with secondary progressive MS (66.7%) as compared to relapsing-remitting (32.1%) ($p<0.05$) and primary progressive MS (50.0%) (Table 2). The relatively high frequency of gadolinium-enhanced lesions in each type of MS may be due to the design of the present study, which counted any enhanced lesions in all of the MRI images taken during the whole clinical course. No patients with primary progressive MS revealed any high intensity lesions in the optic nerve, while a few patients with relapsing-remitting (7.1%) and secondary progressive MS (16.7%) did so. The high intensity lesions of the T2-

weighted images were more frequently found in the brain and spinal cord in patients with primary and secondary progressive MS than in those with relapsing-remitting MS. It is of note that the brainstem was affected in all of the patients with primary and secondary progressive MS, but in only 46.4% of patients with relapsing-remitting MS.

Discussion

The present study was based on a retrospective analysis of the medical records of 104 MS patients since 1988, and the mean follow-up period of these patients was relatively short (6.3±7.0 years). These features may require careful interpretation of the present data, including the relatively low proportion of secondary progressive MS in the present study (11.5%) as compared to other studies with longer follow-up periods (6). Nevertheless, this is the first extensive report of MS patients in the Tokyo metropolitan area, and it is expected to provide the basic characteristics of MS patients in this area, since environmental and geographical factors are thought to play important roles in MS (2).

The present study revealed a recent increase in the admission of MS patients in our hospital. The reason for this increase is currently not clear, and there are many possibilities including a true increase in the number of MS patients in the Tokyo metropolitan area, an increased use of MRI, an increasing attraction of MS patients from other hospitals or more awareness of MS in the general public. A complete epidemiological study in the Tokyo metropolitan area is warranted to answer this question.

In the present study, primary progressive MS was found in 7.7% of the total MS patients. Due to variations in the definitions used and the lack of uniformity in the criteria applied, the proportion of patients with primary progressive MS varied between 9–37.4% of MS patients in previous reports from Western countries (12). In one detailed regional study, 18% were considered to have progressive disease from onset (13). Taking the most recent studies into account, the best estimate is that 10–20% of the MS population has the primary progressive form (12). In Japan, it has been known that the proportion of primary progressive MS is much lower than that in Western countries. For example in the 1992 and 2003 regional studies in Hokkaido, the northernmost part of the mainland Japan, only 3% of the MS patients manifested the primary progressive type (5, 6). Likewise, a report in 1981 from Kyushu, the southernmost part of mainland Japan, showed that only 2% of the MS patients were compatible with the recent criteria for primary progressive MS (1). Compared to these low rates in previous Japanese reports, the present study showed a higher prevalence of primary progressive MS, which might be attributed to the increased availability of MRI in the routine clinical workup, the accelerating westernization of daily life in the Tokyo metropolitan area or to regional environmental factors. The proportion of secondary progressive MS in the present study (11.5%) was lower than that in Western countries (30–50%) (1) and in Hokkaido (29%) (6). This difference may be due to a relatively shorter duration of illness (shorter follow-up period) in patients analyzed in the present study or to regional environmental factors.

The equal male to female sex ratio in patients with primary progressive MS in the present study was consistent with the previous reports (12, 14). There was a later age of onset in primary progressive patients (36.6±17.1 years old) as compared to relapsing-remitting and secondary progressive types in the present study, which was also compatible with the previous studies (12, 14, 15). The proportion of our patients with onset after 40 years of age was 37.5% in patients with primary progressive MS, and this value was very close to that found in Western countries (15).

Secondary progressive MS patients begin with a pattern of relapsing-remitting MS that later undergoes a transition to a progressive course with or without superimposed relapse. In this context, it is reasonable that patients with secondary progressive MS in the present study had a significantly higher number of exacerbations and longer duration of illness than those with relapsing-remitting MS. The period before the onset of the progressive phase (6.4±7.2 years) was consistent with a previous paper from France (13), which reported 6.8± 5.4 years.

In the total 104 MS patients in the present study, 17 patients (16.3%) were thought to have the opticospinal form. This value was similar to that recently reported from Hokkaido (16–18%) (6, 16), but was lower than that in a recent report from Kyushu (31%) (2). A retrospective review published in 1981 reported that the proportion of the opticospinal form among all cases of MS was seven times higher in Kyushu, Japan than in England (42% vs. 6%) (1). These figures are compatible with the recent trend that the proportion of opticospinal form has decreased with the now increasing ratio of conventional form of MS in Japanese (2). This trend may be attributed to the advancement of various diagnostic techniques to detect MS lesions such as MRI, and/or changes in various environmental factors and lifestyle in Japan (2).

The opticospinal type was not found in any patients with primary progressive MS in the present study, while it was found in 17.9% and 16.7% of patients with relapsing-remitting MS and secondary progressive MS, respectively. This may be due to the fact that patients with primary progressive MS had suffered extensive lesions in the central nervous system which were not limited to the spinal cord and optic nerve. Thus, by our criteria, these patients were not classified as having the opticospinal form of MS.

The primary progressive cohort experienced gait disturbance (87.5%) and motor weakness (50.0%) more frequently as an initial symptom than those with other types of MS. At their last examinations, the primary progressive (75.0%) and secondary progressive (58.3%) groups were often dependent on wheelchairs for their daily activities. These features were compatible with previous studies showing that primary and secondary progressive MS has a poor prognosis (12, 17, 18).

Total protein in the cerebrospinal fluid was significantly higher in patients with secondary progressive MS than in those with other types of MS, probably reflecting a more destructive pathology in the central nervous system. The frequency of oligoclonal IgG bands was rather low in each type of MS in the present study as compared to that reported in Western countries (19). This could be partly due to the methodology employed in our hospital (agarose gel electrophoresis), since more sensitive methods such as isoelectric focusing with IgG immunoblotting are recently recommended (20), and this method is currently used in our hospital to solve this issue. The other reason for the low frequency of oligoclonal IgG bands in the present study may be a racial difference. A previous study in Japan reported a relatively low frequency of oligoclonal IgG bands in MS patients of not only opticospinal and spinal forms (29%) but also the conventional form of MS (33%) (8). Similar data was also reported by other Japanese institutes (21). In any case, the same method was applied to all MS patients in the present study, and this revealed a similar frequency of oligoclonal IgG bands among the three types of MS. The lower values of IgG index in relapsing-remitting and secondary progressive cohorts as compared to that in primary progressive cohort, may be due to inclusion of opticospinal MS patients in the former two cohorts (21).

The frequency of gadolinium enhancement in the brain and spinal cord MRI was significantly higher in patients with secondary progressive MS (66.7%) than in those with relapsing-remitting MS and primary progressive MS, which may suggest that the inflammatory process was more severe in this type. In other words, patients with primary progressive MS did not always show the gadolinium enhancement in spite of the progressive nature of the disease process, and this is in accordance with previous reports (14). MR spectroscopy or magnetization transfer ratio may provide more specific images for primary progressive MS (12), but these studies were not available in the present study.

The present study revealed a relatively higher rate of cerebellar lesions on the MRI in each type of MS (20.2–33.3%) as compared to a previous Japanese report, which reviewed MS patients in the Tohoku area, the northern part of the Honshu island, from 1988 to 1997 and found cerebellar lesions in only 6.4% (22). According to a recent report (23), cerebellar lesions are now increasingly detected on the MRI in younger Japanese people with MS.

In summary, the clinical features and laboratory findings in the present study were very similar to those discovered in the USA and Europe except for certain features such as low proportions of the primary and secondary progressive MS types as well as the relative paucity oligoclonal IgG bands in the CSF of our cohorts. Previously the opticospinal form of MS seemed to be very common in Japan, but the present study of Tokyo inhabitants revealed that the conventional form of MS could be five times more common than the opticospinal form. Cerebellar lesions in MRI were not rare in the present study. The reasons for these dynamic differences are yet to be determined but the westernized social and environmental factors in the Tokyo metropolitan area may be contributory. The immunological characteristics of the cerebrospinal fluid and the peripheral blood such as the production of cytokines and HLA alleles in MS patients at our institution are currently under investigation.

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Clinical and laboratory features of in-patients with multiple sclerosis in a University Hospital in Tokyo from 1988-2002.

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OBJECTIVE: The aim of this study was to analyze the clinical and laboratory features of each subtype of multiple sclerosis (MS) (relapsing-remitting, primary progressive, and secondary progressive) in the Tokyo metropolitan area. METHODS AND PATIENTS: We retrospectively analyzed the medical records of 104 consecutive patients with a diagnosis of MS, who had been admitted to our university hospital from 1988 to 2002. They all met criteria for definite MS, by clinical or laboratory standards. RESULTS: Eighty-four (80.8%) patients were classified as having relapsing-remitting MS, while 8 patients (7.7%) and 12 patients (11.5%) were classified as having primary progressive MS and secondary progressive MS, respectively. A significant female predominance existed in the relapse-remitting MS (female : male=2.4 : 1) cohort, but this ratio was 1 : 1 in both primary progressive and secondary progressive MS. The age at onset was older in the primary progressive MS (36.6+/-17.1 years of old) population than in either the relapsing-remitting MS (27.9+/-11.1) or the secondary progressive MS (27.8+/-11.5) subjects. Although the duration of illness was similar among the three types of MS, the number of exacerbations in the secondary progressive (5.9+/-4.6) cohort was significantly higher than that in the relapsing-remitting MS subjects (3.2+/-2.6). Patients with primary progressive MS showed a significantly higher rate of gait disturbance (87.5%) as the initial symptom than those with relapsing-remitting MS (23.8%), and this was thought to be due to the higher incidence of brainstem and spinal cord lesions. Visual disturbance as the initial symptom was frequently noted in those with secondary progressive MS (50.0%), while it was noted only in 29.8% and 12.5% in the relapsing-remitting and primary progressive patients, respectively. Primary progressive MS subjects had a higher propensity to be wheelchair-bound (75.0%) than those suffering from relapsing-remitting MS (1.2%). Increased total protein in the cerebrospinal fluid (CSF) of the secondary progressive cohort was statistically significant compared to the relapsing-remitting cohort. The frequency of oligoclonal IgG bands was rather low in each type of MS (17.1-33.3%). Gadolinium enhancement of plaques on MRI was more frequently present in secondary progressive MS (66.7%) than in either relapsing-remitting MS (32.1%) or primary progressive MS (50.0%). Of note, the opticospinal form was found in only 16.3% of the total MS patients, a proportion less than that in previous reports from southern Japan. CONCLUSION: The present study confirms that while the clinical and laboratory features of the MS patients in the Tokyo metropolitan area are similar to those in Western countries in most regards, features such as

proportionally fewer primary and secondary progressive MS patients as well as less oligoclonal IgG bands on CSF analysis are different from those in Western countries.

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Seasonal variation of multiple sclerosis exacerbations in Japan.

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Several reports have described the seasonal variation of multiple sclerosis (MS) attacks in the European countries and in the US. Some have insisted that attacks occurred more frequently in winter or spring. We investigated the possibility of a seasonal variation in the frequency of MS attacks among patients in Japan. A total of 172 MS exacerbations in 34 MS patients were analyzed retrospectively. Attacks were divided into two groups: opticospinal type and brain type. The 12 months of the year were assigned to 6 groups based on average monthly temperature. Of the 172 MS exacerbations, 123 were opticospinal type and 49 were brain type of attacks. The total number of attacks was significantly more frequent in the warmest (July and August) and coldest (January and February) months. The heat of summer in warmer, low latitude areas may be a risk factor for MS attacks.

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