Two subtypes of optic-spinal form of multiple sclerosis in Japan: clinical and laboratory features

Abstract Seventy-seven cases of the optic-spinal form of multiple sclerosis (OSMS) were collected from 6 institutes in 3 cities of Japan, and the clinical and MRI features were analyzed. Two-thirds of the OSMS patients had longitudinally extensive spinal cord MRI lesions (LESL), and had clinical features similar to those of relapsing neuromyelitis optica which often causes severe disability. In contrast, OSMS patients without LESL tended to have milder disease and had some feature commonly seen in the conventional form of MS. The percentage of OSMS without LESL in total OSMS has recently been increasing. The present study suggests that LESL is crucially important for distinguishing the two subtypes of OSMS.

Key words multiple sclerosis · optic spinal form · neuromyelitis optica · MRI

Introduction

Multiple sclerosis (MS) is a heterogeneous demyelinating syndrome that affects the central nervous system. In Japan, the optic-spinal form of MS (OSMS) has been considered to be one of the variants of MS in which the lesions are restricted to the optic nerves and the spinal cord [1, 8, 10]. Although the percentage of OSMS in Japanese MS is decreasing [6, 11], about one-fourth of Japanese MS patients have OSMS. The term neuromyelitis optica (NMO) has been widely used in Western countries to describe patients with severe optic neuritis and transverse myelitis [17]. Relapsing NMO is considered to be a distinct entity from MS even
though its symptoms are indistinguishable from those of classic MS (CMS) patients [16]. Recently, NMO-IgG, an NMO-specific serum autoantibody, was discovered, and about 60% of cases with OSMS were positive for NMO-IgG, while cases with CMS were consistently negative for this serum marker [9]. Although the relation between NMO-IgG and the pathogenesis of NMO is unknown, a fraction of cases of OSMS, especially those with NMO-IgG, may be caused by the same pathological mechanisms as those in NMO [5]. NMO is usually severe and often unresponsive to corticosteroids [18]. Interferon β treatment often fails to prevent a relapse of NMO [18]. In OSMS, however, some patients show milder disease and some do respond to interferon β therapy [14]. Considering the diversity of OSMS, we examined the records of 77 OSMS patients from six hospitals in Japan, and analyzed their clinical and laboratory features.

Materials and methods

Patients

Clinical and laboratory data of OSMS patients were collected from 6 hospitals in Japan (Tohoku University Hospital in Sendai City, Hokuyukai Neurology Hospital and Nishi Maruyama Hospital in Sapporo City, Tokyo Women’s Medical University Hospital and Tokyo Metropolitan Neurological Hospital and Tokyo Metropolitan Ebara Hospital in Tokyo). All the patients fulfilled the criteria of OSMS proposed by Kira [8]. Patients whose disease duration was less than a year, and patients with systemic lupus erythematosus were excluded from the study.

Analyzed Items

Clinical and laboratory data were retrospectively analyzed. The analyzed items were gender, onset year, onset age, present EDSS, and history of transverse myelitis, sustained severe optic neuritis, or minor brainstem symptoms. In MRI examinations, longitudinally extensive (longer than three vertebral segments) spinal cord lesions (LESL), brain lesions, gadolinium-enhanced brain lesions, brainstem lesions, periventricular ovoid lesions, and tumefactive brain lesions were analyzed. In addition, serum anti-nuclear antibodies (ANA), anti-SS-A antibodies or anti-SS-B antibodies, cerebrospinal fluid (CSF) pleocytosis, and CSF oligoclonal IgG bands (OB) were also studied. Transverse myelitis was defined as myelitis that caused simultaneous bilateral dysfunction of both the motor and sensory systems. Sustained severe optic neuritis was defined as that which showed markedly impaired corrected visual acuity (below 20/200) after treatment. Minor brainstem symptoms included nystagmus, temporary diplopia, hiccup, nausea, and vertigo. MRI and CSF findings were those obtained in the acute phase of the disease. As for OB, only the cases tested by isoelectric focusing method were included.

Data analysis

We defined severe OSMS as the condition of both transverse myelitis and sustained severe optic neuritis, mild OSMS as the disorder without the two symptoms, and intermediate OSMS as that with one of the two symptoms. The other items were compared between the three groups. We also compared those with OSMS with LESL and OSMS without LESL.

Statistics

StatView® version 5.0 (SAS Institute Inc., Cary, NC) was used for statistical analysis. We used the Mann-Whitney U test or Bonferroni-Dunn test for differences between the groups, the Fisher’s exact test for the frequencies of positive OB and autoantibodies in the two groups, and the Spearman rank correlation coefficient test for correlations in the two groups.

Results

Patients (Table 1)

The records of a total of 77 OSMS patients from the 6 hospitals were collected. There were 68 women and 9 men. The average age of the 77 OSMS patients was 49 years and the average disease duration was 14 years. The present EDSS ranged from 0 to 10 and the median was 5.0. The EDSS correlated with the disease duration (p < 0.001) (Figure 1). Transverse myelitis was seen in 60% of the patients, sustained severe optic neuritis was seen in 52% of the patients, and minor brainstem symptoms were seen in 31%. Sixty-eight percent of the patients had brain lesions on MRI, but only 5% had gadolinium-enhanced brain lesions. Brainstem MRI lesions were seen in 23% of the patients, and periventricular ovoid lesions in 22%. Tumefactive brain lesions were rarely seen (3%). OB detected by the isoelectric focusing method was positive in 15% of the patients, which was similar to the percentage reported in a previous study [12]. Serum anti-nuclear antibody was positive in 45% of the patients and anti-SS-A or SS-B antibody was positive in 29%. HLA-DRB1*1501 was positive in only 36%.

Comparison between severe OSMS, mild OSMS, and intermediate OSMS

Among the 77 patients, 31 (40%) had both transverse myelitis and sustained severe optic neuritis, and were defined as severe OSMS. Among the rest, 22 patients (29%) had no episode of transverse myelitis or sustained severe optic neuritis, and were defined as mild OSMS. In the comparison of the clinical and MRI features between severe OSMS and mild OSMS, significant differences were observed in age (mean 58 years old vs. 36 years old, higher in severe OSMS, p < 0.0001), onset age (mean 38 years old vs. 28 years old, higher in severe OSMS, p = 0.0075), disease duration (mean 19 years vs. 7 years, longer in severe OSMS, p < 0.0001), EDSS score (median 6.5 vs. 1.5, higher in severe OSMS, p < 0.0001), frequency of