A clinical comparative study of multiple sclerosis and neuro-Behçet's syndrome

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SUMMARY Clinical comparisons were made between Japanese patients with multiple sclerosis (66 cases) and neuro-Behçet's syndrome (23 cases.) Those with neuro-Behçet showed marked male predominance, while those with multiple sclerosis showed slight female preponderance. Both showed encephalomyelopathy disseminated in time and space. Patients with multiple sclerosis, however, showed a more polyphasic course, whilst those with neuro-Behçet showed a more progressive one. In multiple sclerosis optic neuritis, acute transverse myelitis, painful tonic seizures, mental disturbance and internuclear ophthalmoplegia were common. On the other hand, in neuro-Behçet the main neurological manifestation was progressive pseudobulbar palsy. Serum and CSF showed more inflammatory changes in neuro-Behçet than in multiple sclerosis. Clinical estimation suggested that in multiple sclerosis the main lesions were in the optic nerve, tegmentum of the brain stem and spinal cord, whereas in neuro-Behçet they were in the basal parts of the brain stem.

Multiple sclerosis and neuro-Behçet's syndrome are disseminated demyelinating and inflammatory diseases affecting the central nervous system (CNS) of unknown etiology. Nationwide survey¹ and other clinical studies of multiple sclerosis in Japan²⁻⁴ disclosed a low incidence, but its clinical and pathological pictures are essentially the same as those of the Western countries except for a relatively higher incidence of optic neuritis and transverse myelitis.⁵ On the other hand, epidemiological and clinical studies for Behçet's disease revealed a relatively higher incidence of neuro-Behçet in Japan than in the Western countries.^{6,7} When muco-cutaneo-ocular symptoms such as aphthous stomatitis, genital ulcer or uveitis are not evident, Behçet's disease shows a picture of brain stem encephalitis, simulating multiple sclerosis in some cases. A comparison of the clinical and laboratory findings in the two conditions has been carried out.

Materials and methods

The subjects of the present study were composed of consecutive series of 66 Japanese multiple sclerosis patients and 23 neuro-Behçet patients examined in our clinic. Diagnostic criteria of multiple sclerosis were those of the Multiple Sclerosis Committee of Japan.¹ Diagnosis of neuro-Behçet was made in a patient with neurologic manifestations which fulfilled the diagnostic criteria of Behçet's disease in Japan.⁹

Comparisons were made between the two series regarding sex ratio, age at onset, initial neurological symptoms, neurological symptoms and signs throughout the course of the illness, laboratory data, and clinical course. The mean periods between the onset and the most recent examination or death were 7 years in multiple sclerosis and 2 years and 8 months in neuro-Behçet syndrome.

Results

Sex ratio The multiple sclerosis series consisted of 21 males and 45 females; the neuro-Behçet series of 20 males and 3 females.

Age at onset The age at onset was 15 to 52 years

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Table 1 Age at onset

Age (yr)	MS	Behçet's disease	
		Somatic symptoms	Neurologic symptoms
10-19	7	1	0
20-29	21	9	7
30-39	19	9	10
40-49	17	3	4
50-59	2	1	2
Total	66	23	23
Mean age	31	32	35

(mean 31 years) for multiple sclerosis (table 1). In neuro-Behçet the age at onset of somatic (muco-cutaneo-ocular) symptoms and neurologic symptoms were separated. The former appeared 3 years earlier on average (table 1); the age at appearance of somatic symptoms was 19 to 57 years (mean 32 years), that of neurologic symptoms 23 to 58 years (mean 35 years). In 16 cases of neuro-Behçet syndrome muco-cutaneo-ocular symptoms preceded neurological symptoms, on the other hand, neurological symptoms developed simultaneously in 3 cases or preceded muco-cutaneo-ocular symptoms in 4 cases. When neurological symptoms preceded, muco-cutaneo-ocular symptoms appeared within a year (table 2).

Initial neurologic symptoms Almost half of the multiple sclerosis patients started with visual impairment, and numbness was the second most frequent. On the other hand about 40% of neuro-Behçet patients started with speech disturbance, and none complained of numbness, or visual impairment due to optic neuritis (table 3). **Neurological symptoms and signs** In multiple sclerosis patients visual impairment (74%), acute transverse myelitis (35%), painful tonic seizure (27%), mental disturbance (21%) and inter-

Table 2 Development of neurologic symptoms in neuro-Behçet's syndrome

No of cases	
<i>Interval muco-cutaneo-ocular to neurological symptoms</i>	
Within one year	2
1-2 years	2
2-3 years	2
3-4 years	3
Over 4 years	7
Total	16
<i>Interval neurological to muco-cutaneo-ocular symptoms</i>	
Within 6 months	1
6 months to 1 year	3
Total	4
Simultaneous	3

Table 3 Initial neurologic symptoms (%)

	Multiple sclerosis (n = 66)	Neuro-Behçet's syndrome (n = 23)
Speech disturbance	0	39
Mental disturbance	0	22
Gait disturbance	6	22
Paralysis	18	9
Diplopia	5	4
Sphincter disturbance	9	9
Visual impairment	42	52*
Numbness	26	0

*All were due to uveitis.

nuclear ophthalmoplegia (18%) were commonly seen. Bilateral visual impairment was seen in 47% of cases. Euphoria was seen in 15% (10 cases) and amnesic syndrome in one case.

In neuro-Behçet patients frequent neurological manifestations were hyperreflexia (96%), dysarthria (74%), mental disturbance such as forced laughing or crying (61%), and hyperactive jaw jerks (52%) suggesting pseudobulbar signs (table 4). Paraplegia, convulsion, internuclear ophthalmoplegia, Lhermitte's sign and painful tonic seizure were rare. Cranial nerve involvement was also rare; only 3 had partial unilateral peripheral facial nerve palsy. Six of the 23 patients complained of headache during the course, but meningeal irritation sign was seen in only 2. Visual impairment due to uveitis was frequently seen in neuro-Behçet syndrome. The differences of the two conditions were compared in table 5.

Laboratory data The erythrocyte sedimentation rate (ESR) was increased in 45% of patients with multiple sclerosis, and in 70% of patients with neuro-Behçet. C-reactive protein (CRP) in the serum was positive in 3% of patients with multiple sclerosis and in 67% of patients with

Table 4 Neurologic signs during the course of the illness in neuro-Behçet's syndrome (%)

Hyperreflexia	96
Dysarthria	74
Mental disturbance	61
Hyperactive jaw jerks	52
Sphincter disturbance	35
Dysphagia	30
Ataxia (cerebellar)	30
Hemiplegia (paresis)	17
Facial palsy (peripheral type)	13
Sensory disturbance	6
Nystagmus	4
Stiff neck	4
Paraplegia	4
Convulsion	4
Internuclear ophthalmoplegia	0
Lhermitte's sign	0
Painful tonic seizure	0

Table 5 Comparison of some neurological signs (%)

	Multiple sclerosis (n=66)	Neuro-Behçet's syndrome (n=23)
Mental disturbance	21	61
Internuclear ophthalmoplegia	18	0
Paraplegia with sensory level	35	4
Painful tonic seizure	27	0

neuro-Behçet syndrome (table 6). In the cerebrospinal fluid, pleocytosis was present in 35% of patients with multiple sclerosis (highest 164/mm³) and in 79% of patients with neuro-Behçet (highest 68/mm³). Polymorphonuclear cells were seen in 15% (5 of 34 cases) of patients with multiple sclerosis and in one of 13 cases in neuro-Behçet. Protein content was increased in 27% of patients with multiple sclerosis (highest 1120 mg/l) and in 33% of those with neuro-Behçet (highest 850 mg/l) (table 6).

In multiple sclerosis oligoclonal band was present in 45% (5 of 11 cases), and IgG was increased in 60% (6 of 10 cases, highest 260 mg/l, normal range 5–42 mg/l). In neuro-Behçet the Mastix test was done in 3 cases, all were normal; IgG content was measured in 2 cases, both showed abnormally high level (50 mg/l, 58 mg/l), in one of which oligoclonal band was tested for but was negative.

Clinical course Patients with multiple sclerosis showed remissions and exacerbations in 97% of cases, whereas patients with neuro-Behçet also showed acute exacerbations and partial remissions but the overall clinical course was progressive in 83% (table 7). Corticosteroids of different kinds and doses were given to 9 patients

Table 6 Comparison of laboratory data (%)

	Multiple sclerosis	Neuro-B	None
ESR, increased	45	70	
C-reactive protein, positive	3	67	
CSF			
Pleocytosis	35	79	
High protein content	27	33	

Table 7 Clinical course of the disease (%)

	Multiple sclerosis (n=66)	Neuro-Behçet's syndrome (n=23)
Remissions and exacerbations	97	17
Progressive with partial remissions	0	26
Progressive	3	57

with neuro-Behçet's syndrome for variable periods of time: 2 showed slight improvement but the remaining were not effective.

Discussion

There are a number of reports regarding multiple sclerosis^{1-15 10} and neuro-Behçet's syndrome^{7 11-15} independently. Detailed clinical comparative studies for these two diseases from a single neurologic source have, however, not yet been reported. Our study showed that the age at onset was common in young adults in both, but a striking difference in sex ratio occurred; there was a slight female preponderance in multiple sclerosis and marked male predominance in neuro-Behçet's syndrome, which was in agreement with the previous reports.^{1 6 10 16}

In addition some differences in clinical features were disclosed. Common clinical features in multiple sclerosis were optic neuritis, internuclear ophthalmoplegia and transverse myelitis suggesting the lesions in the optic nerve, brain stem of both tegmentum and basal part, and spinal cord. This higher incidence of optic neuritis and transverse myelitis is one of the characteristic features in Japanese multiple sclerosis.² On the other hand the common neurologic manifestations of neuro-Behçet's syndrome were generalised hyperreflexia and pseudobulbar palsy manifesting forced laughing and crying, dysarthria and hyperactive jaw jerks with rare involvement of tegmentum or spinal cord.

Shimizu⁹ reported pleomorphic neuropsychiatric features in neuro-Behçet's syndrome such as severe headache, stiff neck, Kernig's sign (meningeal irritation), tremor, nystagmus, ataxia, dysarthria (cerebellar sign), spastic paresis, Babinski's sign, clonus (pyramidal sign), dysarthria, dysphagia, forced laughing and crying (brain stem sign), and mental symptoms such as anxiety, memory impairment and character change. On the other hand, Ikeda¹⁷ stressed that the common neurologic features of neuro-Behçet's syndrome were motor impairment especially bilateral pyramidal signs and that the mental changes mainly consisted of loss of emotional control with relative sparing of intelligence and memory. Our results were in general agreement with this report. Since there was no severe dementia at least at the initial stage of the disease, the pseudobulbar palsy could be attributable to lesions mainly in the basal part of the brain stem rather than bilateral hemispheric damage. Our clinical

assessment was compatible with a previous pathological study done by Totsuka¹⁸ who concluded that the lesions of multiple sclerosis were located surrounding the ventricles, while those in neuro-Behçet's syndrome were in the lateral basal parts of the brain stem with relatively sparing the tegmentum.

Other differences were seen in the clinical course and laboratory data. Multiple sclerosis is a disease with remitting and exacerbating course, while neuro-Behçet's syndrome is always a progressive disease in spite of corticosteroid treatment. Laboratory data such as increased ESR, positive C-reactive protein and CSF pleocytosis suggest a more inflammatory process in neuro-Behçet's syndrome than in multiple sclerosis.

From these studies we conclude that neuro-Behçet's syndrome is a disease predominantly affecting men with the main lesions in the basal parts of the brain stem manifesting pseudobulbar palsy in association with inflammatory changes. The striking differences obtained in the present study are an aid to diagnosis and may be a guide to further investigation in search of the aetiology.

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