

VIEWS AND REVIEWS

Devic's disease and multiple sclerosis in Asia

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Abstract

There has been a number of recent publications citing differences in clinical features, CSF, MRI and pathology to support Devic's disease as a distinct disease from multiple sclerosis. However, the interpretation of the studies is complicated by the varied definitions. Many of the patients included in these studies would be classified as optic-spinal recurrent form of multiple sclerosis in the Asian literature. The evidences cited also suffer from circular nature of the argument. Data from the Malaysian multiple sclerosis patients showed that features of severe spinal cord disease was seen among classical Western multiple sclerosis patients as well as the optic-spinal recurrent form. It points to a general preponderance for severe spinal cord involvement among Asians with multiple sclerosis, rather than optic-spinal recurrent (or Devic's disease) as a distinct disease from multiple sclerosis.

Key words: Devic's disease, neuromyelitis optica, Asian multiple sclerosis

INTRODUCTION

There has been a number of recent publications in Devic's disease (neuromyelitis optica)¹⁻⁵ indicative of renewed interest in the disease. The main focus of the publications was to show that there were sufficient differences in the pathology, MRI, CSF and clinical features of Devic's disease when compared to multiple sclerosis for the former to be considered a distinct disease. Devic's disease has been known to be more common among Asians.⁶ With the recent availability of disease modifying treatment in multiple sclerosis, the discussions on Devic's disease are highly relevant to neurology practice in Asia. The Consensus Report by the Asia Pacific Multiple Sclerosis Consensus Group in this issue of the Journal is thus an important contribution.⁷

Varied definitions of Devic's disease

A recurring problem in the discussion of Devic's disease is the varied definitions used by different authors.^{8,9} The late Kuroiwa, a well-known authority on multiple sclerosis in Asia defined Devic's disease as a monophasic illness with acute bilateral optic neuritis and transverse (severe) myelitis occurring successively within a period of less than several weeks.⁶ This is close to the original understanding of Devic's disease.^{8,9} In the recent studies by Mandler et al¹ and O'Riordan et al³, although the requirement

of optic neuropathy and severe myelopathy was retained, a multiphasic illness and long interval between optic and spinal involvement were also allowed. Another recent study by Wingerchuk et al⁴ defined Devic's disease as involvement confined to the optic nerve and spinal cord. A multiphasic disease was allowed and myelopathy need not be severe. Most of the recent Asian publications on multiple sclerosis and Devic's disease adopted the definitions of Kuroiwa and his colleagues. As such, many of the patients from Mandler et al¹, O'Riordan et al³ and Wingerchuk et al⁴ would be classified as optic-spinal recurrence form of multiple sclerosis rather than Devic's disease in these Asian literature.^{10,11} Interpretation and application of these recent studies should thus be exercised with care.

Evidence supporting Devic's disease as a distinct entity

The evidence cited to support the view that Devic's disease is distinct from multiple sclerosis were based on clinical, CSF, MRI and pathological findings. Clinically, relapses in Devic's disease tended to be confined to the eye and the spinal cord. The prognosis was worse than the usual multiple sclerosis patients. The CSF may show pleocytosis of >50 cells/mm³ with fewer patients having oligoclonal bands. There were fewer lesions in the MRI of the brain. The lesions in the spinal MRI may extend

over more than two vertebral segments. The pathology in spinal cord showed more necrosis and cavitation, with less involvement of other parts of central nervous system.^{1-5,9}

A major drawback in using the above evidences is the circular nature of its argument. As patients with disease confined to the eye and spinal cord were the initial inclusion criteria, it is not surprising to find the patients to have relapses confined to the eye and spinal cord and less MRI brain lesions. Severe spinal cord involvement as included in the selection criteria would also by itself cause longer MRI spinal lesions, more pleocytosis in CSF, worse prognosis and more severe pathology. Furthermore, none of the features mentioned above is specific for Devic's disease. They can all be found in "classical" multiple sclerosis.

Multiple sclerosis in Malaysia

As mentioned above, many of the patients labelled as Devic's disease in the recent publications with relapsing optic nerve and spinal cord involvement would be classified as optic-spinal recurrence form of multiple sclerosis in many of the Asian studies. The optic-spinal recurrence form of multiple sclerosis is more commonly seen among Asians, accounting for up to 63% of the clinically definite multiple sclerosis patients.¹¹ In Asia where Devic's disease or optic-spinal form of multiple sclerosis is

commonly seen, does it occur as a distinct entity? We have analysed our earlier series of multiple sclerosis to answer this question.¹² The clinical definite multiple sclerosis may be divided into two groups, 20 patients with optic-spinal recurrent form of multiple sclerosis ("Devic's disease"), and another 15 patients with involvement beyond the optic nerve and spinal cord ("Western multiple sclerosis"). As shown in Table 1, there was no difference in the age of onset, sex ratio, relapse rate, disease severity, mortality, occurrence of acute transverse myelitis and paroxysmal tonic spasm in the two groups. Acute transverse myelitis and paroxysmal tonic spasm are features said to be particularly common among Asians with multiple sclerosis.^{10,13} We have earlier reported 10 other patients with clinically probable multiple sclerosis manifesting as relapsing myelopathy. The age of onset of these 10 patients were 32 years. The annual relapse rate was 0.45 with a F:M sex ratio of 2.3:1. Three of these 10 patients had paroxysmal tonic spasm. All these features are similar to the clinically definite multiple sclerosis thus indicating that they are same disease.¹³

Thus, our data do not support the concept of two distinct diseases, Devic's disease (or optic-spinal recurrent multiple sclerosis) and classical Western multiple sclerosis. Rather it is multiple sclerosis among Asians as a single disease characterised by frequent and severe spinal cord involvement. Among the Asians with multiple

TABLE 1: Comparison between optic-spinal recurrent form of multiple sclerosis ("Devic's disease") and "Western multiple sclerosis" in Malaysia

	"Devic's disease" (n=20)	"Western multiple sclerosis" (n=15)	P values
Age at onset (years)	31.4 ± 13.2	30.6 ± 11.5	0.86
Race (Chinese)	85%	87%	0.83
Sex (female)	95%	80%	0.29
Relapse rate (per year)	0.97	1.2	0.36
Blindness (per eye)	33%	23%	0.57
Bedridden	30%	13%	0.42
Mortality	40%	20%	0.28
Acute transverse myelitis	50%	40%	0.81
Paroxysmal tonic spasm	35%	27%	1.0

Footnote on statistical analyses – nonparametric variables were analysed using Mann-Whitney U statistics, Chi square or Fisher exact tests. Parametric variables were analysed using ANOVA.

sclerosis, there is a group of patients whose relapses is confined to the optic nerve and spinal cord. There is another group with a more disseminated involvement simulating classical Western multiple sclerosis. However, even within these patients, there is more severe spinal cord involvement. There is a third group of patients whose manifestation is confined to spinal cord only. This is in addition to other characteristics of Asian patients with multiple sclerosis; lower prevalence, rare occurrence of similar family history, higher female to male sex ratio and lower occurrence of oligoclonal band.^{10,13} This is consistent with a large comparative pathological studies on American and Japanese multiple sclerosis patients, where there were more Japanese patients with simultaneous optic and spinal involvement, often with necrotic and destructive lesions. However, similar necrotic and destructive cases were also seen among the patients from North America.¹⁴ Kira et al¹⁵ reported that the Western-type multiple sclerosis among Japanese was associated with HLA DRB1*1501 allele and DRB 5*0101 allele but not the Asian-type multiple sclerosis. Yamasaki et al¹⁶ found that Japanese patients with optico-spinal multiple sclerosis were more likely to have HLA DPB1*0501. The difference in genetic make-up such as HLA typing, may determine the target organs in multiple sclerosis and the severity of the inflammation.

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