

# Multiple sclerosis in South East Asia and diagnostic criteria for Asians

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## Abstract

Multiple sclerosis is an uncommon disease in Southeast Asia, having been characterised only recently. The estimated prevalence is about  $2 - 3/10^5$ , with high female to male ratio, but rare family history. As high as 40% of the patients had the optic-spinal phenotype; though patients in this region seldom progressed to the secondary progressive phase, disability was more severe due to severe spinal cord involvement. There is a great degree of overlap in clinical, radiological and laboratory features between the classical and the optic-spinal phenotypes, including long spinal cord involvement, few brain lesions, lower proportion of positive cerebrospinal fluid oligoclonal bands and anti-aquaporin-4 antibody. We proposed that future international diagnostic criteria need to take this into account.

## INTRODUCTION

Multiple sclerosis (MS) is an uncommon disease in South East Asia. However, the relatively high proportion of optic-spinal form of MS makes this the ideal place not only to study the relationship between the two forms MS, but also to test out the sensitivity and specificity of any diagnostic criteria which purport to differentiate between the two.

## MULTIPLE SCLEROSIS IN SOUTH EAST ASIA

MS is a relatively new disease in South East Asia. As recent as the late 1970's it was believed that it was so rare that it was not seen in many countries in the region, such as Malaysia and Indonesia. CT Tan undertook the first comprehensive study of the disease in Malaysia and this was published as a series of papers and his doctorate thesis from 1988 to 1990. Many of his observations still stand today.<sup>1,2</sup>

There is yet a large scale population-based prevalence study in the region. The prevalence often quoted is about 2 to  $3/10^5$ , a figure derived from comparative study using the relatively stable worldwide prevalence of amyotrophic lateral sclerosis.<sup>1,2</sup> The female to male ratio is 3.8:1, and it may be even higher in some ethnic groups.<sup>3</sup> Family history is rare, and there is yet a documented case of familial MS from many countries in the region, including Malaysia. Clinically, 40% of patients had the optic-spinal form. Ten years after the onset of the illness,

79% remained in the relapsing remitting phase. Interestingly, there was little difference between the classical, prototypic, western form compared to the optic-spinal form including the onset age, female to male ratio, severity as measured by EDSS, frequency of relapses and the proportion of positive oligoclonal bands. The only significant difference was the severity of spinal cord attacks and the resultant clinical manifestations. Myelitis and optic neuritis were important features, each being the presenting feature in a third of the patients, and each occurred sometime during the course of illness in half of the patient.<sup>3</sup>

Radiologically, there were many similarities between the two forms as well. On brain and spinal cord MRI, the appearance and distribution of lesions were similar, though patients with prototypic MS had more brain lesions while those with optic-spinal form more severe spinal cord disease. Importantly, spinal cord lesions longer than 2 vertebral segments were seen in 29% of prototypic and 54% of the optic-spinal form; while the average length of cord lesion was  $2.5 \pm 2.3$  vertebral segments in the former and  $4.2 \pm 3.6$  in the latter.<sup>4</sup> Not surprisingly, current international criteria has not been proven sensitive enough for use in the region. McDonald's MRI dissemination in space criteria was only positive in 52% of the patients who fulfilled Poser's criteria; 67% in the prototypic and 37% in the optic-spinal form.<sup>5</sup> Cerebrospinal fluid oligoclonal bands were positive in 33% and 14% respectively.<sup>3</sup> Recent report from Singapore suggested that serum anti-aquaporin-4 antibodies were positive in less than

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10% in patients with optic-spinal MS.<sup>6</sup> This was consistent with the findings from the Asia Pacific region that the overall positivity of anti-aquaporin-4 antibodies was low even among optic-spinal patients – about 5.6 – 27%. Interestingly, the autoantibodies were more likely to be positive in patients with MRI fulfilling Barkhof's criteria and those with long cord lesion, and not whether they had prototypic or optic-spinal MS.<sup>7</sup>

## DIAGNOSTIC CRITERIA FOR ASIANS

The diagnosis of MS in the region follows current, established, international criteria. The common diagnostic criteria used were that of Poser, and now, the modified McDonald criteria, which in essence, is to prove “dissemination in space and time without a better explanation”. McDonald criteria rely on the use of MRI where clinical evidence is insufficient. In practice, the criteria is less sensitive in this region as compared to elsewhere because of the fewer brain lesions in the Asian MS patients<sup>5</sup>, even among those with prototypic disease; as well as the disputed nature of long spinal cord lesions.<sup>4</sup> Furthermore, due to the large degree of overlap between prototypic and optic-spinal MS in the region, differentiation between the two has not been easy.<sup>2-6</sup> The finding of anti-aquaporin-4 antibodies and the proposal of a new diagnostic criteria for neuromyelitis optica<sup>8</sup>, which some asserted to be the same as optic-spinal MS<sup>9</sup>, confuses the issues even more. The great degree of clinical and radiological overlap between the two entities and the recent finding of the low sensitivity of the anti-aquaporin-4 antibodies even among the OSMS patients<sup>6,7</sup> not only makes the current diagnostic criteria<sup>9</sup> less discriminative, but also argues for the case that OSMS is a variant of MS instead of a distinct disease entity.

## REFERENCES

1. Tan CT. Multiple sclerosis in Malaysia. *Arch Neurol* 1988; 45:624-7.
2. Tan CT. Multiple sclerosis and other related diseases in Malaysia: Their clinical manifestations and laboratory findings. MD dissertation, University of Malaya, 1990.
3. Chong HT, Li P, Ong B, *et al.* Severe cord involvement is a universal feature of Asians with multiple sclerosis: A joint Asian study. *Neurol J Southeast Asia* 2002; 7:35-40.
4. Chong HT, Ramli N, Lee KH, *et al.* Magnetic resonance imaging of Asians with multiple sclerosis was similar to that of the West. *Neurol Asia* 2004; 9:47-53.
5. Chong HT, Ramli N, Lee KH, *et al.* Low sensitivity

- of McDonald MRI criteria in the diagnosis of multiple sclerosis among Asians. *Neurol Asia* 2006; 11:129-33.
6. Tan K, Shuguna M, Yee WC, *et al.* The seroprevalence of NMO-IgG in Singapore – a pilot study. *Neurol Asia* 2008; 13:205-6.
7. Chong HT, Kermode A, Tan CT. The role of anti-aquaporin-4 antibody in Asian patients with multiple sclerosis: Confusions and controversies. *Neurol Asia* 2007; 12:135-9.
8. Wingerchuk DM, Lennon VA, Pittock SJ, *et al.* Revised diagnostic criteria for neuromyelitis optica. *Neurology* 2006; 66: 1485-9.
9. Weinschenker BG, Wingerchuk DM. OSMS is NMO, but not MS: proven clinically and pathologically. *Lancet Neurol* 2006; 5:110-1.