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VIEWS AND REVIEWS

Proposed modifications to McDonald diagnostic criteria for Asians with multiple sclerosis

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Abstract

There are significant differences in the clinical and investigatory findings among Asian patients with multiple sclerosis (MS) versus those in the West. The McDonald diagnostic criteria do not take into account the different clinical presentation in Asian patients, and has low sensitivity among Asians. Modification to the McDonald criteria for Asian patients with MS is thus necessary. It is proposed that for Asian patients, magnetic resonance imaging (MRI) spinal cord lesions longer than 2 vertebral segments, spinal cord swelling and complete cross sectional involvement should not be exclusion criteria for the diagnosis of MS. To increase the sensitivity of McDonald criteria, 4 or more T2-hyperintense brain MRI lesions should be sufficient as one of the criteria for dissemination in space. Cerebrospinal fluid pleocytosis of more than 50/mm^3 should not automatically exclude the diagnosis of MS. Patients with relapses disseminated in space but confined to spinal cord should also be accepted as spinal MS.

INTRODUCTION

The use of magnetic resonance imaging (MRI) has greatly increased the sensitivity and specificity of diagnosis of multiple sclerosis (MS)[1-5], and thus has been incorporated into the latest diagnostic criteria.[6-9] However, most, if not all, of the MRI studies that form the basis for the diagnostic criteria are done among patients in Europe and North America.[1-5,9] There are significant differences in the clinical and investigatory findings of patients from Asia as compared to those from the West, such as more severe spinal cord disease with longer spinal cord lesions and fewer brain lesions in MRI of the Asian patients.[10-13] Although the revised McDonald criteria gives more weight to spinal cord lesion, it still does not address the differences in clinical presentation of MS among Asian patients.[8] In a recent joint Asian study, the McDonald criteria was only 49% sensitive in diagnosing MS among Asians. The sensitivity was slightly higher at 52% with the revised McDonald criteria.[14] The International Panel on MS Diagnosis in fact commented that the Asian neurological community will determine whether the Criteria can be generalized to their population, and how modifications to the Criteria will make them more appropriate in the Asian population.[8] This is a proposal to modify the McDonald diagnostic criteria for the Asian populations, with the basis that MS is an idiopathic inflammatory demyelinating disease disseminated in time and space.

MAGNETIC RESONANCE IMAGING

Spinal cord lesion longer than two vertebral bodies

The McDonald criteria stated that the spinal cord lesion should be at least 3 mm but under two vertebral segments in length.[7] In a joint Asian MRI study, it was found that the spinal cord lesions had a mean length of 3.6 ± 3.3 vertebral segments and 47% of the cord lesions were longer than 2 vertebral segments (29% in patients with classical MS and 52% in those with optic-spinal MS).[13] Long spinal cord lesions were

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also commonly observed in Japanese patients with MS.[15,16] Long spinal cord lesions are not uncommon among patients from the West, with 10% of all lesions in one study being more than 2 vertebral segments in length.[17] Very long lesions involving the whole spinal cord were assumed to result from the coalescence of more than one lesion and are called "diffuse lesions". The term was initially restricted to lesions that involved the entire length of the spinal cord, but in later studies, all lesions longer than two vertebral segments in length appeared to be classified as diffuse.[18-20] In one study, 13 out of 104 patients had diffuse cord lesions, with a mean length of 11.2 (± 5.7) vertebral segments involvement.[18] In other studies, 21 – 36% showed diffuse cord lesions.[19,20] In view of the fact that long spinal cord lesions are frequently seen in Asian patients with classical as well as optic-spinal MS, and are not uncommonly encountered in MS patients in the West, there should be no restriction to the length of spinal cord lesion in diagnosis of MS in Asians.

Spinal cord swelling and complete cross sectional involvement

The McDonald criteria stated that there should be no swelling of the cord and the lesion should occupy only part of the cross section of the cord.[7] In the revised McDonald criteria, these issues are not specifically addressed.[8] In the joint Asian MRI study, cord swelling was seen in 23% of the lesions (13% in classical MS and 29% in optic-spinal MS). Complete cross sectional involvement was also seen in 23% of the lesions (7% in classical MS and 33% in optic-spinal MS).[13] Cord swelling was also reported in 15% of one Japanese series.[15] Therefore, spinal cord swelling and complete cross sectional cord involvement should not exclude the diagnosis of MS in Asians.

Brain MRI Findings

The McDonald criteria[7] require 9 T2-hyperintense MRI brain lesions or one gadolinium-enhancing lesion as one of the evidence of dissemination in space. In the revised McDonald criteria[8], an enhancing spinal cord lesion is considered equivalent to an enhancing brain lesion. In the recent joint Asian study, these McDonald dissemination in space criteria had a sensitivity of only 49% among Asians with MS. The sensitivity was slightly higher at 52% with revised McDonald criteria.[14] The low sensitivity is partly due to fewer brain lesions among Asians with MS.[13] In the joint Asian study, only 53% of the patients had 9 or more T2-hyperintense lesions, (35% in

Table 1: Proposed modifications to McDonald diagnostic criteria for Asians with multiple sclerosis

McDonald diagnostic criteria[7,8]	**Proposed modifications for Asians**
Spinal MRI	
Spinal cord lesion should be under 2 vertebral bodies in height	No restriction to length of spinal cord lesion
No swelling of the spinal cord lesion	No restriction to spinal cord lesion with swelling
Spinal cord lesion should occupy part of the cross section	No restriction to spinal cord lesion involving complete cross section
Brain MRI	
9 T2-hyperintense lesions or one gadolinium-enhancing lesion	4 or more brain MRI T2-hyperintense lesions in patients less than 60 years of age or one gadolinium-enhancing lesion
Cerebrospinal fluid	
Lymphocyte pleocytosis should be < 50/mm^3	No restriction on CSF pleocytosis
Disease restricted to spinal cord	
Dissemination of space should not be restricted to spinal cord	No restriction to lesions clearly separated in space but limited to spinal cord

optic-spinal MS versus 69% in classical MS).[14] The low sensitivity of the McDonald criteria among Asians contrasts with the published results of 82% sensitivity in Western MS patients with 73% having 9 or more T2-hyperintense cerebral lesions.[5]

To improve the sensitivity of brain MRI in diagnosing MS among Asians, we propose that the McDonald criteria should be modified to include 4 or more T2-hyperintense lesions in Asian patients under the age of 60 years. In patients over the age of 60 years, the increased possibility of cerebral ischemic conditions might confound the significance of fewer than 9 T2-hyperintense lesions. In the joint Asian MRI study, 69% of patients had 4 or more T2-hyperintense brain lesions (84% in classical MS and 52% in optic-spinal MS). In fact, a lower number of T2-hyperintense lesions had been found to be predictive of conversion from clinically isolated syndrome (CIS) to clinically definite MS in Western patients. In a review including no less than 10 trials, Frohman *et al* noted that 38% to 89% of CIS patients with 3 to 4 or more lesions convert to clinically definite MS over a variable period.[21] Treatment trials using similar criteria have shown that close to 50% of untreated CIS patients with 3 to 4 or more lesions convert to clinically definite MS in 37 months.[22,23] A number of studies have shown that the presence of T2 lesions were predictive of conversion to clinically definite MS, while there was only a weak association between the number of lesions with subsequent development of clinically definite MS.[21,24]

CEREBROSPINAL FLUID PLEOCYTOSIS

The McDonald criteria[7] require that the lymphocyte pleocytosis in cerebrospinal fluid (CSF) should be less than 50/mm^3. There has been a number of studies reporting significant proportion of Asian MS patients having CSF pleocytosis of more than 50/mm^3 (12% in Japan[25], 9.5% in Taiwan[26] and 4.7% in China[27]). Kira *et al*[15] from Japan noted that CSF pleocytosis was more marked among their Asian patients as compared with Western MS patients. In view of the above findings, it is proposed that CSF pleocytosis of more than 50/mm^3 should not automatically exclude the diagnosis of MS in Asian patients.

SPINAL MULTIPLE SCLEROSIS

The McDonald criteria stated that two or more spinal cord lesions clearly separated in time and space could possibly satisfy the criteria for MS but the International Panel on MS Diagnosis decided to await further data.[7] Relapses limited to the spinal cord accounts for a significant proportion of MS patients in Asia. A Malaysian report found 20% of patients having relapses limited to the spinal cord.[28] The corresponding figure from Thailand was 4 out of 54 patients (7.4%).[29] In a series of pathological study comparing 70 American and 75 Japanese MS patients, 9 Japanese patients (12%) were found to have relapses limited to the spinal cord. This was not found among the Americans.[30] Therefore, Asian patients with two or more spinal cord lesions clearly separated in time and space should be accepted as having MS.

CONCLUSION

The above proposed modifications to the McDonald diagnostic criteria has been suggested with the view of enhancing its sensitivity for diagnosis of MS in Asian patients, who has different clinical presentations from West MS patients. We do acknowledge that prospective studies should be done on Asian MS patients to determine the sensitivity and specificity of these modified criteria, in particular regarding use of 4 or more T-hyperintense lesions as one of the criteria for dissemination in space.

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