

MEDICAL *express* REPORTS

ISSN 0956-8298
VOLUME 16 ISSUE 1

**3rd MS Forum
Pan-Asian
Conference**

5-6 November 2005

The unique characteristics of multiple sclerosis (MS) in Asia were the main focus of discussions at the 3rd MS Forum Pan-Asian Conference held in Sydney, Australia.

The *MS Forum* began to foster collaboration among Asian neurologists in 2003, recognizing that some forms of MS in Asia differ from the western disease and that this has implications for diagnosis, prognosis and disease management. This third *MS Forum Pan-Asian Conference* was held over 2 days, and was chaired by Professor Jun-ichi Kira of Kyushu University, Fukuoka, Japan, and Dr Allan Kermode of the Sir Charles Gairdner Hospital, Perth, Australia.

This issue of *Medical Express Reports* describes topics discussed at the conference, which brought together international neurologists and neurologists from the Asia Pacific and Middle East regions to address issues specific to MS in Asia, such as classification, development of diagnostic criteria and recent advances in MS management. The majority of delegates (71.4%) found the meeting extremely useful and 88.6% said that they would like to attend a similar event in 2006. ■



© Gary Brand

The Sydney Opera House is an impressive landmark of the Australian city, Sydney – host of the 3rd MS Forum Pan-Asian Conference.

Consensus reached on MS in Asian populations

Since the last *MS Forum Pan-Asian Conference* in Ho Chi Minh City, Vietnam, in 2004, the 2nd Consensus Group Meeting produced a statement on a range of issues relating to the classification and diagnosis of multiple sclerosis (MS) in Asian populations.

The Consensus Group agreed that the Poser criteria are useful in the diagnosis of MS in Asia, but that they do not facilitate early diagnosis, which reduces

the chance of initiating early treatment. The McDonald criteria for magnetic resonance imaging appear to have less utility for early diagnosis of MS in Asia because they do not address the spinal cord features more commonly seen in Asian patients. The McDonald criteria need to be validated in the Asian population and it was suggested that there might be a need for modified criteria, which would then serve as a basis for further clinical and laboratory research in Asian MS. ■

Choosing the optimum MS therapy

Increasing the Betaferon® dose from 250 µg to 375 µg every other day (eod) has been shown to reduce the signs of disease activity on magnetic resonance imaging (MRI) scans and the incidence of relapses in patients with relapsing-remitting multiple sclerosis (RRMS) after a suboptimal treatment response to 6 months of 250 µg Betaferon® eod. This provides more evidence of a dose-response effect for interferon beta (IFN-β), and Professor Luca Durelli from Turin University, Italy, explained that he strongly believes the highest currently approved dose of 250 µg Betaferon® is unlikely to be the maximum effective dose.

Prophylactic treatments to prevent flu-like symptoms and titration schedules have helped to limit the side-effects associated with higher doses of IFN-β in the short term, thus making it possible to evaluate efficacy of higher doses. The OPTimization of Interferon dose for Multiple Sclerosis (OPTIMS) study, which aimed to test the efficacy of two different doses of Betaferon® (250 µg and 375 µg eod) in RRMS patients, has just been completed. At the end of the initial 6-month treatment period with

The 250 µg dose of Betaferon® is unlikely to be the maximum effective dose

250 µg Betaferon®, patients with a sub-optimal treatment response, demonstrated by persistent signs of disease activity on MRI scans or persistent relapses,

were randomized to receive either 250 µg or 375 µg Betaferon® eod for a further 6 months. The 375 µg dose of Betaferon® reduced the risk of MRI activity by 72%, significantly reduced the number of patients with new PD/T2 and new gadolinium-positive lesions, and significantly increased the time to first active lesion, while maintaining a safety profile comparable with that of 250 µg Betaferon®. Both the 250 µg and 375 µg doses of Betaferon® were well tolerated. ■

Betaferon® – treatment effect after 16 years

Long-term follow-up of the original 372 patients enrolled in the pivotal Betaferon® trial has identified 331 (89%), which is a considerable achievement, reported Professor George Ebers, University of Oxford, Oxford, UK. The long-term effects of immunomodulatory treatment are of interest to physicians, because MS is a chronic disease which can affect patients for decades, and yet studies have so far provided data over a relatively limited time span. Of those patients identified in the long-term follow-up, 50% have been taking Betaferon® for more than 10 years and some for up to 16 years.

Case-report forms for 210 patients show that 33% are currently taking 250 µg Betaferon® and 41% have taken 250 µg Betaferon® for more than 80% of the time span between the end of the pivotal trial and 23 September 2005. The median exposure to 250 µg Betaferon® in the 210 patients has been 3644 days (i.e. 10 years).

Of the 331 patients identified to date, 297 (90%) are alive and 34 (10%) deceased. Of those who are alive, 175 (59%) are ambulatory and 76 (26%) use a wheelchair or are bedridden. Analysis of the patient disposition according to original treatment allocation of those who have been identified shows that a larger proportion of the patients originally treated with 250 µg Betaferon® remain alive (105/111; 95%) compared with the placebo-treated group (91/110; 83%). The difference in

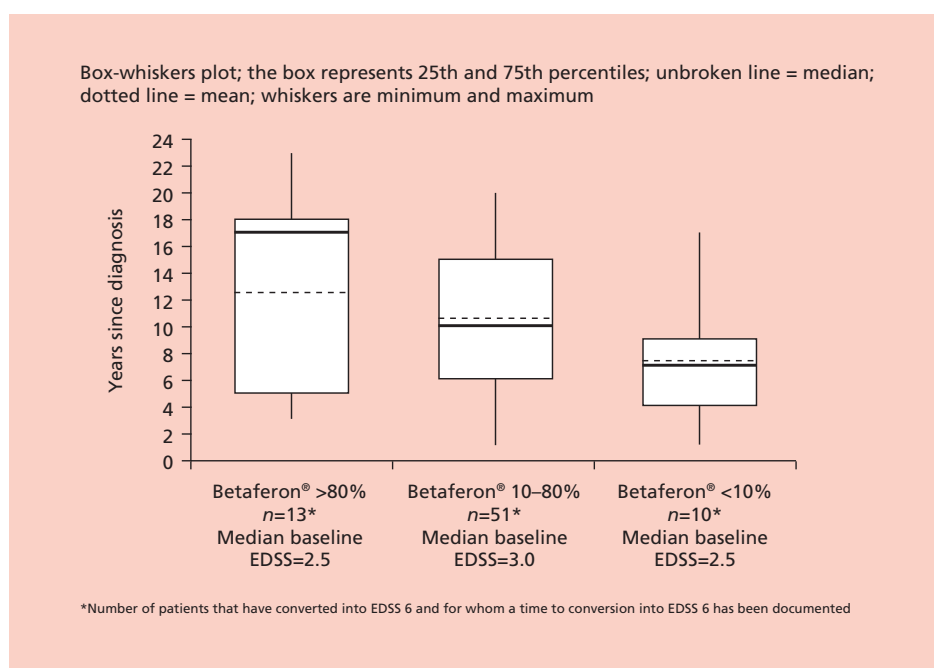


Figure 1: Time to an EDSS score of 6 stratified according to exposure to Betaferon® (exposure calculated for the time between start of treatment in the pivotal trial and 2005).

survival rate between the placebo- and Betaferon®-treated groups requires further investigation.

Preliminary results suggest that long-term Betaferon® treatment increases the time to Expanded Disability Status Scale (EDSS) progression, reported Professor Ebers. Patients treated with Betaferon® for more than 80% of the

Of those patients identified...50% have been taking Betaferon® for more than 10 years and some for up to 16 years

time between the start of the pivotal trial and 2005 demonstrated a longer time to reach an EDSS score of 6 than those treated for less than 10% of the time (Figure 1). The findings also appear to support the hypothesis that initiation of Betaferon® treatment early in disease progression has long-lasting beneficial effects. ■

Working towards diagnostic standards for demyelinating disease

The broad range of presenting features and considerable potential for alternative causes complicates the differential diagnosis of MS. It is an idiopathic inflammatory demyelinating disease that is restricted to the central nervous system and is characterized by dissemination of lesions in both time and space, for which there is no other identified cause, stated Dr Allan Kermode of the Sir Charles Gairdner Hospital, Perth, Australia.

In classical MS (CMS), the most frequent symptoms are limb weakness, unilateral optic neuritis and paraesthesia. Certain key symptoms should also alert the clinician to an alternative diagnosis. The situation is further complicated by differences in the symptom profiles of western and Asian patients. For example, only 4% of western CMS patients will have tonic spasms compared with 16% of Asian CMS patients, and 46% of Asian patients present with optic-spinal MS (OSMS).

The degree of spinal cord involvement is also variable and may not always comply with the McDonald criteria for

MS (McDonald WI *et al. Ann Neurol* 2001; 50:121). Dr Kermode suggested that these guidelines may be applicable to most cases in the West, but are probably too restrictive for cases in Asia, even for Asian CMS. The minimum requirements for the clinical evaluation of demyelinating disease are shown in Table 1. Most delegates reported having access to oligoclonal band tests (85%), evoked potential studies (94%) and magnetic resonance imaging (MRI; 100%). There is clearly an urgent need to characterize and define the spectrum of demyelinating diseases in the Asian region and their relationship to western forms, said Dr Kermode.

More research is needed to verify the use of the McDonald criteria in Asian patients

Professor Jun-ichi Kira and colleagues of Kyushu University, Fukuoka, Japan, have retrospectively applied the McDonald/Barkhof MRI criteria to 108 consecutive Japanese patients with clinically definite relapsing-remitting MS according to the Poser criteria (Poser CM *et al. Ann Neurol* 1983;13:227) to evaluate their relevance in the early diagnosis of MS in Asian patients. A total of 38 patients had OSMS, 52 had CMS and 18 had spinal or brainstem spinal MS (SMS); and only 40.7% fulfilled the Barkhof criteria (Barkhof F *et al. Brain* 1997;120:2059). The study found that the McDonald MRI criteria were not applicable to Asian patients with a clinically isolated event suggestive of MS and that the Poser criteria should be applied. More research is needed to verify the use of the McDonald criteria in Asian patients and to delineate the natural history of Asian MS. In principle, 95% of delegates supported the development of an MS registry for Asia. ■

Record of first symptoms, their nature and duration

Detailed neurological examination (ideally EDSS/FSS)

Complete general examination (cardiorespiratory, gastrointestinal tract, lymphadenopathy)

Investigations:

- Serum B12
- Antinuclear antibody screen
- Cerebrospinal fluid examination, if possible
- Targeted MRI imaging
- Visual evoked potentials (desirable)

Other investigations dictated by history and examination

EDSS, Expanded Disability Status Scale; FSS, Functional Systems Score.

Table 1: Minimum requirements of an objective clinical evaluation in patients with demyelinating disease.

MS in MRI – an educational CD-ROM for neurologists and radiologists

In 2004, Professor Ernst-Wilhelm Radue (University Hospital, Basel, Switzerland) and his team published an educational CD-ROM, entitled 'MS in MRI – a learning CD-ROM', that helps neurologists become more familiar with magnetic resonance imaging (MRI) findings in MS. It also includes information for radiologists on recent MRI developments in MS research. Professor Radue demonstrated the CD-ROM during his presentation.

The CD-ROM covers the technical requirements for MRI and shows examples of the appearance of typical lesions in different sequences. It contains detailed information on the possible pitfalls of MRI in the differential diagnosis of MS, and provides standardized examination protocols and a review of potential future technological advances. A highly invaluable interactive section also enables the user to assess their level of understanding of MRI. The *MS Forum* is grateful to Professor Radue who made available, with the generous support of Schering AG, copies of the CD-ROM for attendees. The CD-ROM can be ordered by contacting Professor Radue (eradue@uhbs.ch). ■

MS disease variability in western and Asian populations

Tonic seizures, transverse cord myelitis and dysphagia are seen more frequently in Asian patients with classical MS (CMS) than western patients, explained Professor David Bates, Newcastle-upon-Tyne, UK. He compared the symptoms of CMS in western and eastern populations, highlighting these important differences as well as the many similarities (weakness, paraesthesia and optic neuritis).

Although we know much more about the characteristics and natural history of MS in Caucasian populations than in Asian populations, he said that MS can be highly variable even in Caucasians. For example, the Marburg variant (severe acute onset MS) has been recorded in up to 5% of Caucasian patients; as many as 25% of patients have apparently benign disease; and

Devic's neuromyelitis optica (NMO) accounts for less than 1%.

A study of western non-Caucasians (African-Americans) demonstrated that they were much more likely to develop optic-spinal MS and transverse myelitis than Caucasian Americans (Cree BA *et al. Neurology* 2004;63:2039). African-Americans also had a more aggressive disease course. Neuromyelitis optica, a condition that selectively targets the optic nerves and spinal cord, is also more common in non-Caucasians and is often misdiagnosed as MS (Lennon VA *et al. Lancet* 2004;364:2106). Clearly, there is variability in the forms of MS not only between different racial groups but also among Caucasians, which raises the possibility that there are distinct forms of the disease. Professor Bates explained that we need to develop appropriate criteria to define MS variants clinically, using magnetic resonance imaging and biological tests. ■

Challenges of managing MS in South-East Asia

Not only do the unique characteristics of MS in Asia present problems for disease management, but so does the healthcare infrastructure in many South-East Asian countries, reported Professor Benjamin Ong of the National University of Singapore, Singapore. Furthermore, because of these issues, the prevalence rates of MS in Asia are likely to be underestimated.

The three main areas of concern are diagnosis, treatment and support services. In terms of diagnosis, the patient needs access to physicians with the appropriate expertise, access to specialized investigations that require specific

equipment and the application of diagnostic criteria relevant to their MS. This latter issue has been partially dealt with by the 2nd Consensus Group Meeting's 2005 consensus statement for Asia.

Professor Ong explained that the prevalence of MS is variable across South-East Asia (Table 2). He said that, in Taiwan, as in other Asian populations, MS prevalence is low although optic-spinal MS is common. In contrast, the symptoms at onset in Japanese patients with MS are like those seen in western patients.

Physicians in Asian countries may be restricted by the lack of specialized equipment, explained Professor Ong.

| Country | Prevalence of MS per 100000 population |
|-----------|--|
| Japan | 2.5 (1975) to 10.2 (2002) |
| Taiwan | 0.8 (1976) to 1.9 (2004) |
| Hong Kong | 0.88 (1989) to 0.77 (2002) |
| Thailand | 2 |
| Malaysia | 2 |

Table 2: Prevalence of MS in Asia.

As of 2000, Thailand had 26 magnetic resonance imaging devices, 15 of which

were privately operated. A similar situation exists for evaluating biological

samples such as oligoclonal bands. Access to treatment is also variable – in several countries the individual patient bears the cost of treatment – as are levels of support, such as physiotherapy and cognitive rehabilitation. If available, the facilities may not be specific to MS patients, but will be shared with patients diagnosed with other conditions. Community-based resources and caregiver training and support are also likely to be extremely limited in Asia. ■

Optic-spinal MS and neuromyelitis optica – the same or different?

Optic-spinal MS (OSMS) is very similar to neuromyelitis optica (NMO), explained Professor Kazuo Fujihara of Tohoku University, Sendai, Japan. However, he said that when the possibility that they might be identical was discussed at the Second Pan-Asian Conference in Ho Chi Minh City, the evidence to support this theory was considered insufficient. More light may be shed on this by the recent identification of an NMO-specific autoantibody, NMO-IgG.

Professor Fujihara compared OSMS with classical MS (CMS), describing how the two conditions have distinct characteristics, such as bilateral optic neuritis and acute transverse myelitis in OSMS, compared with disseminated (periventricular) lesions in CMS. OSMS is often more severe than CMS. The cord lesions in OSMS are usually

centrally located and >3 vertebral segments long compared with non-central lesions that are <2 vertebral segments long in CMS.

Optic-spinal MS is a devastating demyelinating disease that selectively targets the optic nerves and the spinal cord. In addition to these unique clinical

features it is also associated with a female preponderance, negative oligoclonal IgG bands in cerebrospinal fluid and longitudinal extended spinal cord lesions.

Professor Fujihara concluded by suggesting that further investigation is needed to examine the correlation between OSMS and NMO. ■

Using the unique MRI and clinical features of MS in Asia

Asian patients with MS demonstrate unique features compared with their western counterparts. Interestingly, many of these are also shared with MS patients from Brazil, Kenya, Martinique and with black South Africans. Dr Victor HT Chong, University of Malaya, Kuala Lumpur, Malaysia, reviewed two multicentre studies that described the clinical and magnetic resonance imaging (MRI) features of classical MS (CMS) and optic-spinal MS (OSMS) in Asian patients.

The first study investigated the clinical features of Asian MS and recruited 263 patients from seven countries. Of these, 79% of patients had relapsing-remitting MS. In 33% of patients the first attack was in the spinal cord, in 29% it was in the optic nerve, and in 4% it was in both sites. Oligoclonal bands were present in 27% of

patients. When comparing OSMS with CMS, a higher proportion of OSMS patients had transverse myelitis (67% versus 31%, respectively) and paroxysmal tonic spasms (46% versus 16%), and fewer had oligoclonal bands (14% versus 33%).

When brain lesions from CMS patients

were compared with those from OSMS patients in the second study, there were more lesions and more enhancement in OSMS patients, but the distribution was similar. There were, on average, 1.4 spinal cord lesions per patient. Spinal cord MRI lesions in patients with CMS were generally smaller than those from OSMS patients. CMS patients also had fewer complete cross-section lesions compared with OSMS patients (7% versus 33%, respectively), and fewer T1 hypointense lesions (15% versus 37%). There were no differences in spinal cord swelling or atrophy between CMS and OSMS patients, and long spinal cord lesions were found in both groups.

Dr Chong concluded that spinal cord involvement is common in Asian MS (88% of patients), even in those patients with CMS. ■

Consensus needed on clinical criteria of MS variations in Asia

Distinguishing between the various idiopathic inflammatory demyelinating diseases of the central nervous system, such as classical MS (CMS), clinically isolated syndromes and fulminant/monophasic syndromes can be quite difficult, explained Professor Kwang-Kuk Kim, University of Ulsan, Seoul, Korea. Although the McDonald criteria are very helpful in establishing evidence of recurrence, he questioned whether their limitations could result in some patients not receiving immunomodulatory treatment. According to Dr Toshiyuki Fukazawa, Nishimaruyama Hospital, Sapporo City, Japan, we need to develop a consensus on the different MS syndromes and produce revised clinical criteria that take into account observed ethnic variations.

Professor Jamshid Lotfi, University of Tehran, Iran, said that the McDonald criteria might underestimate the importance of spinal cord lesions. They can also be of only limited help when classifying and distinguishing between some of the demyelinating disease variants such as optic-spinal MS (OSMS), neuromyelitis optica, recurrent optic neuritis and myelitis. It is currently not clear if these variants represent MS or are distinct conditions.

Dr Fukazawa was presenting data from the Japanese nationwide MS survey of 2004, which found that primary progressive MS was rare, particularly in patients with OSMS. Japanese patients tended to have few brain lesions, but optic nerve and spinal cord lesions were relatively common. Spinal cord lesions ≥ 3 vertebral segments long were found in 41.2% of OSMS patients, but they were also seen in 16.7% of CMS patients.

McDonald criteria might underestimate the importance of spinal cord lesions

Oligoclonal band testing was not thought to be useful in Japanese patients with either OSMS or CMS.

In Shanghai, China, Professor Qi Cheng and her colleagues from Ruijin Hospital identified 179 patients with MS according to the McDonald criteria; of these, 63.1% were found to have spinal cord lesions, 53.6% cerebrum lesions, and 44.1% optic nerve involvement. Magnetic resonance imaging was positive in 95% of patients. Periventricular lesions were the most frequently identified (42.9%), and some patients (15.7%) only had lesions in the

spinal cord and not in the brain (Table 3). A total of 49% of patients had oligoclonal IgG bands. The majority of patients were treated with corticosteroids alone (86%). Professor Cheng estimated the prevalence of MS to be at least 1.06/100 000 in Shanghai with a female:male ratio of 2.24:1.

The HLA-DP β 1 genotype might be helpful as a diagnostic aid for OSMS

Professor Kim reported findings from 49 cases diagnosed with MS according to the Poser criteria. Twenty-four patients were diagnosed with OSMS on the basis of the Kira criteria, with main symptoms of optic neuritis and myelitis (Kira J *et al.* *Ann Neurol* 1996;40:569). The remaining 25 patients were diagnosed with idiopathic recurrent myelitis (IRM). There was a significant female preponderance in OSMS (20/24 patients) and a significant male preponderance in IRM (20/25 patients) ($P=0.0001$). The majority of OSMS patients (62.5%) had optic neuritis. Cervical spinal cord lesions were more common in OSMS patients than in IRM patients, and thoracic lesions were more frequently seen in IRM. OSMS was associated with human leukocyte antigen (HLA)-DP β 1*0501 and was negatively associated with HLA-DP β 1*0201. Professor Kim concluded that IRM might be a distinct disease entity from OSMS and that the HLA-DP β 1 genotype might be helpful as a diagnostic aid for OSMS. ■

| Lesion type | Number of patients | Percentage (%) |
|---|--------------------|----------------|
| Periventricular lesions | 60 | 42.9 |
| Periventricular and infratentorial lesions | 31 | 22.1 |
| Infratentorial lesions | 15 | 10.7 |
| Periventricular, infratentorial and corpus callosum lesions | 4 | 2.9 |
| Periventricular and corpus callosum lesions | 2 | 1.4 |
| Other lesions not associated with MS | 2 | 1.4 |
| No lesions in the brain (lesions in the spinal cord) | 22 | 15.7 |
| Unknown | 4 | 2.9 |
| Total | 140 | 100.0 |

Table 3: Types of brain lesion identified in 140 Chinese patients with MS who had brain scans in a population-based survey in Shanghai, China.

Simple, clinically useful diagnostic criteria for MS

Diagnostic criteria must be simple or they will be ignored, stated Professor Alan Thompson, University College London, London, UK, during his presentation on how the diagnostic criteria for MS have evolved over the past 50 years. Clinically useful diagnostic criteria should describe the clinical phenotype of a condition while still maintaining a clear distinction between the condition and other similar conditions. MS presents neurologists with problems because it has such a broad spectrum of clinical presentation.

In 2005 the McDonald criteria for MS were revised by an expert panel that re-assessed the existing criteria, recommended appropriate changes, retained useful features of prior criteria, integrated imaging into the criteria, and added criteria for primary progressive MS (Table 4). The panel also sought to clarify definitions, simplify categories and create a scheme that would be useful for practitioners. The revised McDonald criteria were published in late 2005 (Polman CH *et al. Ann Neurol* 2005;58:840). Clinical expertise is required to interpret a patient's history and to evaluate clinical signs in order to determine if the criteria for attacks are fulfilled and whether there is evidence for dissemination in time and space.

Diagnostic criteria must be simple or they will be ignored

Magnetic resonance imaging (MRI) provides evidence for dissemination in space and time.

Professor Thompson concluded that, as diagnostic criteria evolve over time, they should aim to maximize specificity (to avoid false positives) while gradually increasing sensitivity, and that it is essential that they are validated on new cohorts of unselected patients. ■

Demonstration of dissemination in time

- Gadolinium-enhancement at least 3 months after onset of the initial clinical event, if not at site of event
- New T2 lesion at any time compared with a reference scan done at least 30 days after onset of the initial clinical event

Spinal cord imaging

- Exclusion of alternative diagnosis
- Useful in showing dissemination in space if brain lesions are not informative
- Equivalent to a brain infratentorial lesion
- Can contribute along with individual brain lesions to reach required lesion number

Diagnosing primary progressive MS

- 1 year of disease progression (retrospective or prospective)
- Plus 2/3 of the following:
 - + brain MRI (9 T2 lesions or ≥4 lesions with +VEP)
 - + spinal cord MRI (≥2 focal T2 lesions)
 - + CSF by oligoclonal bands using isoelectric focusing and/or elevated IgG index

VEP, visual evoked potentials; CSF, cerebrospinal fluid.

Table 4: *The Amsterdam Revisions to the McDonald diagnostic criteria for MS (2005).*

Case studies demonstrate the difficulties in diagnosing MS

Professor David Bates of the University of Newcastle-upon-Tyne, UK, and Dr Kwang Ho Lee of the Samsung Medical Centre, Seoul, Korea, moderated a case study session showing just how difficult it can be to provide a differential diagnosis of MS in patients from Asia and the Middle East. The delegates rarely reached consensus, particularly in cases with complex features.

Dr Lee presented the case of a 30-year-old woman with symptoms suggestive of MS and who gradually developed spinal cord and brain lesions. Sjögren's syndrome was diagnosed with the Schirmer test, salivary gland scintigraphy and lip biopsy. Just over half of the delegates thought that this was Sjögren's syndrome mimicking MS.

The case of another woman who presented with optic symptoms and

brain lesions suggestive of MS was discussed by Professor Aksel Siva, University of Istanbul, Turkey. This case followed a course typical of classical MS and eventually the patient fulfilled both the Poser and McDonald criteria and is now being treated with interferon beta.

Professor Naraporn Prayoonwiwat, Siriraj Hospital, Bangkok, Thailand, reported on several cases of optic-spinal MS, a

case of neuromyelitis optica (NMO), and one unusual case of NMO that also had brain lesions suggestive of MS. Human T lymphotropic virus type 1 (HTLV-1) is associated with myelopathy (HAM)/tropical spastic paraparesis.

Professor Fujio Umehara, Kagoshima University, Japan, presented the case of a 54-year-old woman, whose mother was an HTLV-1 carrier, who presented with dysaesthesia and muscle weakness, ambulatory problems and bladder dysfunction.

The case of a woman with primary Sjögren's syndrome (PSS) that mimicked MS was presented by Professor Ching-Piao Tsai, Veteran's General Hospital, Taipei, Taiwan, who explained that PSS is an important differential diagnosis in patients in Taiwan. ■

Treating the first clinical event can reduce risk of MS progression

The first clinical event suggestive of MS has to be taken seriously and this was emphasized by Professor Mark Freedman of Ottawa University, Canada. He was highlighting the results of the BETAferon®/Betaseron® in Newly Emerging multiple sclerosis For Initial Treatment (BENEFIT) study that showed patients with a first clinical event are at a high risk of developing MS, with 85% of placebo-treated patients developing MS according to the McDonald criteria within 2 years (51% at 6 months). There is increasing evidence that irreversible asymptomatic axonal damage occurs early in MS.

Professor Freedman suggested that immunomodulatory therapy should be started at the time of the first inflammatory attack because, if the patient is allowed to have a second attack, considerable subclinical damage might have already occurred. With Betaferon® treatment the onset of clinically definite MS (CDMS) was delayed by 1 year at the 25th percentile compared with placebo, and there was a risk reduction of 50% over 2 years from the development of CDMS in the Betaferon® group. Furthermore, analysis of data so far has demonstrated that Betaferon® significantly reduced the risk of progression to CDMS by 55% ($P < 0.00001$) in patients with monofocal disease onset (i.e. signs and symptoms that were explained by a single demyelinating lesion).

The first clinical event suggestive of MS has to be taken seriously

The BENEFIT study is the largest clinical trial in patients with clinically isolated syndromes and magnetic

resonance imaging suggestive of MS, and it uniquely offers pre-planned long-term analysis of the effects of early intervention with interferon beta-1b (250 µg subcutaneously [sc]) every other day (eod).

To be representative of real-life clinical practice, the study included patients with both mono- and multifocal disease onset.

Two earlier studies, CHAMPS (Jacobs CD *et al. N Engl J Med* 2000;18:898) and ETOMS (Comi G *et al. Lancet* 2001;357:1576), had demonstrated that once-weekly, low-dose interferon beta-1a (30 µg intramuscularly [im] or 22 µg sc, respectively) in patients who had experienced a first clinical event reduced the risk of conversion into CDMS. While Professor Freedman acknowledged that care should be taken in comparing results from different studies, comparisons are inevitable. With this in mind, he commented that in patients with a first clinical event suggestive of MS, the relative treatment effect generated by 250 µg interferon beta-1b eod is of a greater magnitude than a similar treatment effect seen with once-weekly interferon beta-1a (30 µg im or 22 µg sc) in separate studies.

With Betaferon® treatment the onset of clinically definite MS was delayed by 1 year

Clinicians know they can rely on Betaferon® to be highly effective in patients with confirmed MS but, explained Professor Freedman, they should also now look at treating patients who might be at the very earliest stage of the disease. This is an important message when considering that 64% of the delegates said that their hospitals would see over 10 new patients per year and a fifth reported they would see 5–10 patients per year with clinically isolated syndromes such as optic neuritis.

Discontinuation data from the BENEFIT study reveal a high level of patient adherence to Betaferon®, demonstrating that Betaferon® is well tolerated in this group of patients where treatment was initiated following the first clinical event suggestive of MS. Further valuable data should be available in 2008. ■



Medical Express Reports is produced and published by Cambridge Medical Publications, a division of PAREXEL MMS Europe Ltd, and this issue is supported by Schering AG, Berlin, Germany.

Every effort has been taken to ensure accurate reporting of the presentations covered in this publication. Opinions expressed by participants are their own and do not represent endorsement by and are not to be attributed to either the publisher or the grantor. In so far as any product is named, its use, dose, or means of administration for an indication are for research purposes only and Cambridge Medical Publications and the grantor cannot be held responsible for the validity of clinical treatments, dose regimens, or other medical statements. Independent verification should be made of product dosages, means of administration and their approved usage in different indications and different countries. Individuals should always consult their physician prior to using any of the products mentioned or before changing the dose or stopping treatment. The relevant data sheet for a product or the current package insert recites the manufacturer's recommendations as to safe and effective use and should be consulted prior to use. Where a product may be mentioned that is not licensed, individuals are advised to contact the local office of the manufacturer for information on the current licensed indication status.

Reprint orders and all correspondence concerning this issue should be directed to Cambridge Medical Publications, Wicker House, High Street, Worthing, West Sussex, BN11 1DJ, UK.

© 2006 Cambridge Medical Publications. All rights reserved.