IS MULTIPLE SCLEROSIS IN BRAZIL AND ASIA ALIKE?

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SUMMARY — The clinical picture of 67 consecutive patients with definite multiple sclerosis in Belo Horizonte, Brazil, was analysed. There were 20 patients with the predominant optic-spinal form of the disease and eight with Devic’s disease. Visual loss occurred in 43% of the cases as the presenting symptom and in 84% in the course of the illness. Symptoms related to spinal cord and cerebellar involvement were observed in 64% and 52% respectively. The high prevalence of visual and spinal abnormalities at onset and during the course of the illness, the lesser common involvement of the cerebellum and the relative frequency of Devic’s disease make multiple sclerosis in Brazil similar to that observed in Eastern countries in distinction to the clinical pattern seen in the United States and Europe.

KEY WORDS: multiple sclerosis, clinical characteristics, geographical similarities (Brazil and East Asia countries).

A esclerose múltipla é semelhante no Brasil e na Asia?

RESUMO — O quadro clínico de 67 pacientes consecutivos com diagnóstico clinicamente definido de esclerose múltipla foi analisado. Vinte destes pacientes apresentavam a forma predominante óptico-espinal da doença e oito pacientes apresentavam doença de Devic. Baixa visual foi observada em 43% dos casos como manifestação inicial e em 84% durante o curso da doença. Sintomas e sinais secundários a acometimento da medula espinal e do cerebelo foram observados em 64% e 52% dos casos respectivamente. A elevada prevalência de anormalidades visuais e espinais, o envolvimento menos frequente do cerebelo e a alta frequência relativa da doença de Devic sugerem que a esclerose múltipla no Brasil apresenta características semelhantes às relatadas em países orientais em distinção ao padrão clínico mais comumente observado nos Estados Unidos e na Europa.

PALAVRAS-CHAVE: esclerose múltipla, características clínicas, semelhanças geográficas (Brasil e países da Asia Leste).

The marked differences in the geographical distribution of multiple sclerosis (MS) around the world have long intrigued investigators and led to a conviction that latitude, environmental conditions and race are important factors in determining risk. Ethnic influence has been demonstrated by numerous observations such as the low frequency of the disease in Hungarian gypsies, its exceptional rarity in black South Africans, its lower prevalence in Japanese and black Americans as compared to their white counterparts, and in indigenous people of New Zealand in comparison with descendants of European immigrants. In addition to its variable prevalence rates in different ethnic populations MS may also exhibit distinct clinical features in different racial groups. It has been well established that the clinical profile of MS in Eastern countries includes some peculiarities which make it distinctive from the classical picture as observed in the West. Series from Japan, Taiwan, China, Korea and Malaysia show

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in addition to a low prevalence rate, that involvement of the optic nerves and spinal cord both as a presenting symptom and during the course of the disease is much more frequently found than in the West. Likewise whereas Devic's disease is a very rare form of MS in the United States and Europe it comprises 8% of all MS cases in Japan. Other clinical characteristics of MS in Asian populations are the severity of visual and spinal functional disability, the less frequent involvement of the cerebellum and the low conversion rate of isolated idiopathic optic neuritis to disseminated MS.

Although the interest for the study of MS in Brazil is recent and only a few series of patients have been published to date it appears that Brazilian patients exhibit some of the characteristic features found in Orientals, distinguishing them from patients in other Western countries. In the present report it is analysed the clinical similarities of a series of MS patients in Brazil as compared with published series from some Asian countries. It is emphasized the fact that environmental factors, besides race, may play a role in its clinical characterization.

METHOD

The series consists of consecutive patients examined by one of us (MALP) at our private office and Federal University of Minas Gerais Medical School Hospital, in Belo Horizonte, Brazil, a southeastern city situated at 20°S latitude, in the period between 1979 and 1990.

The medical records of patients with the diagnosis of MS were reviewed and only those cases fulfilling the Poser Committee diagnostic criteria as definite MS were then considered. For the purposes of the present investigation the cases were divided into three groups according to the predominance of clinical symptoms: 1. classical form in which there was predominance of symptoms other than those related to optic nerve and spinal cord lesions; 2. optic-spinal form in which there were predominant signs of visual and spinal involvement; 3. neuromyelitis optica (Devic's disease) in which acute visual loss (optic neuritis) and transverse myelitis occurred either simultaneously or successively within an interval of few weeks. Any optic-spinal form of MS with a polyphasic course or the presence of other signs was not considered as Devic's disease.

The cases were analysed in relation to sex ratio, race distribution, age of onset, clinical form of the disease, and symptoms and signs at presentation and during the course of the disease. These data were then compared with some classical studies in the United States and Europe as well as with some published series from Asian countries.

RESULTS

There were 67 patients in whom the diagnosis of definite MS was confirmed after review of their medical records. The mean age of onset was 28.9 years (SD 10.4, range 12 to 54). There were 47 women and 20 men, the sex ratio was 2.3 women to men. Figure 1 shows the age of onset by sex. No patient was of Oriental ancestry, there were 51 white, 13 dark-skinned and three black patients.

Twenty (30%) of the 67 patients exhibited the optic-spinal form of the disease whereas eight (12%) had neuromyelitis optica. The remaining 39 patients (58%) experienced variable clinical signs with no predominance of visual and spinal cord disturbances.

The most common initial symptom was motor involvement (51%). Symmetrical weakness of both lower limbs occurred in 30% of the patients. In six patients the presenting symptom was monoparesis and in two hemiparesis. Visual loss, usually associated with orbital pain following eye movements was the next most frequent initial symptom occurring in 29 cases (43%). In eight of them the visual loss was associated simultaneously or within a short interval with paraparesis, sensory loss with a distinct level and sphincter disturbances. Twenty-six patients complained sensory abnormalities at onset, usually in both lower limbs and coming along with paraparesis. Two patients manifested subjective sensory disturbances in both hands simultaneously and one patient reported numbness in one upper extremity as the first manifestation of the illness. Brainstem and cerebellar symptoms occurred at onset in 23 patients whereas in seven cases there were symptoms related to involvement of the seventh and fifth cranial nerves. Sexual and sphincter disturbances were reported by 15 patients.

Table 1 summarizes the percentage frequencies of the various symptoms and signs at onset of MS among our 67 patients in comparison with series from Germany and Sweden.
Visual impairment as the presenting symptom was as frequent in our series as reported in Japan but less prevalent than in series from Taiwan and Korea but much more frequent than in Germany, Sweden, and the United States.

The frequency of motor symptoms at onset in our series is similar to those observed in Korea and the United States.

Table 2 compares the percentage frequencies of symptoms and signs during the course of the illness in the present group of patients with series from other countries. Impaired vision was found in 56 of our 67 patients. This frequency is much higher than those reported in Germany, Japan, and the United States and close to those in Japan, Taiwan, and China. Diplopia occurred during the course of the illness in 21 of our patients. Fifteen of them had external ocular palsies whereas six developed internuclear ophthalmoplegia. The prevalence
of diplopia in our population is similar to that reported by Kuroiwa and colleagues in Japan. Involvement of the trigeminal and facial nerves was observed in 17 of our cases. The closest figures to ours are those reported by Zhao and coworkers in China who found trigeminal abnormalities in 13 and facial palsy in six of their 70 cases. Thirty-six patients experienced cerebellar symptoms; the frequency of this finding in the present series lies midway between series from Western and Eastern countries. Fifty-three patients developed weakness of limbs. The distribution of the motor abnormalities was as follows; paraparesis occurred in 29 patients, tetraparesis in 12, hemiparesis in six whereas other six exhibited weakness of just one limb. Sixty patients developed sensory disturbances which were variably described and distributed but had a marked tendency to involve the lower limbs. Sphincter abnormalities and mental changes in the present group did not differ extensively from reported series in other countries.

Analysis of the clinical features of the illness in relation to the anatomical sites of involvement shows that 55 patients in the present series had involvement of the optic nerves, 43 of the spinal cord whereas lesions of the brainstem, cerebellum and cerebrum could be inferred in 30, 35 and 15 cases respectively. Table 3 is a comparison of the percentage frequencies of the anatomical sites of involvement in our series alongside with figures for other series in Western and Eastern countries. The optic nerves and the spinal cord were the most affected structures in our population. These figures remarkably differ from those as reported by Kurtzke and collaborators in the United States but are, on the other hand, impressively similar to those observed in Japan, Taiwan, China and Malaysia. The cerebrum was the least affected portion of the CNS in ours as in almost all Eastern series. This is in extreme opposition to the high prevalence of cerebral involvement in the United States.

As the frequency of cerebellar symptoms is concerned our figure is higher than those reported in the East but still considerably lower than the 72% reported in the United States.

Table 4 summarizes the most distinguishing clinical features of MS in Orientals and Caucasians as compared with Brazilian patients in the present study.

<table>
<thead>
<tr>
<th>Table 2. Frequency of symptoms during the course of multiple sclerosis in some countries (%).</th>
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<tbody>
<tr>
<td>Symptoms</td>
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<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Impaired vision</td>
</tr>
<tr>
<td>Diplopia</td>
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<tr>
<td>V - VII nerves</td>
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<tr>
<td>Ataxia</td>
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<tr>
<td>Weakness of limbs</td>
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<tr>
<td>Sensory disturbances</td>
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<tr>
<td>Sphincter disturbances</td>
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<td>Mental changes</td>
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</tbody>
</table>

Table 3. Sites of involvement in multiple sclerosis in Brazil and other Western and Eastern countries (%).

<table>
<thead>
<tr>
<th>Anatomical sites</th>
<th>Brazil (67)</th>
<th>USA 6 (527)</th>
<th>Japan 14 (1064)</th>
<th>China 17 (70)</th>
<th>Taiwan 10 (25)</th>
<th>Malaysia 36 (30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic nerve</td>
<td>82</td>
<td>34</td>
<td>73</td>
<td>70</td>
<td>92</td>
<td>77</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>64</td>
<td>23</td>
<td>68</td>
<td>83</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Brainstem</td>
<td>45</td>
<td>42</td>
<td>55</td>
<td>40</td>
<td>48</td>
<td>27</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>52</td>
<td>72</td>
<td>34</td>
<td>31</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>22</td>
<td>77</td>
<td>35</td>
<td>29</td>
<td>20</td>
<td>13</td>
</tr>
</tbody>
</table>
Multiple sclerosis in Brazil is still poorly known and even its prevalence remains to be determined. A scant number of studies have been published, most of them describing small groups of patients. One autopsied case has been well documented. The present investigation shows that Brazilian patients share some clinical features of the illness as it manifests in the Asian race. The main distinctive traits of MS in Orientals as compared with Europeans and northern Americans include the higher frequency of visual loss and transverse myelitis at onset and during the course of the illness, the more common occurrence of the optic-spinal form of the disease and of neuromyelitis optica, and the lower prevalence of cerebellar symptoms. All these were conspicuous features. In fact, visual loss and symptoms of transverse myelitis were the presenting symptoms in 43% and 35% of our cases respectively. The optic-spinal form was observed in 30% and Devic's disease occurred in eight patients (12%). The frequency of cerebellar symptoms in the course of the illness was lower in our population than in most of Eastern series.

In the largest series published to date in Brazil, Callegaro reported paraparesis as the presenting symptom in 34 of his 120 patients in the state of Sao Paulo, whereas sensory disturbances and visual loss were observed at the onset of the illness in 35 and 18 patients respectively. Although the frequency of visual symptoms at the onset of the illness in his series is lower than in ours, it is still higher than in most of the western series. Devic's disease occurred in four of his patients, a figure much higher than any in the United States or Europe. His study does not analyze specifically the frequency of the optic-spinal form of the disease but he observed a predominance of spinal symptoms and visual impairment in the second and third bouts of the illness.

In the second and third bouts of the illness.

Two recent communications report on the occurrence of MS in Rio de Janeiro. In a study of a series of 31 patients Papais-Alvarenga and colleagues observed that visual impairment, motor and cerebellar symptoms "were the most frequent findings." Leite and collaborators noted paraparesis in 54%, sensory disturbances in 42% and visual loss in 35% as the presenting symptoms of his 51 patients with definite or probable MS. They observed in eight patients (16%) the association of "spinal symptoms with optic neuritis at presentation. Some of these patients probably had Devic's disease. These observations are therefore very similar to ours.

The conversion rate of isolated idiopathic optic neuritis to disseminated MS may be also a distinctive feature of MS in different geographic areas and ethnic groups. In Europe, Japan and the United States the risk of progression may be as high as 50% whereas in Japan it is as low as 8.3%. In a recent study in Brazil, Lana-Peixoto and Lana-Peixoto disclosed a conversion rate of 10.8%. Brazilian and Japanese patients with isolated optic neuritis therefore share...
a low risk to develop MS as compared to their European and north American counterparts.

Genetic influence on the distribution of MS are beyond question. The correlation between the frequency of HLA-DR2 and the susceptibility to the illness in northern Europeans, and the results of twin studies reaffirm the importance of the genetic factors. Likewise racial influences have been ascribed to the distinctive clinical manifestations of MS in Eastern countries. On the other hand epidemiological studies suggest that environmental factors also play a fundamental role in the prevalence of the illness. The present investigation demonstrates that MS in Brazil exhibits the same clinical peculiarities which distinguish Asian MS from the pattern usually found in the West. This study showing strong similarities between Brazilian and Asian patients despite their striking racial differences provides an evidence that factors other than race and genetic account for these common clinical features. It is possible that Brazil and Asian countries share some common environmental conditions which would be the low prevalence of MS in their populations but also promote the development of the same peculiarities in the phenotypic expression of the illness.

REFERENCES