SEASONAL DISTRIBUTION AND EVOLVING FORMS OF MULTIPLE SCLEROSIS PATIENTS DIAGNOSED FROM APRIL 2004 TO NOVEMBER 2007

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Abstract – **Background:** Multiple sclerosis (MS) was first reported in Cuba in 1965. The most frequent appearance is observed in the first six months of the year. **Objective:** To determine the seasonal distribution and evolving forms of MS patients diagnosed with the disease between April 2004 and November 2007. **Method:** Twenty-one patients with suspected MS and 42 outbreaks were studied. Patients were classified according to Lublin and Revingold's criteria for clinical forms and according to McDonald. **Results:** Most patients were classified in outbreak and remission and only two patients classified as primary-progressive multiple sclerosis. The higher number of outbreaks occurred in the first two quarters of the year. **Conclusion:** It is recommended to study further weather variables that may be related to the emergence of these outbreaks in our environment.

KEY WORDS: multiple sclerosis, epidemiology, environmental factors.

Distribución estacional y formas evolutivas de esclerosis múltiple en pacientes diagnosticados entre Abril del 2004 y Noviembre del 2007

Resumen – **Introducción:** La esclerosis múltiple (EM) fue reportada en Cuba por primera vez en 1965. Se ha venido observando la aparición más frecuente en los primeros seis meses del año. **Objetivo:** Determinar la distribución estacional y formas evolutivas de EM en pacientes con diagnóstico de esta enfermedad entre abril 2004 y noviembre 2007. **Método:** Se estudiaron 21 pacientes con sospecha de EM y un total de 42 brotes. Los pacientes fueron clasificados según los criterios de Lublin y Revingold para las formas evolutivas y según los criterios de McDonald. **Resultados:** Solo dos pacientes clasificaron en la forma evolutiva progresiva primaria; los primeros dos trimestres del año fueron los de mayor número de brotes. **Conclusión:** Se recomienda profundizar en las variables climatológicas que pudieran tener vínculo con la aparición de estos brotes en nuestro medio.

PALABRAS-CLAVES: esclerosis múltiple, epidemiología, factores ambientales.

First anatomopathological descriptions of multiple sclerosis (MS) were done by Cruveilhier[1] and Carswell[2], however, Charcot in 1868, provided the first detailed description of the clinical and evolutive aspects of the disease and stated the concept of plate sclerosis. English authors called it disseminated sclerosis due to the spread of lesions in the central nervous system (CNS), afterwards North American authors called it multiple sclerosis (MS) and it is the most used name.

The relation among latitude, climate genetics and the prevalence of MS is well known[2-7]. The disease is more frequent in geographic regions with cold winters, mild summers and rainfalls evenly spread throughout the whole year[3].

However, some seasonality related with the outbreaks of MS has been empirically observed in Cuba.

This paper aims at determining seasonal distribution and evolving forms of MS patients diagnosed with the disease from April 2004 to November 2007.

METHOD

Twenty-one patients with clinical suspicion of MS were studied. They were classified according to Lublin and Revingold and Mc Donald's criteria[8,9].

A sample of serum and cerebrospinal fluid (CSF) was collected from each patient. Albumin and IgG of both fluids were quantified by simple radial immunodiffusion in NOR and LC Partigen plates from Dade Behring (Marburg). Albumin and IgG concentrations were turned into quotients CSF/serum and were plotted in the reibergrams according to Wormek's CSF Laboratory program version 3.0.

The clinical records of patients specifying the dates of outbreaks, how they evolved and the most important clinical features as well as the categorization of the disease were checked.

RESULTS

The 90.5% of the patients was classified as relapsing-remitting MS, according to Lublin and Revingold's criteria.

The frequency of outbreaks of MS was distributed in quarters. These results are shown in Figure.

DISCUSSION

Relapsing-remitting multiple sclerosis and primary-progressive MS were the evolving forms in our sample, with predominance of the former. This result matches the literature, where it is also the most common form of presentation[10]. Cases of secondary-progressive multiple sclerosis and progressive remitting multiple sclerosis were not found.

According to the epidemiology of MS, there may be a relation between the disease and any environmental factor. It seems to be that, some environmental factor acts during childhood in genetically predisposed individuals. After years of latency, this same factor seems either to start the disease or to contribute to its causes. Many authors have considered the infection by certain viruses as the candidate. Despite the findings of intrathecal response to a large list of viruses, neither the viral genetic material has been isolated in active MS plates with a well established etiological relation, nor there is a viral model of the disease[9-16].

Figure. Frequency of MS outbreaks per quarters. Comparison of proportions, p<0.01

A viral infection might be the initial event in the genesis of MS and some secondary factor might act during life activating the disease or causing the outbreaks.

Based on prevalence, three risk areas can be considered according to Kutzke[17,18].

High risk area: when prevalence is higher than or equal to 30 cases per 100 000 inhabitants. Between 65° and 43° north latitude, northern Europe, USA and Canada and between 33° and 44° south latitude (Australia and New Zealand). Medium risk area: when prevalence is 5-29 cases per 10 000 inhabitants, southeast USA, south Europe and southern Australia. Low risk area: when the prevalence is less than 5 cases per 10 000 inhabitants, Asia, Latin America, Africa and regions close to the equator. Cuba is included in this the area.

The estimated prevalence of clinically definite MS in Cuba was 4.42 cases per 100 000 inhabitants using as source the case registers of all provinces and of the Association of Multiple Sclerosis patients in Cuba[19].

According to our the results, outbreaks occur more frequently in the first two quarters of the year and their frequency is particularly higher in the second quarter that corresponds to April to June.

April, in our country, is the last month of the dry season (winter) and it is considered to be a transition month from winter to summer. Lately, this month have had a tendency to high temperatures and a variable thermal oscillation. This month marks the beginning of the quarter where outbreaks of MS are more frequent, and it might be related with the features mentioned above. From January to March there have been changes in the thermal regime with a greater range of variations, and El Niño Southern Oscillation event has been considered their cause[20-22].

Many studies found a relation between outbreaks emergence with different weather variables and seasons. When conducting analyses of the seasonal outbreaks of MS, the results have been contradictory depending on the geographical locations where these studies have been performed. These contradictory data make difficult the establishment of a seasonal or month incidence of MS outbreaks that may be applicable everywhere[23-27].

It has been reported that there are certain climate parameters in some seasons that favor MS outbreaks in patients suffering from this disease[26,27]. Other studies have stated that under certain weather conditions the start of MS patients occurs regardless of their clinical presentation[28].

Studies carried out by Partridge in Spain, where immigrants were enrolled, found out that latitude susceptibility to suffer this disease is particularly special during childhood[29]. Van der Mei and colleagues identified that exposure to sunlight, mainly in winter, between the ages of 6 and 15 years, is related to a decrease in the risk of MS[23].
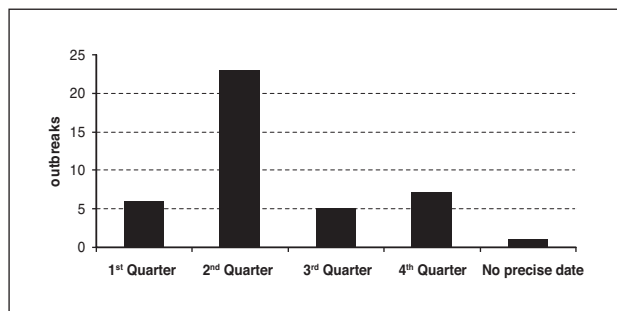
According to Wüthrich[3], the number of outbreaks in-

creases in winter and spring in Switzerland. A non significant tendency to increase during the summer, mainly in July, has been observed in England according to Shapira[4]. An increase of outbreak incidence from April to June in Galicia, Spain has been described by Abella-Corral[14] and this finding coincides with what we found in our study.

Aver, Shumman and Kumpfel have found related seasonal variations with the appearance of lesions by nuclear magnetic resonance (NMR). They found that the number and activity of lesions in NMR were significantly higher in the first half of the year than in the second one[26]. On the other hand, Rovaris and colleagues found that more active lesions appeared in the NMR in March and less in December, though this results were not statistically significant[27]. An analysis of MS seasonal outbreaks in Palencia, Spain showed a non- statistically significant trend towards the diminishing of outbreaks in the summer[28].

There are also data from USA were more outbreaks are observed from July to October in Ohio and in spring in Minnesota[8]. A study conducted in Arizona showed a non-significant trend to increase relapses in spring and at the beginning of summer[5]. O'Reilly et al. carried out a study in the west of Ireland. As a result they established the relation between the outbreak frequency and concrete weather variables. Correlation between them was not observed, however there was an increase in the duration of the symptoms of the outbreak in periods of peak temperature and solar radiation, or lower relative humidity and volume of rainfall[27].

In summary, there is certain seasonality in the behavior of the outbreaks in our country. A higher number of patients will allow us to reassert this first approximation of our observations. It would be interesting to relate the season with various climatic variables and their relation to viral infections circulating in these months.

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