

Magnetic Resonance Poor Prognostic Factors In Mexican Multiple Sclerosis Patients

Factores de Mal Pronóstico Por Resonancia Magnética en Pacientes Mexicanos Con Esclerosis Múltiple

Ricardo Jorge García-Bermúdez, Brenda Bertado-Cortés, Raúl Carrera-Pineda

Abstract

Introduction: Multiple sclerosis is one of the main causes of disability in young people. It has characteristic lesions in magnetic resonance images which are part of diagnosis criteria, and some of them could predict a long-term disability. In Mexican population there is no description about multiple sclerosis imaging characteristics.

Materials and methods: We performed an observational, descriptive, cross-sectional, and retrospective study at the Neurology Service of Specialties Hospital of Siglo XXI National Medical Center of Mexican Social Security Institute, in Mexico, evaluating magnetic resonance images characteristics of patients with multiple sclerosis diagnosis between January 2017 and January 2020.

Results: 75 patients were included, 8% had 1-3 T2-weighted lesions, 18.6% had 4-9 T2-weighted lesions, and 73.3% had 10 or more T2-weighted lesions. 50.6% had infratentorial lesions and 61.3% had spinal cord lesions. Gadolinium enhancing lesions were found in 48%, with a median of lesions 2 (IQR 1,3).

Conclusions: Mexican patients with multiple sclerosis have a great incidence of magnetic resonance image poor prognosis factors, which should lead to a closer follow-up and influence treatment options.

Keywords: multiple sclerosis, Mexican patients, epidemiology, prognosis, magnetic resonance, disability

Resumen

Introducción: La esclerosis múltiple es una de las principales causas de discapacidad en personas jóvenes. Se caracteriza por lesiones en resonancia magnética que forman parte de sus criterios diagnósticos, prediciendo algunas de ellas discapacidad a largo plazo. En la población mexicana no existe descripción de las características por imagen de esclerosis múltiple.

Materiales y métodos: Desarrollamos un estudio observacional, descriptivo, retrospectivo de cohorte en el servicio de Neurología del Hospital de Especialidades del Centro Médico Nacional "Siglo XXI" del Instituto Mexicano del Seguro Social, en México, evaluando las características por imagen de resonancia magnética en pacientes con diagnóstico de esclerosis múltiple entre enero de 2017 y enero de 2020.

Resultados: 75 pacientes fueron incluidos. En secuencia T2 el 8% tuvo 1-3 lesiones, 18.6% tuvo 4-9 lesiones en secuencia T2 y 73.3% tuvo 10 o más lesiones. El 50.6% tuvieron lesiones infratentoriales y el 61.3% tuvo lesiones en médula espinal. Lesiones captantes de gadolinio se encontraron en el 48%, con una mediana de lesiones de 2 (RIC 1,3).

Conclusiones: Los pacientes mexicanos con esclerosis múltiple tienen una gran incidencia de factores de mal pronóstico por resonancia magnética, lo cual debería de guiar a un seguimiento más estrecho e influenciar en las opciones de tratamientos.

Palabras clave: esclerosis múltiple, pacientes mexicanos, epidemiología, pronóstico, discapacidad

Rev. Ecuat. Neurol. Vol. 30, N° 1, 2021

Introduction

Multiple sclerosis (MS) is one of the most common causes of neurological disability, especially in young people.¹ This chronic, neuroinflammatory, and demyelinating disease has multiple mechanisms involved in its phy-

siopathology, which makes it difficult to treat.² Mexico has a MS mean prevalence of 18.7 per 100,000 inhabitants, with a gender ratio female: male of 2.3:1 and a predominance between the third and fourth decades of life.^{3,4} Magnetic resonance image (MRI) has an important role in MS diagnosis.

Department of Neurology, Specialties Hospital of "Siglo XXI" National Medical Center, Mexican Social Security Institute, Mexico city, Mexico.

Corresponding author:
Ricardo Jorge García-Bermúdez, MD
Department of Neurology, Specialties Hospital of "Siglo XXI" National Medical Center, Mexican Social Security Institute.
330 Cuauhtemoc avenue, PC 06720, Mexico city, Mexico.
Telephone Number: (+52) 8341213014
E-mail: ricardojgb92@gmail.com

This diagnostic method shows the characteristic lesions of the disease, which are areas of hyperintensity on a T2-weighted or proton-density-weighted MRI scan that is at least 3mm in long axis located in four different zones: cortical or juxtacortical, periventricular, infratentorial or spinal cord. Optic nerve lesions could be part of the typical lesions of MS, depending on the diagnostic criteria. Also, when those lesions get chronic, they can be visualized hypointense in T1-weighted MRI.^{5,6}

There are several disease characteristics which can predict a poor prognosis and a long-term disability, including MRI features.⁷ A greater number of T2 lesions at MS diagnosis has been associated with a higher disability, especially within the groups of patients with 4-9 and 10 or more T2 lesions.⁸ Gadolinium enhancing lesions (GEL) mainly predict the probability of conversion to clinically defined MS, but also long-term disability.⁹ Lesions topography plays an important role in long-term disability, being infratentorial and spinal cord lesions the ones that are predictors.^{10,11}

There are some studies about clinical and demographic characteristics of Mexican MS patients, nevertheless, there are no reports of radiological characteristics of these patients at diagnosis.¹²

Materials and methods

We performed an observational, descriptive, cross sectional, and retrolective study at the Neurology service at Specialties Hospital of Siglo XXI National Medical Center of Mexican Social Security Institute, in Mexico city, Mexico. All patients whom MS diagnosis, by 2017

McDonald diagnosis criteria, were made during hospitalization between January 2017 and January 2020, were included. The objective of this study was to show MRI poor prognostic factors in Mexican population with MS. Patients hospitalized with known MS diagnosis or MS relapse were excluded. Demographic and MRI characteristics were obtained from medical records. All MRI were performed with Philips Ingenia 3.0 tesla MRI system. Data collected was gender, age, smoking, comorbidities, number of MRI T2-weighted lesions, number of gadolinium enhancing lesions, localization of T2-weighted lesions, and presence of T1-weighted hypointense lesions.

Quantitative variables were expressed as mean and standard deviation (SD) and as median and interquartile range (IQR); qualitative variables were expressed as frequencies and percentages. The Statistical Package for the Social Sciences (SPSS) version 24 for Windows was used.

Results

75 patients got MS diagnosis by 2017 McDonald diagnosis criteria during hospitalization. 37 (49.3%) were men and 38 (50.6%) were women. Mean age was 33 years old (SD 11.68) with 21 (28%) older than forty years. Smoking was found in 20 (26.6%) patients and 24 (32%) had comorbidities, being arterial hypertension, depression, and hypothyroidism the most frequent with 22.5%, 12.9%, and 12.9%, respectively. In table 1 are shown demographic characteristics of patients.

In MRI (table 2), 6 (8%) patients had 1-3 T2-weighted lesions, 14 (18.6%) had 4-9 T2-weighted lesions, and 55 (73.3%) had 10 or more T2-weighted lesions. 38 (50.6%) patients had infratentorial lesions and 46 (61.3%) had spinal cord lesions. GEL were found in 36 (48%) patients, with a median of lesions of 2 (IQR 1,3). T1-weighted

Table 1. Demographic characteristics of patients.

Characteristics	Value
Men <i>n</i> (%)	37 (49.3)
Women <i>n</i> (%)	38 (50.6)
Age* (SD)	33 (11.68)
Older than forty years <i>n</i> (%)	21 (28)
Smoking <i>n</i> (%)	20 (26.6)
Comorbidities <i>n</i> (%)	24 (32)
- Arterial hypertension	7 (22.5)
- Depression	4 (12.9)
- Hypothyroidism	4 (12.9)
- Dyslipidemia	2 (6.4)
- Migraine	2 (6.4)
- Rheumatoid arthritis	2 (6.4)
- Gastritis	2 (6.4)
- Diabetes	1 (3.2)
- Allergic rhinitis	1 (3.2)
- Ankylosing spondylitis	1 (3.2)
- Schizophrenia	1 (3.2)
- Arrhythmia	1 (3.2)
- Asthma	1 (3.2)
- Fibromyalgia	1 (3.2)
- Thyroid nodule	1 (3.2)

*Media. SD standard deviation.

Table 2. MRI characteristics of patients.

MRI Characteristics	Value
Number of T2-weighted lesions <i>n</i> (%)	
1-3	6 (8)
4-9	14 (18.6)
10 or more	55 (73.3)
Lesions topography <i>n</i> (%)	
Periventricular	73 (97.3)
Cortical/juxtacortical	71 (94.6)
Infratentorial	38 (50.6)
Spinal cord	46 (61.3)
Gadolinium enhancing lesions	
Patients <i>n</i> (%)	36 (48)
Lesions* (IQR)	2 (1,3)
T1-weighted hypointense lesions <i>n</i> (%)	59 (78.6)
2 or more characteristics ¹ <i>n</i> (%)	55 (73.3)
4 characteristics ² <i>n</i> (%)	15 (20)

*Median. ¹Combinations of 10 or more T2-weighted lesions, infratentorial lesions, spinal cord lesions, and/or GEL. ²10 or more T2-weighted lesions, infratentorial lesions, spinal cord lesions, and GEL. IQR: interquartile range (25,75). GEL: gadolinium enhancing lesions.

hypointense lesions were found in 59 (78.6%) patients. From the four poor prognostic factors identified (10 or more T2-weighted lesions, infratentorial lesions, spinal cord lesions, and GEL), 55 (73.3%) patients had more than one and 15 (20%) had all of them. In table 2 are shown MRI poor prognosis characteristics of patients.

Discussion

One of the most relevant results in our study is that the gender ratio female:male is 1.02:1, which since several years ago has been increasing as MS incidence in women increases, even greater than 2:1.¹³ Age at MS diagnosis has a wide range, which could be secondary to an emergency attention in a reference tertiary-care center as ours; furthermore, mean age is older than reported worldwide with almost double the number of patients older than forty years.^{14,15}

Smokers are fewer than reported in other studies in contrast to comorbidities, which have the same incidence, with a predominance of arterial hypertension, depression, and thyroid pathology as other populations. Smoking as well as some autoimmune diseases as thyroid pathology, have been associated with a poor MS prognostic.¹⁶⁻¹⁸

Number of T2-weighted lesions are very similar as in other populations, being most common 10 or more lesions; nevertheless, there are few studies in which the number of patients with 10 or more T2-weighted lesions are greater than 70% as in ours. Lesions topography differs with international studies, being more frequent spinal cord lesions and less frequent infratentorial lesions in our population.^{19,20}

Another relevant difference with other reports is the great number of patients with GEL, more than the double of patients, as well as the mean GEL, which is almost three times greater than in other populations.^{19,21}

The most important result of this study is that almost three quarters of our patients had more than one poor prognostic factor and the fifth had four of them. These results could be the association of demographic factors as male gender, age at MS diagnosis, smoking, and comorbidities, which have a great incidence in our study.⁷

There is known that T2-weighted MRI lesions volume and brain atrophy are also risk factors for long-term disability;²² nevertheless, in our hospital there is no software to measure them.

Conclusion

Our study shows that Mexican MS patients have a great incidence of poor prognosis factors in MRI, even more than one, which leads us to investigate the relation with other MS poor prognostic factors. This guides us to a closer monitoring of our patients and to choose the appropriate treatment, assessing the necessity of high effectiveness treatments in order to prevent long-term disability.

Further studies with more patients are needed in order to establish the exact incidence of poor prognosis factors in MRI at MS diagnosis of Mexican population and their impact on long-term disability.

References

1. GBD 2016 Multiple Sclerosis Collaborators. Global, regional, and national burden of multiple sclerosis 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:269-285. [https://doi.org/10.1016/S1474-4422\(18\)30443-5](https://doi.org/10.1016/S1474-4422(18)30443-5).
2. Dendrou C, Fugger L, Friese M. Immunopathology of multiple sclerosis. *Nature Reviews Immunology* 2015;15:545-558. <https://doi.org/10.1038/nri3871>.
3. Correa E, Paredes V, Martínez B. Prevalence of multiple sclerosis in Latin America and its relationship with European migration. *Multiple Sclerosis Journal Experimental, Translational and Clinical* 2016;2:1-10. <https://doi.org/10.1177%2F2055217316666407>.
4. Velázquez-Quintana M, Macías-Islas M, Rivera-Olmos V, et al. Esclerosis múltiple en México: un estudio multicéntrico. *REV NEUROL* 2003;36(11):1019-1022. <https://doi.org/10.33588/rn.3611.2002610>.
5. Thompson A, Banwell B, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol* 2018;17:162-173. [https://doi.org/10.1016/s1474-4422\(17\)30470-2](https://doi.org/10.1016/s1474-4422(17)30470-2).
6. Filippi M, Rocca M, Ciccarelli O, et al. MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines. *Lancet Neurol* 2016. [https://doi.org/10.1016/S1474-4422\(15\)00393-2](https://doi.org/10.1016/S1474-4422(15)00393-2).
7. Rotstein D, Montalban X. Reaching an evidence-based prognosis for personalized treatment of multiple sclerosis. *Nat Rev Neurol* 2019;15:287-300. <https://doi.org/10.1038/s41582-019-0170-8>.
8. Fisniku L, Brex P, Altmann D, et al. Disability and T2 MRI lesions: a 20-year follow-up of patients with relapse onset of multiple sclerosis. *Brain* 2008;131:808-817. <https://doi.org/10.1093/brain/awm329>.
9. Swanton J, Fernando K, Dalton C, et al. Early MRI in optic neuritis: the risk for disability. *Neurology* 2009;72:542-550. <https://doi.org/10.1212/01.wnl.0000341935.41852.82>.
10. Minneboo A, Barkhof F, Polman C, et al. Infratentorial lesions predict long-term disability in patients with initial findings suggestive of multiple sclerosis. *Arch Neurol* 2004;61:217-221. <https://doi.org/10.1001/archneur.61.2.217>.
11. Brownlee W, Altmann D, Alves P, Swanton J, et al. Association of asymptomatic spinal cord lesions and atrophy with disability 5 years after a clinically isolated syndrome. *Multiple Sclerosis Journal* 2017;23(5):665-674. <https://doi.org/10.1177%2F1352458516663034>.

12. Bertado-Cortés B, Villamil-Osorio L, Carrera-Pineda R, y cols. Características clínicas y demográficas de los pacientes con esclerosis múltiple. *Rev Med Inst Mex Seguro Soc* 2016;54(2):186-190. PMID 27561023.
13. Leray E, Moreau T, Fromont A, et al. Epidemiology of multiple sclerosis. *Revue Neurologique* 2016;172:3-13. <https://doi.org/10.1016/j.neurol.2015.10.006>.
14. Scalfari A, Neuhaus A, Daumer M, et al. Age and disability accumulation in multiple sclerosis. *Neurology* 2011;77:1246-1252. <https://doi.org/10.1212/wnl.0b013e318230a17d>.
15. Alroughani R, Akhtar S, Ahmed S, et al. Is time to reach EDSS 6.0 faster in patients with late-onset versus young-onset multiple sclerosis? *Plos One* 2016. <https://doi.org/10.1371/journal.pone.0165846>
16. Heydarpour P, Manouchehrinia A, Beiki O, et al. Smoking and worsening disability in multiple sclerosis: A meta-analysis. *Acta Neurol Scand* 2018;00:1-8. <https://doi.org/10.1111/ane.12916>.
17. Kowalec K, McKay K, Patten S, et al. Comorbidity increases the risk of relapse in multiple sclerosis. *Neurology* 2017;89:2455-2461. <https://doi.org/10.1212/wnl.0000000000004716>.
18. Puz P, Lasek-Bal A, Steposz A, et al. Effect of comorbidities on the course of multiple sclerosis. *Clinical Neurology and Neurosurgery* 2018;167:76-81. <https://doi.org/10.1016/j.clineuro.2018.02.014>.
19. CHAMPS study group. Baseline MRI characteristics of patients at high risk for multiple sclerosis: results from the CHAMPS trial. *Multiple Sclerosis* 2002;8:330-338. <https://doi.org/10.1191%2F1352458502ms819oa>.
20. Silveira F, Pappolla A, Sánchez F, et al. Brain magnetic resonance imaging features in multiple sclerosis and neuromyelitis optica spectrum disorders patients with or without aquaporin-4 antibody in a Latin America population. *Multiple Sclerosis and Related Disorders* 2020. <https://doi.org/10.1016/j.msard.2020.102049>.
21. Hamdy S, Abdel-Naseer M, Shalaby N, et al. Characteristics and predictors of progression in an Egyptian multiple sclerosis cohort: a multi-center registry study. *Neuropsychiatric Disease and Treatment* 2017;13:1895-1903. <https://doi.org/10.2147/ndt.s140869>.
22. Popescu V, Agosta F, Hulst H, et al. Brain atrophy and lesion load predict long term disability in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2013;84(10):1082-1091. <https://doi.org/10.1136/jnnp-2012-304094>.