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Original Article

Migraine related white matter lesions in the differential diagnosis of multiple sclerosis: Magnetic resonance imaging features

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Abstract

Aim: This study aims to describe the lesion characteristics of conventional magnetic resonance imaging (MRI) of patients who are directed to a university hospital with a pre-diagnosis of demyelinating disease who are finally diagnosed as MrWMLs.

Material and Methods: Individuals who were referred to an MS outpatient clinic of a university hospital with a pre-diagnosis of demyelinating disease and finally diagnosed with migraine according to the International Classification of Headache Disorders (ICHD) -3 (β) criteria who also have MrWMLs and 45 age and gender-matched individuals who are diagnosed with MS according to the 2017 McDonald diagnostic criteria, without migraine-type headache were retrospectively analyzed.

Results: Forty-five individuals with migraine and 45 age and gender-matched individuals who are diagnosed with MS were included. The median time since diagnosis was 10 (0.5-32) years for the migraine group and 5 (0.3-20) years in the group with MS (p=0.031). The median age of the group with migraine was 35 (23-54) years, while the median age of the group with MS was 34 (20-55) years. There was no significant difference between the groups in terms of average age and gender distribution (p=0.342 and p=0.389). The total number of T1 and T2 lesions were significantly higher in the MS group. Similarly, the number of infratentorial and periventricular lesions was higher in the MS group (p<0.001). The number of deep white matter lesions was higher in the migraine group (p<0.05).

Conclusion: In this study, conventional MRI tips were defined for differentiating MS lesions from MrWMLs which has an important place in the differential diagnosis of MS. MrWMLs were deep white matter lesions that are predominantly located at the frontal and parietal lobes. Studies involving more individuals and using automated segmentation software may provide more information to differentiate MrWMLs from MS lesions.

Keywords: Multiple sclerosis; migraine; white matter lesions

INTRODUCTION

Multiple sclerosis is the most common immune-mediated inflammatory disease of the central nervous system (CNS), affecting more than 2 million people worldwide (1). The underlying cause of MS is not known precisely but is thought to occur with the influence of environmental factors in genetically susceptible individuals (2). Although MS was previously identified as a T cell-mediated disease, genetic and pathology studies show that T and B cells play a critical role in the pathogenesis of MS. However, other cells of the central nervous system, such as oligodendrocyte, microglia, and astrocyte, have also been shown to contribute to pathology (3). Initially, 85-90 % of patients have relapses followed by periods of remission. Secondary progressive disease characterized by gradual worsening of neurological function in many patients over time (2). The diagnosis is made by careful evaluation of history, neurological examination, neuroimaging, and laboratory tests. Dissemination in time and space and the lack of a better explanation of the presentation form the basis of diagnostic criteria (4). The detection of at least one T2 lesion in two of the four CNS regions defined as periventricular, infratentorial, juxtacortical, or cortical and spinal cord, meets the requirement for dissemination in space criteria in the 2017 McDonald diagnostic criteria (4). The condition of dissemination in the space is provided by demonstrating that demyelinating attacks occur at different times by clinical or MR imaging (4, 5). However, MS misdiagnosis remains an important problem

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with serious consequences for patients and healthcare systems (5). In a study in which 241 patients diagnosed with MS were evaluated in two different academic MS centers, it was shown that approximately one-fifth of the patients were misdiagnosed, and the most common actual diagnosis was migraine(16%) (6). Similarly, in another study evaluating 110 misdiagnosed individuals, it was shown that the most common actual diagnosis was migraine (7).

Migraine is a chronic neurological disorder characterized by attacks of moderate or severe headache and reversible neurological and systemic symptoms. Migraine is one of the most prevalent and disabling medical illnesses in the world. World Health Organization ranks migraine as the third most prevalent medical condition and the second most disabling neurological disorder in the world (8, 9). The migraine headache is often reported by patients to be unilateral (60%), throbbing (50%), and aggravated by physical activity (90%) or head movement (10, 11). Globally, migraine affects about 15% of the general population and is more common in women like MS (9, 12). Migraine is considered as a risk factor for the formation of WMLs which are observed hyperintense in T2-weighted images (13), and WMLs are common in individuals with migraines (14). The aim of this study is to describe the lesion characteristics of patients with WML accompanying migraine who are referred to a university hospital with a pre-diagnosis of demyelinating disease and finally not diagnosed with demyelinating disease.

MATERIAL and METHODS

Study procedure

The study was approved by the Erciyes University ethics committee (meeting date of the ethics committee: 12.02.2020, decision number: 2020/92). Forty-five individuals who were referred to Erciyes University Faculty of Medicine, MS outpatient clinic with a pre-diagnosis of demyelinating disease and finally diagnosed with migraine according to International Classification of Headache Disorders (ICHD) -3 (β) criteria (12) who have WMLs were included in the study. Individuals in the migraine group did not show any symptoms similar to the MS symptom at any time, except for a headache. The exclusion criteria for the migraine group were as follows: any imaging finding other than focal T2 hyperintensity, any type of ongoing or recurrent headaches other than migraine, any systemic inflammatory or autoimmune diseases, and uncontrolled hypertension. Additionally, we excluded smokers and patients with dyslipidemia, diabetes mellitus, and history suggestive of any malignancy. Forty-five age and gender-matched individuals diagnosed with MS according to the 2017 McDonald diagnostic criteria, without migraine who are registered in our iMed © database were included in the study. The number of WML was counted on FLAIR images and the WMLs were grouped according to the anatomical localization and distribution pattern. Four subgroups were determined according to the WML distribution. These subgroups were juxtacortical, deep white matter, periventricular, and infratentorial. Based on the number of WML, five subgroups were identified; 0, 1–2, 3–8, and ≥9. The anatomical localization of WMLs was defined as frontal, temporal, parietal, occipital, and infratentorial.

The data were analyzed with IBM SPSS V23. Compatibility with normal distribution was examined by Kolmogorov Smirnov and Shapiro Wilk tests. Mann Whitney U test was used to compare data without normal distribution. Independent samples t-test was used to compare normally distributed data, and the results of the analysis were presented as mean ± s. Deviation. Categorical data were examined by the chi-square test and the results were presented in frequency (%). The significance level was considered as $p < 0.05$.

RESULTS

Ninety individuals, 45 individuals with migraine (29 women, 55.6%), 45 MS (25 women 55.5%), were included in the study. The median age of the group with migraine was 35 (23-54) years, while the median age of the group with MS was 34 (20-55) years. There was no significant difference between the groups in terms of age and gender distribution ($p = 0.342$ and $p = 0.389$). The median time since diagnosis was 10 (0.5-32) years for the migraine group and 5 (0.3-20) years for the group with MS. The duration of the migraine group since diagnosis was significantly longer ($p = 0.031$). In the migraine group, 3 (6.7%) individuals had migraine with aura, while 42 (93.3%) individuals had migraine without aura.

Table 1. Demographic characteristics of migraine and MS groups

	Migraine (n=45)	MS (n=45)	p
Age (year)	35 (23 - 54)	34 (20-55)	0.324*
Gender n, (%)			
Female	29, (55.6)	25, (55.5)	0.389#
Male	16, (44.4)	20, (45.5)	
Time since diagnosis (years)	10 (0.5-32)	5 (0.3-20)	0.031*

Data are given as median (minimum-maximum) and n, (%). * Mann Whitney U test, #Pearson chi-square test

The total number of T1 and T2 lesions were higher in the MS group ($p < 0.001$, $p < 0.001$). Similarly, the number of infratentorial and periventricular lesions was higher in the MS group ($p < 0.001$). The number of deep white matter lesions was higher in the migraine group ($p < 0.05$). There was no significant difference between the groups in the number of juxtacortical lesions ($p = 0.229$). Also, no T1 hypointense lesion was found in the migraine group (Figure 1).

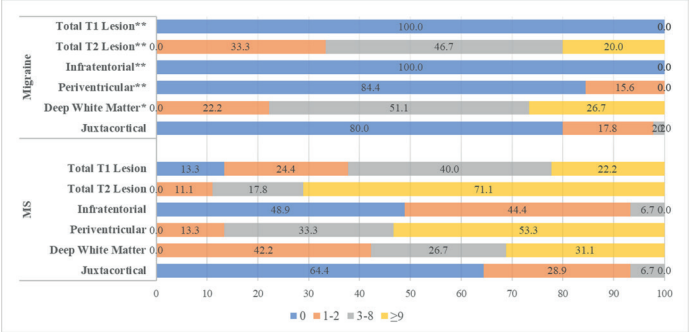

Figure 1. Distribution of the number of lesions in migraine and MS group, * p <0.05, ** p <0.001

When the anatomical distribution of the lesions is examined, it is noteworthy that the lesions in the migraine group are located in the frontal lobe (p <0.05). Temporal lobe involvement was more prominent in the MS group (p <0.05). Also, corpus callosum, brainstem, and cerebellum involvement were observed in the MS group (p <0.001). Parietal, occipital and capsula interna lesions did not differ between groups (p = 0.646, p = 0.292, p = 0.163). Besides, no lesions were observed in the brainstem and cerebellum in the migraine group (Figure 2).

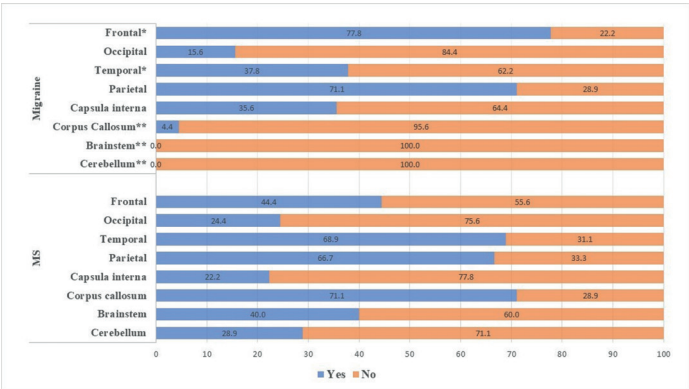

Figure 2. Anatomical locations of lesions in migraine and MS group, * p <0.05, ** p <0.001

DISCUSSION

In this study, the radiological features of MrWMLs, which has an important place in the differential diagnosis of MS, are emphasized. MrWMLs are defined as small, ovoid, hyperintense lesions in T2, and FLAIR images predominantly located in the deep white matter (15). MS lesions are located perpendicular to the lateral ventricles and are larger than migraine-related WMLs (16). In our study, it has been shown that MrWMLs are most frequently localized in the frontal and parietal lobes and are not observed in the infratentorial region, unlike MS lesions. This difference in the distribution of lesions suggests different physiopathology of MS and migraine. Immune-mediated demyelination and secondary axonal loss in MS affect the entire CNS. However, although the mechanism of formation of MrWMLs is not clearly understood, hypotheses have been proposed, including focal hypoperfusion and oligoemia during migraine attacks (17, 18). Ischemia-reperfusion periods can lead to increased permeability of the blood-brain barrier and glutamate excitotoxicity (19, 20). In a study evaluating 28 individuals with migraines, it was revealed that MrWMLs were mostly localized in the frontal lobe, brainstem, and cerebellum (20). In another study comparing MrWMLs and MS lesions, it was shown that frontal lobes were affected mainly in the migraine group, lesions were localized in the anterior circulation and posterior circulation was preserved (21). Although the reason for this difference is not fully known, it has been suggested that this distribution pattern may be explained by the lower overall prevalence of posterior system infarction compared with the anterior system infarction (21, 22). In our study, it has been shown that MrWMLs are frequently located in deep white matter in accordance with previous studies (23), and it was found that the periventricular area was preserved, unlike MS lesions. Likewise, Lapucci et al. (24) showed that the presence of periventricular lesions has a key role in the differentiation of migraine with aura from clinically isolated syndrome (CIS), the first episode of demyelinating disease, especially when there are more than three. Our study has some limitations. Firstly, clinical data such as attack frequency and duration in the migraine group could not be obtained in detail because of the retrospective design of the study. Additionally, MR images were evaluated without using automated software that could allow volumetric measurements. Volumetric analysis of MrWMLs can provide more information in the differential diagnosis. For example, in the study of Kamson et al. (21) MrWMLs were shown to have a smaller volume compared with MS lesions. However, there are studies showing that manual and automated software achieve similar results in determining the number of WMLs (25).

CONCLUSION

In this study, conventional MR imaging clues were defined for differentiating MS lesions from MrWMLs. MrWMLs were deep white matter lesions that are predominantly located at frontal and parietal lobes. It has been shown that MS lesions have a higher T1 and T2 lesion load and affect the periventricular and infratentorial areas. Besides, MS lesions are localized to all hemispheres, with the temporal lobes predominance. Studies using automated segmentation software and involving more individuals will be able to provide more information in the differential diagnosis of MrWMLs from MS lesions.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: The study was approved by the Erciyes University ethics committee (meeting date of the ethics committee: 12.02.2020, decision number: 2020/92).

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