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Original Article

Oligoclonal band on the 5-year prognosis of patients with multiple sclerosis

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Abstract

Background: Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system (CNS). Prognostic markers are essential for predicting disease progression and managing its impact. Oligoclonal bands (OCBs) are significant laboratory findings in MS, yet their prognostic role remains uncertain. This study aimed to evaluate the role of OCBs in the short-term progression of MS.

Methods: We enrolled patients diagnosed with Relapsing-Remitting MS and conducted a follow-up for five years, during which we monitored their Expanded Disability Status Scale (EDSS) scores. Clinical manifestations were compared between patients with positive and negative OCBs. Statistical analysis was performed using SPSS 26.

Results: Among the 140 participants, 41 (29%) were OCB-negative and 99 (71%) were OCB-positive. No significant differences were found regarding sex, age, family history, associated disease, and EDSS scores between the two groups at the beginning of the study. Throughout the five-year duration of the study, there was no disparity in the EDSS scores of patients belonging to the two groups. Notably, the mean number of relapses was 1.37 in OCB-negatives compared to 1 in OCB-positives, which was statistically significant (P=0.03). In other words, after 5 years, despite the high rate of recurrence in patients with negative OCB compared to patients with positive OCB, there was no difference in terms of prognosis (EDSS progress) between the two groups.

Conclusion: While the presence of OCBs in patients with MS does not demonstrate a significant prognostic impact over a five-year follow-up period, it could potentially influence the rate of recurrence.

Keywords: Cerebrospinal fluid, Multiple sclerosis, Oligoclonal band, Prognosis.

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Multiple sclerosis (MS) is the most common immune-mediated inflammatory demyelinating disease of the central nervous system (CNS), which typically emerges in young adults and follows a highly variable and unpredictable course. Currently, both the prevalence and incidence of this disease are increasing worldwide (1). Additionally, patients with MS face a higher risk of death from cardiovascular disease, respiratory disease, infectious causes, accidents, and suicide compared to their counterparts of the same genders (2). In nearly 85% of patients, the disease initiates as a clinically isolated syndrome (CIS), characterized by the first episode of CNS demyelination (3, 4). The ability to predict the disease's progression, especially at its onset, holds the potential to provide more effective treatment approaches and reduce the risk of mortality. According to the 2017 McDonald criteria, the diagnosis of MS relies on integrating clinical findings, imaging, and laboratory data (5). Among these, the presence of oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF) stands as the most valuable laboratory finding. For patients with clinically isolated syndrome, OCB detection can fulfill the dissemination criterion in time (5).

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Positive OCB means the presence of two or more bands in the CSF sample compared to the serum sample. Several studies suggest a high likelihood for OCBs to influence the progression of MS (6, 7). However, other studies have found no significant association between OCBs and disease evolution (8, 9). Despite this variability, OCBs still maintain a consistent value as a biomarker for clinical diagnosis and potentially hold relevance for predicting the progression of MS. The aim of this study was to assess the value of Oligoclonal Band on the 5-year prognosis of patients with multiple sclerosis. This comparison intended to determine the prognostic impact of OCBs on the future course of the disease.

Methods

Study design: In this prospective cohort study, our study population consisted of patients with relapsing-remitting MS who were referred to MS Clinic of Besat Hospital, affiliated with Hamadan University of Medical Sciences, Hamadan, Iran, between 2018 and 2019. Patients were asked to complete pre-prepared checklists regarding their disease as well as demographic features and were then examined at three-month intervals for a five-year period. The inclusion criteria were naive patients with a definite diagnosis of relapsing-remitting MS based on the 2017 McDonald criteria who were treated with interferon $B1_a$ as well as EDSS score lower than 2 (5). Patients were excluded if they did not complete the five-year follow-up period or if they had refused to participate in the study.

Data collection: All patients were initially evaluated via the Expanded Disability Status Scale (EDSS) by a neurologist (MS Fellowship) during their first visit. The EDSS is the most common and widely accepted tool for measuring disability in MS (10). This scale assesses the patient's maximum functional ability and has 10 grades, ranging from 0 (normal) to 10 (death due to the disease). To evaluate the five-year progression of MS, the patients' new disability scores were calculated at the end of the five-year follow-up period. Additionally, the number of relapses experienced during these five years was extracted from their medical records. To investigate the presence of OCBs in the central nervous system (CNS), samples of cerebrospinal fluid (CSF) were collected from patients and sent to the laboratory for analysis. OCBs were quantified using the Isoelectric Focusing (IEF) method. All samples were immediately sent to the same laboratory after lumbar puncture (LP) to prevent measurement errors. To mitigate the impact of confounding variables, patients were matched based on age, sex, and EDSS score. The analysis results were recorded in the patients' medical files. Patient information was collected using pre-prepared checklists, which included details such as age, sex, family history, changes in treatment, EDSS scores at the beginning of the diagnosis and after five years, type of MS, presence of OCBs in CSF, number of relapses, hospital admissions, and associated diseases.

Ethical considerations: The study objective was explained to all patients, and written informed consent was obtained from each participant. The patients were assured that their information would be kept confidential by the researcher, and they could voluntarily withdraw from the study at any time without any impact on their treatment course. Lumbar puncture (LP) is one of the routine measurement tests used in the course and diagnosis of MS. No additional charges were applied to the patients for this procedure. The study was conducted under the auspices of the ethical board of Hamadan University of Medical Sciences and registered with the number IR.UMSHA.REC.1400.725 in the Research Ethics Committee of the University of Medical Sciences

Statistical analysis: To determine the sample size, we used the comparison ratio formula based on a study by Michael J Olek et al. considering a power of 90% and a type I error of 5% (11). This calculation yielded a sample size of 140 participants. Due to the limitation in the number of OCB-negative patients and drawing from insights from previous studies, we allocated one-third of the samples as OCB-negative and two-thirds as OCB-positive (12). Statistical analysis was performed using SPSS Version 26.0 (IBM, USA). For descriptive statistics, mean and standard deviation (SD) were used for quantitative variables with normal distribution, while median and interquartile range [IQR] were used for non-normally distributed variables. The Mann-Whitney U test was applied for categorical variables, and the Spearman correlation test was utilized for bivariate correlations involving quantitative data. To compare the change in EDSS at the time of diagnosis with the EDSS after five years, we employed the Repeated-Measures analysis of variance (ANOVA) test. The chi-square test was employed to explore relationships between categorical variables. Significance level of 5% was considered for all analyses.

Results

Among the 140 patients, 41 (29%) were OCB-negative, while 99 (71%) were OCB-positive. The mean age at disease manifestation was 31 years (SD: 9.9; range 14 - 60), and 112 (80%) of the participants were females. Table 1

reports the characteristics of patients in the two groups of OCB-positive and OCB-negative. As demonstrated, there were no significant differences in sex (P=0.19), age (P=0.87), family history (P=0.58), associated diseases (P=0.55), clinical presentation (P=0.16), and the course of the disease (P=0.28) between patients with or without OCB in CSF (table 1). Additionally, the EDSS changes over time in both the OCB-positive and OCB-negative groups showed statistical significance (P<0.001) (figure 1). However, the EDSS variations between the two groups of OCB were not statistically significant (P=0.14). Furthermore, our results indicated that the EDSS changes did not significantly differ between the OCB groups, based on whether the patient required a modification in their treatment regimen (P=0.98). Regarding other outcomes, we observed no significant association between OCB status and re-admission (OR: 0.34; CI95%: 0.07 - 1.76; P=0.15) or the occurrence of relapse (OR: 0.23; CI95%: 0.07 - 0.69; P=0.05). However, the number of relapses was significantly associated with a positive OCB status in CSF (P: 0.03).

Discussion

The prognostic value of OCB in the CSF of patients with MS remains uncertain. In this present study, we observed no significant difference between OCB status and MS progression, indicating that the presence of OCBs does not necessarily imply a more aggressive disease after primary five years of follow-up. The EDSS is the most widely used and universally accepted scale for measuring the outcome of MS in clinical studies (10). Our findings revealed no significant association between OCB-positive as well as OCB-negative patients and EDSS, either at the onset of the disease or after five years. Similar results were reported in other studies, indicating no correlation between OCB and disability (13-15).

Table 1. Comparison of demographic and clinical characteristics of multiple sclerosis and clinically isolated syndrome patients based on oligoclonal bands in their cerebrospinal fluid

Characteristics	Total; N=140	Oligoclonal bands			P-value [a]
		Negative; n=41 (29.3%)	Positive; n=99 (70.7%)		
Gender; n (%)	Male	28 (20)	11 (39.29)	17 (60.71)	0.19
	Female	112 (80)	30 (26.79)	82 (73.21)	
Age (years), median [Q1 – Q3]		31 [14-60]	30 [18-60]	31 [14-56]	0.87
Positive family history, n (%)		30 (21.43)	10 (33.33)	20 (66.67)	0.58
Associated disease, n (%)	Total	25 (17.86)	7 (20)	18 (72)	0.55
	Hypothyroid	9 (6.43)	2 (22.22)	7 (77.78)	0.63
	Diabetes	3 (2.14)	1 (33.33)	2 (66.67)	0.88
	Cardiovascular disease	2 (1.42)	1 (50)	1 (50)	0.52
	Hypertension	2 (1.42)	1 (50)	1 (50)	0.52
	Others	9 (6.43)	2 (22.22)	7 (77.78)	0.63
EDSS, median [Q1 – Q3]	First	1 [0-2]	1 [0-2]	1 [0-2]	0.47
	Second	1 [0-2.5]	1 [0-3.25]	1 [0-2]	0.38
	Difference	0.5 [0-1]	0 [0-1]	0.5 [0-1]	0.75
Admission, n (%)		125 (89.29)	39 (31.2)	86 (68.8)	0.15
Admission number, median [Q1 – Q3]		1 [1-2]	1 [1-2]	1 [1-2]	0.42
Change in treatment, n (%)		51 (36.4)	39 (39.4)	12 (29.3)	0.26
Relapse, n (%)		104 (74.29)	37 (35.6)	67 (64.4)	0.05
Relapse number, median [Q1 – Q3]		1 [0-2]	1 [1-2]	1 [0-2]	0.03

EDSS: Expanded Disability Status Scale; OCB, oligoclonal bands. [a] Chi-square test or Mann-Whitney U test

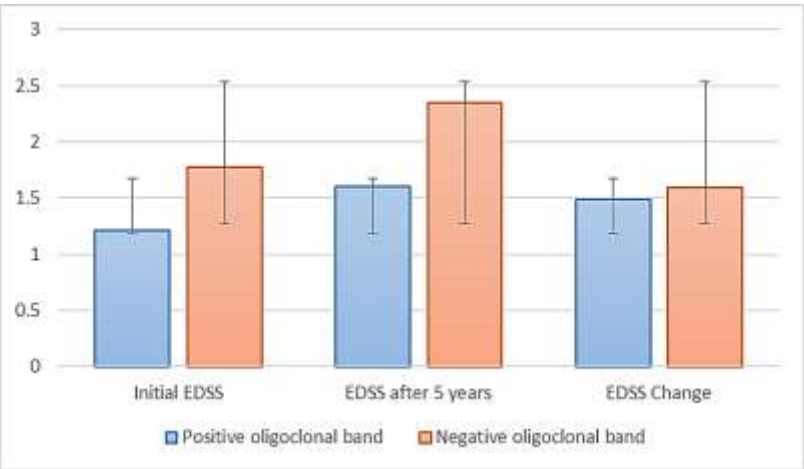

Figure 1. Progress of Expanded Disability Status Scale (EDSS) after five years of multiple sclerosis patients in two groups of positive and negative oligoclonal bands in cerebrospinal fluid

Conversely, a study from China suggested that patients with OCB may experience a faster disease progression (8). However, some studies have reported the presence of OCBs to be associated with a higher disability score (16-18). On the contrary, another study demonstrated that patients without OCBs exhibited a higher change in EDSS after five years (19). These differences in results may be attributed to variations in the ethnicity of the patient populations studied.

Furthermore, other MS outcomes, including relapses and hospital admissions, were not found to be correlated with the presence of OCB. However, we did observe a significantly higher number of relapses in patients without OCB compared to those with OCB. This finding contrasts with results from other studies that reported no relationship between relapses and OCB (8, 15, 19). Thus, the recurrence of MS does not appear to be influenced by the presence of OCB. While the presence of negative OCB in the first 5 years does not exert an influence on the disease prognosis, studies suggest that a higher frequency of relapses during the initial five years is associated with a poorer prognosis for patients in the future. In other words, based on the results of the present study, individuals with negative OCB may potentially experience a worse long-term prognosis due to an increased number of relapses in the first five years. We acknowledge that our study has certain limitations. Various factors can potentially influence outcomes, such as ethnicity, season, latitude, serum vitamin D levels, smoking, stress, infectious diseases, pregnancy, and assisted reproduction, which should be taken into consideration (20). Additionally, treatment and response to treatment can vary among patients due to the variability in disease severity. In this study, we utilized the EDSS to measure disability, which means we did not have detailed information about specific changes in disability over time for each patient. Our study findings demonstrate after the first 5 years of the disease, despite the high recurrence rate in patients with negative OCB compared to patients with positive OCB, there was no significant difference in terms of prognosis (EDSS progress) between the two study groups. It is advisable to investigate the impact of positive OCB on long-term prognosis by dealing with a larger sample size over a period of 10 years or more.

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Ethics approval: In the study, patients' information was recorded confidentially, and no charges were imposed on any of the patients throughout all stages of the research. Additionally, written informed consent was obtained from all patients or their legal representatives. The study received approval from the ethics committee of the university and was conducted in accordance with the Declaration of Helsinki.

Conflict of interests: The authors declare that they have no competing interests.

Authors' contribution: Masoud Ghiasian and Mojtaba Khazaei contributed to conception and study design, data collection and interpretation of data. Sajjad Daneshyar contributed to conception and design, data collection and drafting the article. Elham Khanlarzade performed data analysis. Mohammad Amin Habibi contributed to conception and design, data collection, and interpretation of data .All authors approved the final version of the manuscript to be published.

Availability of data and materials: All data pertaining to this study have been included in the manuscript. If you are interested in obtaining further information, please feel free to contact the corresponding author.

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