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Research

Examining Biomarker Levels in Patients Diagnosed with Multiple Sclerosis

Multiple Skleroz Tanılı Hastalarda Biomarker Düzeylerinin İncelenmesi

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ABSTRACT

Objective: Multiple sclerosis (MS) is a chronic autoimmune disorder characterized by inflammation, demyelination, and axonal damage in the central nervous system. Oligoclonal bands (OCBs) composed of immunoglobulin G (IgG) antibodies in the cerebrospinal fluid (CSF) are a key diagnostic marker for MS, indicating intrathecal IgG synthesis. Recent research has emphasized the importance of distinguishing between kappa and lambda light chains in understanding the clinical implications of OCBs in MS. This study aimed to explore the relationship between kappa light chain and clinical findings, considering the presence and type of OCBs in MS.

Methods: A total of 72 MS patients were included, and their demographic characteristics, laboratory results, CSF analysis, and cranial/spinal magnetic resonance imaging findings were recorded. Blood samples were collected for kappa light chain analysis. The presence of spinal lesions, kappa light chain level, Expanded Disability Status scale (EDSS) score, and IgG index were compared among patients based on OCB positivity type.

Results: The mean age of 72 MS patients was 38.6±10.2 spinal lesions were in 41 patients. The free kappa LC level was calculated as 15.2 mg/L (8.8-48.6), and the serum kappa LC level was 2.8 mg/L (1.5-7.3). No significant relationship was observed between free and serum kappa light chain levels, IgG index, EDSS score, spinal lesion count, and total lesion count in patients with OCB types 1 and 2. In addition, subgroup analysis among patients with OCB type 2 revealed no significant relationship.

Conclusion: In this study, no relationship was found between the EDSS score and free kappa light chain. Although other studies have shown a correlation between the number of spinal lesions and kappa light chain levels, no such correlation was observed in this study. Understanding the specific role of the kappa light chain in MS can provide insights into disease severity, clinical subtypes, and treatment response. Such knowledge can contribute to personalized treatment approaches and improved prognosis for MS patients.

Keywords: Kappa light chain, oligoclonal band, multiple sclerosis

ÖZ

Amaç: Multipl skleroz (MS), merkezi sinir sisteminde enflamasyon, demiyelinizasyon ve akson hasarı ile karakterize kronik otoimmün bir bozukluktur. Beyin omurilik sıvısında (BOS) bulunan immünoglobulin G (IgG) antikorlarından oluşan oligoklonal bantlar (OCB'ler), MS için önemli bir belirteç olup intratekal IgG sentezini göstermektedir. Son araştırmalar, MS'deki OCB'lerin klinik sonuçlarını anlamak için kappa ve lambda hafif zincirler arasındaki ayrımın önemini vurgulamıştır. Bu çalışma, MS'deki OCB'lerin varlığı ve tipini dikkate alarak kappa hafif zincir ile klinik bulgular arasındaki ilişkiyi araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Toplam 72 MS hastası dahil edildi ve demografik özellikleri, laboratuvar sonuçları, BOS analizi ve kraniyal/spinal manyetik rezonans görüntüleme bulguları kaydedildi. Kappa hafif zincir analizi için kan örnekleri alındı. OCB pozitifliği tipine göre hastalar arasında spinal lezyonların varlığı, kappa hafif zincir seviyesi, Genişletilmiş Sakatlık Durumu ölçeği (EDSS) skoru ve IgG indeksi karşılaştırıldı.

Bulgular: Yetmiş iki MS hastasının ortalama yaşı 38,6±10,2 idi. Kırk bir hastada spinal lezyonlar mevcuttu. Serbest kappa hafif zincir seviyesi 15,2 mg/L (8,8-48,6) olarak hesaplandı ve serum kappa hafif zincir seviyesi 2,8 mg/L (1,5-7,3) idi. OCB tipi 1 ve 2 olan hastalarda serbest ve serum kappa hafif zincir seviyeleri, IgG indeksi, EDSS skoru, spinal lezyon sayısı ve toplam lezyon sayısı arasında anlamlı bir ilişki gözlenmedi. Ayrıca, OCB tipi 2 olan hastalar arasında yapılan alt grup analizinde anlamlı bir ilişki bulunmadı.

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Sonuç: Bu çalışmada, EDSS skoru ile serbest kappa hafif zincir arasında bir ilişki bulunmadı. Diğer çalışmalar, spinal lezyon sayısı ile kappa hafif zincir seviyeleri arasında bir korelasyon göstermiş olsa da, bu çalışmada böyle bir korelasyon gözlenmedi. MS'deki kappa hafif zincirin özel rolünün anlaşılması, hastalık şiddeti, klinik alt tipler ve tedavi yanıtı konusunda bilgi sağlayabilir. Bu tür bilgi, kişiselleştirilmiş tedavi yaklaşımlarına ve MS hastaları için iyileştirilmiş prognoza katkıda bulunabilir.

Anahtar Kelimeler: Kappa hafif zincir, oligoklonal band, multipl skleroz

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disorder affecting the central nervous system, characterized by inflammation, demyelination, and axonal damage. One of the key diagnostic markers for MS is the presence of oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF) (1). OCBs are composed of immunoglobulin G (IgG) antibodies, and their presence suggests intrathecal IgG synthesis. However, recent research has highlighted the importance of differentiating between kappa and lambda light chains in understanding the clinical implications of OCBs in MS.

OCBs are detected through immunofixation or isoelectric focusing of CSF, and their presence is considered a valuable diagnostic criterion for MS. OCBs are found in approximately 80-95% of MS patients, indicating a specific immune response within the central nervous system. OCBs arise from the clonal expansion of B cells and subsequent production of specific IgG antibodies. These antibodies, along with the involved B cells, are believed to play a role in the inflammatory cascade observed in MS (2).

The Ig molecule consists of two heavy chains and two light chains, which can be further classified into two types: kappa and lambda. Recent studies have shown that analyzing the composition of OCBs by distinguishing between kappa and lambda light chains can provide additional insights into the pathophysiology of MS (3).

This article aims to explore the relationship between the kappa light chain and clinical findings, considering the presence and type of OCBs in MS.

METHODS

A total of 72 patients diagnosed with MS were included in this study. Demographic characteristics, laboratory results, and CSF analysis results of the patients were recorded. During the patients' last outpatient follow-ups, cranial and spinal magnetic resonance imagings (MRI) were performed according to the MS protocol. The Kappa light chain was studied from the blood samples obtained from the patients simultaneously with MRI. The number of cranial and spinal lesions was calculated and compared with the blood and CSF results. The presence of OCBs was classified as type 1 or type 2 positivity. One patient with type 3 positivity was included in the number of type 2 positive patients. The presence of spinal lesions, kappa light chain level, EDSS level, and IgG index were compared among patients based on the OCB positivity type.

Statistical Analysis

Statistical analyzes were conducted using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA) software. The normal distribution of the data was evaluated using the Shapiro-Wilk test. Numerical variables showing a normal distribution and those not showing a normal distribution are presented as mean ± standard deviation and median (minimum-maximum), respectively. Categorical variables are expressed as numbers and percentages. The levels of free and serum kappa-LC did not follow a normal distribution, and differences between groups were evaluated using the Mann-Whitney U test or Kruskall-Wallis H test (post-hoc: Dunn's test). The relationship between the numerical variables was examined using Spearman correlation analyzes $p<0.05$ was considered statistically significant.

Informed consent forms were obtained from all the participating patients. University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee approval was obtained using protocol number 2022/191 and decision number 2022-12-03 (date: 20.06.2022).

RESULTS

Of the 72 evaluated MS patients, 51 were female and 21 were male. The mean age was 38.6±10.2. Among the patients, 52 had relapsing-remitting MS (RRMS), 10 had secondary progressive MS (SPMS), 5 had radiologically isolated syndrome, 4 had primary progressive MS (PPMS), and 1 patient had clinically isolated syndrome (Table 1).

Twenty two patients were receiving interferon treatment. Fourteen patients were using fingolimod, 13 patients were on glatiramer acetate, 6 patients were taking teriflunomide, 6 patients were receiving okrelizumab, 4 patients were on dimethyl fumarate, and 1 patient was using azathioprine. Six patients were being followed without any treatment.

Spinal lesions were in 41 patients. One patient had lesions in the thoracic area, whereas cervical spinal lesions were in

all 40 patients. The free kappa LC level was calculated as 15.2 mg/L (8.8-48.6), and the serum kappa LC level was 2.8 mg/L (1.5-7.3) (Table 1).

No significant relationship was observed between the levels of free and serum kappa-LC, IgG index, EDSS score, spinal lesion count, and total lesion count in patients with OCB types 1 and 2. Additionally, in the subgroup analysis conducted among patients with OCB type 2, no significant relationship was found (Table 2).

DISCUSSION

The presence of OCBs has been associated with a more severe disease course in MS (4). Specifically, a higher number of OCBs has been linked to increased disability progression and a higher risk of transitioning from RRMS to SPMS. However, the impact of the kappa light chain specifically on disease severity requires further investigation. In our study, no relationship was detected between OCB positivity (type 2 pattern) and free kappa light chain. In a previous study, it was stated that kappa free light chain levels have an additive predictive value for early MS disease activity that is independent of known predictors (5). On the contrary, our findings suggest that the level of kappa light chains may not be as decisive in indicating disease severity as OCB positivity.

Some studies have suggested that the presence of kappa light chains is more frequently associated with PPMS and SPMS, which are generally characterized by a progressive disease course compared with RRMS (6). This observation indicates that the kappa light chain may be associated with a more progressive and disabling form of MS. In our study, no relationship was found between the patients' EDSS and free kappa light chain. This finding suggests that EDSS alone may not be sufficient to determine disease severity.

The number of spinal lesions in MS can have varying degrees of severity and can impact the overall disease progression and clinical presentation (7). Multiple studies have demonstrated that a higher number of spinal lesions is associated with elevated levels of kappa light chain (8). This correlation suggests that spinal lesions contribute to the production or release of the kappa light chain, potentially indicating an underlying inflammatory process in the spinal cord. There was no correlation between the number of spinal lesions and the level of free kappa light chain in our study. However, further research is needed to establish a definitive causal relationship between the number of spinal lesions and kappa light chain levels in MS patients.

Table 1. Demographic parameters, laboratory data, and cerebrospinal fluid results

Variables	All population n=72
Gender, n (%)	
Female	51 (70.8)
Male	21(29.2)
Age, years	38.6±10.2
MS type, n (%)	
RRMS	52 (72.2)
PPMS	4 (5.6)
SPMS	10 (13.9)
CIS	1 (1.4)
RIS	5 (6.9)
OCB, n (%)	
Type 1	40 (55.6)
Type 2, 3	32 (44.4)
IgG	0.8 (0.4-2.8)
Spinal lession, n (%)	
No	31 (43.1)
Yes	41 (56.9)
EDSS	1 (0-6)
Free kappa-LC	15.2 (8.8-48.6)
Serum kappa-LC	2.8 (1.5-7.3)

RRMS: Relapsing-remitting MS, PPMS: Primary progressive MS, SPMS: Secondary progressive MS, CIS: Clinically isolated syndrome, OCB: Oligoclonal band, EDSS: Expanded Disability Status scale, IgG: Immunoglobulin G, MS: Multiple sclerosis

Table 2. The relationship between kappa-LC and clinical findings according to the presence and type of OCB

Variables	Free Kappa LC		Serum Kappa LC	
	r	p	r	p
OCB type 1				
IgG index	-0.5	0.667	-0.500	0.667
EDSS	0.122	0.467	-0.063	0.707
Number of lession	-0.059	0.725	0.053	0.753
Number of spinal lession	0.082	0.625	-0.119	0.476
OCB type 2, 3				
IgG index	0.114	0.556	0.013	0.946
EDSS	0.001	0.996	0.026	0.888
Number of lession	0.139	0.447	-0.084	0.647
Number of spinal lession	-0.248	0.172	0.074	0.686

OCB: Oligoclonal band, EDSS: Expanded Disability Status scale, IgG: Immunoglobulin G

In addition, other factors, such as the type of MS, disease duration, and treatment status, should be considered when interpreting the results.

Patients with increased kappa light chain have a higher risk of relapses and a poorer response to disease-modifying therapies, such as interferon-beta and glatiramer acetate (9). These findings highlight the importance of considering the type of OCBs when determining treatment strategies for MS patients. Because of the insufficient number of patients in the treatment class group in our study, no conclusive data on this issue could be obtained.

CONCLUSION

The relationship between the kappa light chain and clinical findings or cranial and spinal lesions in MS, particularly in the context of OCBs, is an emerging area of research. While the presence of OCBs in general suggests intrathecal IgG synthesis, understanding the specific role of the kappa light chain can provide additional insights into disease severity, clinical subtypes, and treatment response. Further investigations and prospective studies are required to unravel the underlying mechanisms and clinical implications associated with the kappa light chain. Such knowledge can contribute to personalized treatment approaches and improved prognosis for patients with MS.

ETHICS

Ethics Committee Approval: University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee approval was obtained using protocol number 2022/191 and decision number 2022-12-03 (date: 20.06.2022).

Informed Consent: Written consent was obtained from the legal caregivers of the patients.

Authorship Contributions

Surgical and Medical Practices: İ.A., Concept: V.Y., İ.A., E.D.D.P., Design: İ.A., Data Collection or Processing: A.M.Y., Y.Ç., A.G., Analysis or Interpretation: V.Y., İ.A., Literature Search: A.M.Y., Y.Ç., A.G., E.D.D.P., Writing: İ.A., A.M.Y., Y.Ç., A.G.

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