ORIGINAL ARTICLE

ARE HYPERINTENSE SIGNAL INCREASES ON CRANIAL MRI A NEW FINDING FOR DIFFERENTIAL DIAGNOSIS IN RHEUMATIC DISEASES?

Romatizmal Hastalıklarda Ayırıcı Tanı İçin Kraniyal MRG'de Hiperintens Sinyal Artışları Yeni Bir Bulgu Mudur?

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ABSTRACT

Objective: To retrospectively evaluate demographic and clinical features of patients with rheumatic diseases, analyze cranial magnetic resonance imaging (MRI) findings taken for various reasons, and assess their contribution to diagnosis.

Material and Methods: Thirty-eight patients followed for rheumatologic diseases between March 2023 and December 2024 were included. Cranial MRI scans performed for reasons such as headache, vertigo, migraine, and cerebrovascular events were reviewed. Hyperintense signal changes were assessed on T2-weighted and Fluid Attenuation Inversion Recovery (FLAIR) images, including lesion location, number, and morphology.

Results: Of the 38 patients, 22 had Rheumatoid Arthritis (RA), 4 had Sjögren's syndrome, 9 had Systemic Lupus Erythematosus (SLE), 2 had SLE with multiple sclerosis (MS), and 1 had Ankylosing Spondylitis (AS). Cranial lesions were observed in 32 cases (84.2%). Lesions were most common in RA (18 patients, 81.8%), with 88.9% showing periventricular localization. Among RA patients, 8 had periventricular-cortical/subcortical, 4 had periventricular-juxtacortical, and 2 had only periventricular lesions. In the SLE group, lesions were present in 8 patients (88.8%), and in both SLE-MS cases (100%), all with periventricular localization. Of these, 4 had periventricular-cortical/subcortical and 2 had periventricular-juxtacortical involvement.

Conclusion: Cranial MRI findings may support diagnosis and symptom evaluation in rheumatic diseases. Nonspecific hyperintense signals, particularly with periventricular distribution, may reflect early central nervous system (CNS) involvement and aid differential diagnosis.

Keywords: *Rheumatic Diseases; Cranial MRI; Hyperintense Lesions; Differential Diagnosis; Central Nervous System Involvement; White Matter Lesions*

ÖZET

Amaç: Romatizmal hastalığı olan hastaların demografik ve klinik özelliklerini geriye dönük olarak değerlendirmek, farklı nedenlerle çekilen kranial manyetik rezonans görüntüleme(MRG) bulgularını analiz etmek ve bu bulguların tanıya katkısını araştırmak.

Gereç ve Yöntemler: Mart 2023- Aralık 2024 tarihleri arasında romatolojik hastalıklar nedeniyle takip edilen 38 hasta çalışmaya dahil edildi. Baş ağrısı, vertigo, migren ve serebrovasküler olay gibi nedenlerle çekilen kranial MRG görüntüleri değerlendirildi. T2 ağırlıklı ve FLAIR (Fluid Attenuation Inversion Recovery) sekanslarında izlenen hiperintens sinyal değişiklikleri; lezyonun yerleşimi, sayısı ve morfolojik özellikleri açısından incelendi.

Bulgular: 38 hastanın 22'si Romatoid Artrit (RA), 4'ü Sjögren sendromu, 9'u Sistemik Lupus Eritematozus (SLE), 2'si SLE-Multipl Skleroz (MS) ve 1'i Ankilozan Spondilit (AS) tanılıydı. Toplam 32 hastada (%84,2) kranial lezyon saptandı. RA'lı 18 hastanın %88,9'unda periventriküler yerleşimli lezyonlar izlendi. Bunların 8'i periventriküler-kortikal/subkortikal, 4'ü periventriküler-juxtakortikal ve 2'si sadece periventriküler yerleşimliydi. SLE grubunda 8 (%88,8), SLE-MS grubunda ise 2 (%100) hastada lezyon saptandı ve tamamı periventriküler yerleşimliydi. Bu lezyonların 4'ü periventriküler-kortikal/subkortikal, 2'si periventriküler-juxtakortikaldi.

Sonuç: Kranial MRG bulguları, romatizmal hastalıklarda tanı, semptom değerlendirmesi ve ayırıcı tanıya katkı sağlayabilir. Özellikle periventriküler yerleşimli nonspesifik hiperintens sinyaller, erken santral sinir sistemi tutulumunu gösterebilir.

Anahtar Kelimeler: *Romatizmal Hastalıklar; Kraniyal MRG; Hiperintens Lezyonlar; Ayırıcı Tanı; Merkezi Sinir Sistemi Tutulum; Beyaz Madde Lezyonları*

INTRODUCTION

Rheumatic diseases (RD) are chronic disorders that generally affect connective tissue and are formed through inflammatory and autoimmune mechanisms, with various environmental and genetic factors playing a role (1). The most commonly encountered diseases in this group include Rheumatoid Arthritis (RA), Osteoarthritis (OA), Systemic Lupus Erythematosus (SLE), and Ankylosing Spondylitis (AS). Although these diseases have many clinical findings, sometimes they may manifest secondarily with neurological symptoms. Neurological manifestations secondary to involvement of the peripheral or central nervous system (CNS) may include psychiatric symptoms, encephalopathy, cranial nerve involvement, myelopathy, radiculopathy, or peripheral neuropathy (2). Pathological entities characterized by inflammatory cell infiltration and necrosis of blood vessel walls as well as immune-mediated changes and ischemia of the vascular wallthe hallmark of vasculitides are the primary causes of symptoms related to the CNS and peripheral nervous system (PNS) (1,3-4). The most common cranial imaging findings include focal, nonspecific white matter T2 hyperintense lesions in periventricular (PV) or subcortical (SC)regions, which may enhance; however, these findings can also be related to cerebrovascular lesions or leukoaraiosis. Additionally, accompanying parenchymal atrophy may range from subtle findings to widespread hemispheric involvement, especially in Sjögren's syndrome and SLE. On the other hand , cranial involvement in RA differs from other diseases due to distinct underlying histopathologies, including vasculitis, nonspecific inflammation, rheumatoid nodules, and leptomeningeal involvement (5-6). Although many studies in the literature explore neurological involvement in rheumatologic disorders, the exact significance of cranial magnetic resonance imaging (MRI) findings remains unclear, as periventricular white matter hyperintensities can occur in many diseases.

The aim of our study is to retrospectively evaluate demographic and clinical characteristics of patients diagnosed with various rheumatic diseases, to analyze their cranial MRI findings taken for different reasons, and to investigate the contribution of these findings to the diagnosis.

MATERIALS AND METHODS

This study was pre-approved by the local committee (2025-121) and was conducted in accordance with the 1964 Declaration of Helsinki; individual patient consent was declined. Patient records and information were anonymized and de-identified prior to analysis.

In our study, 38 cases who were followed up for rheumatologic diseases between March 2023 and December 2024 were included. (Patients' ages ranged between 41.6 and 57 years.) The most common symptoms (headache, myalgia, dermatitis), demographic characteristics (age, gender, presence of comorbidities), treatments administered, and cranial MRI findings obtained for various reasons (headache, vertigo, migraine, cerebrovascular event) were analyzed. Exclusion criteria were as follows: age <18 years, history of major brain trauma, previous medical history of brain surgery, evidence of viral infections, neurodegenerative disorders, and previous cerebrovascular event. Nonspecific white matter lesions and ischemic lesions due to small vessel diseases were considered outside the scope of the study. Lesions were detected in cranial MRI in a total of 32 (84.2%) cases.

MR images were acquired by using a multichannel superconducting 3T MRI scanner (Philips Ingenia, Philips Medical System Nederland B.V., Netherlands) equipped with high speed gradients. The MRI protocol was composed of a diagnostic focused whole brain anatomical sequences including axial and sagittal turbo spin-echo T2-weighted (TR/TE: 3000/80; scan thickness 5 mm; slice gap 1 mm), axial fluid attenuated inversion recovery (TR/TE: 11000/120; scan thickness 5 mm; slice gap 1 mm), 3D T1 weighted (TR/TE: 25/1.74; scan thickness 2 mm; slice gap 0.4 mm) for every participant to rule out any organic brain disorders. All sequences had a number of excitations (nex) of 2.

All brain MRI examinations performed on the patients were accessed via the Picture Archiving and Communication System (PACS). On cranial MRI, hyperintense signal changes were evaluated on T2-weighted and Fluid Attenuation Inversion Recovery (FLAIR) images, and lesion location (cortical (C), subcortical (SC), infratentorial, periventricular, juxtacortical, corpus callosum), lesion number (single or multiple lesions), and morphologic characteristics

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(size >3 mm, ovoid shape, long-axis vertical orientation toward the corpus callosum/ventricles indicating lesions "typical" for MS) were assessed (7-8). Accompanying MRI findings such as hydrocephalus, atrophy, and ischemic changes were also evaluated. Nonspecific white matter lesions and ischemic lesions due to small vessel disease were excluded from the study. Lesion characteristics and locations were examined according to patient groups.

Statistical Analyses

Data were analyzed using the Statistical Package for Social Sciences 23.0 for Windows (SPSS Inc., Chicago, IL). The descriptive findings were presented with frequency (n) and percentage (%) for the categorical data. Numerical variables without normal distribution were compared using the Mann-Whitney U test. Pearson correlation analysis was used to investigate possible correlations. The statistical significance was set at $p<0.05$.

RESULTS

There were 38 cases (32 female and 6 male) in the study. The mean age of female and male cases were 50.1 years (30-65), and 55.3 years (47-70) respectivelly. The distribution of the diseases were as; RA in 22 patients (57.9%), Sjögren's Syndrome in 4 patients (10.5%), SLE in 9 patients (23.7%), coexisting SLE and SLE-MS in 2 patients (5.3%), and AS in 1 patient (2.6%). RA was identified in all male patients, whereas 16 female patients were diagnosed with RA (Table 1).

In the study, lesions were identified in 32 (28 female and 4 male) patients (84.2%). The distribution of these cases was as follows: RA in 18 patients (56.3%), Sjögren's Syndrome in 3 patients (9.4%), SLE in 8 patients (25%), coexisting SLE and SLE-MS in 2 patients (6.3%), and AS in 1 patient (3.1%). Multiple lesions were detected in 25 patients, whereas single focal lesions were detected in 7 patients (Table 1), (Figure 1a,1b).

Lesions were observed in 18 patients with RA (81.8%). Of these lesions, 16 patients (88.9%) had periventricular localization, while one lesion each was located in the

Table 1. Distribution of the diseases with sex and lesion.

			RA	Sjögren	SLE	SLE-MS	AS	Total	
Patient	Female (F), n: 32		16	4	9	2	1	32	38
	Male (M), n: 6		6	0	0	0	0	6	
Lesion	Negative		4 (2F-2M)	1 (F)	1 (F)	0	0	6	
	Positive	Single	4	1	2	0	0	7	32
		Multipl	14	2	6	2	1	25	

Rheumatoid Arthritis (RA), Sjögren's Syndrome (Sjögren), Systemic Lupus Erythematosus (SLE), SLE and Multiple Sclerosis (SLE-MS), Ankylosing Spondylitis (AS)

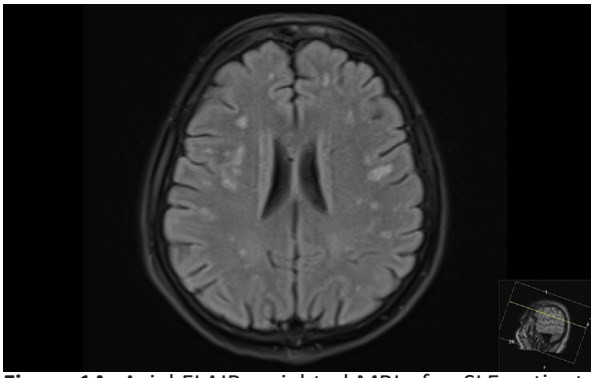

Figure 1A. Axial FLAIR weighted MRI of a SLE patient. The hyperintence signal on the left parietal lobe shows the juxtacortical involvement of SLE.

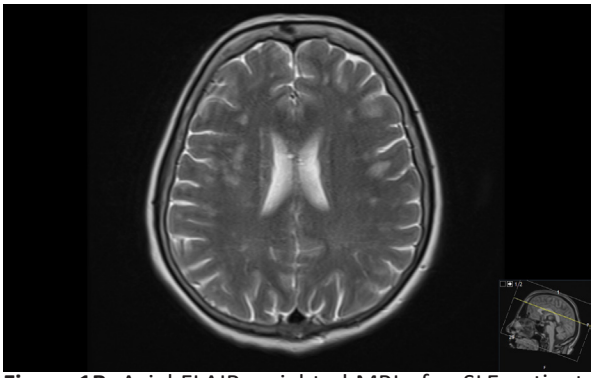

Figure 1B. Axial FLAIR weighted MRI of a SLE patient. (the same patient). The periventricular hyperintencity of SLE patient.

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corpus callosum and infratentorial areas(Figure 2a).

Single lesions were detected in 4 patients (2 patient in the periventricular region, 1 in the corpus callosum, and 1 in the infratentorial region).

Multiple lesions were observed in 14 patients, all of whom exhibited periventricular involvement. Furthermore, 9 of these RA patients had additional lesions located the periventricular localization in different areas (Table 2).

Lesions were detected in 10 cases: 8 in the SLE group (81.8%) and 2 in the SLE-MS group (100%). All these lesions had periventricular localization.

Two cases exhibited single periventricular lesions, while eight cases had multiple lesions.

Among those with multiple lesions, 3 cases showed periventricular involvement only; 3 had both periventricular and cortical/subcortical involvement; 1 had periventricular and juxtacortical lesions; and 1 case presented with periventricular, cortical/subcortical, and juxtacortical lesions (Table 2).

There was no statistically significant difference in lesion detection on MRI between the RA and SLE–SLE/MS groups (p =0,812).

Headache was detected in 26 cases (15 RA, 3 Sjögren's syndrome, 7 SLE or SLE/MS and 1 AS). MRI revealed lesions in 22 of these cases, while no lesions were detected in the remaining . When cases with and without headache were compared, no statistically

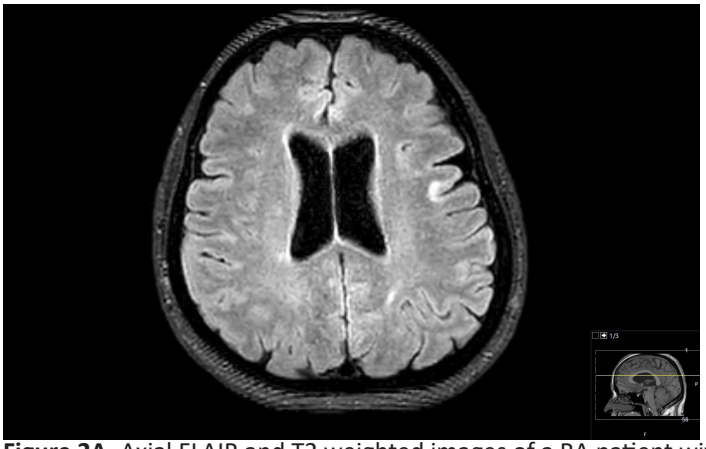

Figure 2A. Axial FLAIR and T2 weighted images of a RA patient with cortical involvement.

Table 2. Cranial MRI findings of the disease location with multipl or single lesion.

		RA	Sjögren	SLE	SLE-MS	AS	Total
Lesion Multiple	PV all	14[a]	1	6	2	1	24
	PV	5		3		1	9
	PV. CSC	3	1	2	1		7
	PV. CSC.JC	4		1			5
	PV. INF	1					1
	PV. CSC. INF	1					1
	PV. JC				1		1
	CSC		1				1
Lesion Single	PV	2	1	2			5
	CC	1					1
	INF	1					1
All lesions		18	3	8	2	1	32

Rheumatoid Arthritis (RA), Sjögren's Syndrome (Sjögren), Systemic Lupus Erythematosus (SLE), SLE and Multiple Sclerosis (SLE-MS), Ankylosing Spondylitis (AS), Periventricular (PV), cortical-subcortical (CSC), juxtacortical (JC), infratentorial (INF), corpus callosum (CC), a; RA-SLE+S-LE/MS (p =0,812)

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Table 3. Distribution of the diseases with headache and lesion.

			RA	Sjögren	SLE	SLE-MS	AS	Total	
Headache			15	3	7		1	26	
Lesion	Negative		2	1	1			4	
	Positive	Single	4	1	1			6	22
		Multipl	9	1	5		1	16	

Rheumatoid Arthritis (RA), Sjögren's Syndrome (Sjögren), Systemic Lupus Erythematosus (SLE), SLE and Multiple Sclerosis (SLE-MS), Ankylosing Spondylitis (AS)

significant difference was found in the presence of lesions (p = 0.478). Other symptoms were myalgia, peripheral neuropathy (PNP), dry mouth, dermatitis, and tremor.

No significant correlation was found between the presence of lesions and disease groups or clinical presentationp (p= 0.621). However, a strong and statistically significant positive correlation was observed between the presence of lesions and the presence of multiple lesions (p = 0.001, r = 0.864)

DISCUSSION

CNS involvement in rheumatic diseases is always a controversial, challenging to diagnose, and concerning issue for all clinicians (9). CNS involvement in rheumatic diseases causes different symptoms among patients. Consistent with the literature, RA is the most common disease, and headache is the most frequently observed symptom. While dry mouth is identified as a prominent symptom in Sjögren's patients, headache and myalgia are prominent in SLE patients. Since our patient group did not show acute disease manifestations and was under treatment, acute symptoms such as meningoencephalitis, stroke, hemorrhage, or myelitis seen in rheumatic diseases were not detected in our patients (1). It has been observed that treatment approaches vary according to the disease type. For example, steroid treatment is frequently preferred in SLE patients, whereas combination therapies are prominent in RA patients.

Regarding MRI findings, hyperintense lesions were detected on T2-weighted images in 32 patients, with different localization patterns. In previous studies, nonspecific hyperintense C-SC and periventricular white matter lesions on T2-weighted images have been reported particularly in SLE, Sjögren's syndrome, and scleroderma (2-5). In RA, besides nonspecific hyperintense signal increases, leptomeningeal involvement is also frequently observed (6). In our patients, the most commonly observed cranial MRI finding was T2 hyperintensity, although the distribution of these lesions showed significant variation. While cortical, subcortical, and periventricular hyperintensities can occur in many diseases, these hyperintensities are often seen in MS mimickers. In MS, lesions typically have periventricular localization, a perpendicular orientation to ventricular axis, and corpus callosum involvement (10). Brain white matter lesions are common in patients with comorbid vascular disease or migraine, as well as in healthy adults, and nonspecific small, rounded deep white matter lesions sparing the periventricular zone and U-fibres may also contribute to some of the lesion burden seen on imaging. Currently, it is rarely possible to distinguish whether individual lesions are attributable to demyelination or to a comorbidity (11). In our study, cortical-subcortical-periventricular lesions were frequently observed together. Since our patients did not have ischemia (due to age factors) or a diagnosis of MS, the presence of widespread hyperintense lesions in these patients suggests early CNS involvement of rheumatic diseases, especially if a rheumatic disease diagnosis is already established. Juxtacortical involvement is more frequently seen in MS cases (12-13); however, in our study, among 6 patients with juxtacortical lesions, only one had a concomitant diagnosis of MS. This finding suggests that juxtacortical involvement can also be seen in rheumatic diseases. Additionally, hydrocephalus and atrophy were detected independently of patient age, and these findings may also have diagnostic significance.

As is known, rheumatic diseases can cause CNS vasculitis by involving large, medium, and small vessels, and they can also result in vasculitic involvement

secondary to connective tissue diseases such as RA, Sjögren's syndrome, SLE, and systemic sclerosis. However, CNS involvement is less specific secondary to other vasculitides and has recently become less frequent (1). What we aim to emphasize in our study is that even if CNS symptoms are not present, due to the possibility of CNS involvement in these disease groups and the potential neurological manifestations related to immunotherapies used in treatment, we suggest that these patients should be periodically evaluated with brain MRI.

Neuropsychiatric involvement (NPSLE) in SLE patients has been reported in studies with a prevalence ranging from 14% to 75% (14,15). Unfortunately, there is currently no specific test for the early and definitive diagnosis of NPSLE. Therefore, patients with suspicious multifocal nonspecific lesions on MRI should be prioritized for early diagnosis and initiation of treatment.

In Sjögren's syndrome, thrombotic events occur less frequently compared to other rheumatic diseases; thus, nonspecific T2 hyperintensities may be more meaningful in terms of CNS involvement in Sjögren's patients, particularly in those without comorbidities (16). In our study, 3 out of 4 Sjögren's patients had periventricular and cortical-subcortical T2 hyperintensities. We believe that T2 hyperintensities may be important indicators of early CNS involvement in Sjögren's syndrome patients without comorbidities and that such patients require monitoring. Further studies involving larger patient groups are needed to evaluate this topic more comprehensively.

CONCLUSION

In conclusion, based on our study, we believe that cranial MRI findings, alongside clinical evaluation, can contribute to the diagnosis of rheumatic diseases, the understanding of symptoms, and the differential diagnosis. Therefore, we suggest that nonspecific hyperintense signal increases observed on cranial MRI in this group of diseases may be meaningful in indicating early CNS involvement.

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The authors declare that they have no conflict of interest to disclose

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