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ORIGINAL ARTICLE

Periventricular Leukomalacia: Comparison of Parenchymal Signal and Volume Changes on Brain MRI in Paediatric Cases with Healthy Peers

Periventriküler Lökomalazi: Pediatrik Vakalarda Beyin MR'ında Parankimal Sinyal ve Hacim Değişikliklerinin Sağlıklı Akranlarla Karşılaştırılması

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ABSTRACT

Background/aims: Previous MRI studies have revealed white matter (WM) and gray matter (GM) of cerebrum and cerebellum, corpus callosum (CC) abnormalities in periventricular leukomalacia (PVL). However, the WM FLAIR signal ratio in MRI may provide quantitative data in the diagnosis and follow-up as a new radiologic method. Thalamic involvement may be a biomarker for neuronal damage and disease severity. We aimed to re-investigate both WM and GM volume changes of cerebrum and cerebellum, CC surface area in PVL, and to evaluate the diagnostic accuracy of the thalamus L sign and FLAIR signal ratio.
Methods: MRI scans of 30 pediatric patients with PVL and 42 healthy controls were analyzed to examine WM and GM volume changes, FLAIR signal ratio, CC surface area, and thalamus L sign. Volumetric analyses were done with the Volbrain program.
Results: Decreased subcortical GM volumes were found in PVL ($p<0.001$). There was a significant positive correlation between FLAIR signal ratio, various GM and cerebellum volumes. In patients with thalamus L sign, decreased GM volume and increased abnormal signaled WM volume were observed. The most important variable in the diagnosis of PVL was abnormally signaled WM volume ($p>0.001$).
Conclusions: Our results emphasize the role of MRI in the detection of PVL, the evaluation of GM changes and brain damage, and the importance of thalamus L sign and FLAIR signal ratio in the evaluation of the severity of the disease. Comprehensive studies in this direction may contribute to the development of targeted treatment strategies aimed at reducing cognitive and motor impairments in PVL.

Keywords: Brain volume, Corpus callosum, FLAIR signal ratio, Gray matter, Periventricular leukomalacia, Thalamus L sign

ÖZ

Amaç: Önceki MRG çalışmaları periventriküler lökomalazide (PVL) serebrum ve serebellumun beyaz cevher (BC) ve gri cevher (GC), korpus kallozum (KK) anormalliklerini göstermiştir. Ancak MRG'de BC FLAIR sinyal oranı yeni bir radyolojik yöntem olarak tanı ve takipte kantitatif veri sağlayabilir. Talamik tutulum nöronal hasar ve hastalık şiddeti için bir biyobelirteç olabilir. Bu çalışmada PVL'de serebrum ve serebellumun BC ve GC hacim değişikliklerini, KK yüzey alanını detaylı araştırmayı, talamus L işareti ve FLAIR sinyal oranının tanısal doğruluğunu değerlendirmeyi amaçladık.
Gereç ve Yöntemler: PVL'li 30 pediatrik hastanın ve 42 sağlıklı kontrolün MRG taramaları, BC ve GC hacim değişikliklerini, FLAIR sinyal oranını, KK yüzey alanını ve talamus L işaretini incelemek için analiz edildi. Volümetrik analizler Volbrain programı ile yapıldı.
Bulgular: PVL'de subkortikal BC hacimlerinde azalma saptadık ($p<0.001$). FLAIR sinyal oranı ile çeşitli GC ve serebellum hacimleri arasında anlamlı pozitif korelasyon bulduk. Talamus L işareti bulgusu olan hastalarda azalmış GC hacmi ve artmış anormal sinyalli BC hacmi gözledik. PVL tanısında en önemli değişken olarak anormal sinyalli BC hacmini bulduk ($p>0.001$).
Sonuç: Sonuçlarımız PVL'nin saptanmasında, GC değişikliklerinin ve beyin hasarının değerlendirilmesinde MRG'nin rolünü ve hastalığın ciddiyetinin değerlendirilmesinde talamus L işaretinin ve FLAIR sinyal oranının önemini vurgulamaktadır. Bu yönde kapsamlı çalışmalar PVL'de bilişsel ve motor bozuklukları azaltmayı amaçlayan hedefe yönelik tedavi stratejilerinin geliştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: Beyin hacmi, FLAIR sinyal oranı, Gri madde, Korpus kallozum, Periventriküler lökomalazi, Talamus L işareti

Introduction

Periventricular leukomalacia (PVL) is an important neuropathological condition observed in childhood, predominantly affecting premature infants and leading to a range of motor and cognitive deficits. It is associated with the loss of cerebral white matter (WM), characterized by damage to the WM adjacent to the lateral ventricles. This condition occurs when there is insufficient oxygen or blood flow to the periventricular region of the brain (1, 2). The etiology involves a combination of several factors such as premature birth, hypoxic-ischemic events, intraventricular hemorrhage, infection and inflammation. In radiological diagnosis, sonography is useful as the first choice when the fontanelle opening allows imaging; MRI is frequently used in the suspicion of PVL because it detects WM signal change and its extent from the early stages. It has an important role in the diagnosis with its high image sensitivity, detailed visualization of the WM, the ability to evaluate the brain as a whole, its use in long-term follow-up, and its contribution to differential diagnosis.

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On MRI, the first signs of PVL are usually T2W and FLAIR hyperintensity areas. In time, cavity formation and periventricular cysts may be observed in these areas. In the last stage, ventriculomegaly and thinning of the corpus callosum (CC) may be observed with progressive necrosis of the periventricular tissue (3, 4). In the literature, PVL has been associated with widespread abnormalities in WM signal intensity (5). It has also been shown that the effect of PVL extends beyond WM and affects cortex and subcortical grey matter (GM) structures. It is known that as a result of these injuries, there is a decrease in WM and CC volumes, especially in the long term. There are a sufficient number of satisfactory studies on this subject in the literature. However, GM changes in PVL encephalopathy and its developmental effects are not completely understood (1, 2).

In MRI, WM signal changes are detected in T2W-FLAIR series. As a hypothesis, FLAIR signal intensity ratio can be useful in determining the severity of PVL. There is no study in the literature regarding this radiological method. Moreover, considering the role of the thalamus in cognitive and motor dysfunctions, the presence of the thalamus L sign in PVL may be a potential biomarker for the degree of neural damage and disease severity (6).

The goal of this study was to compare the WM and GM volume changes, CC surface area of children with PVL with those of healthy children, as well as to evaluate the diagnostic efficiency of the presence of the thalamus L sign and the FLAIR signal ratio value. In this way, we hope to provide a more comprehensive understanding of PVL's neurodevelopmental sequelae and inform early intervention and potential therapeutic targets for affected individuals.

Material and Methods

Study Design and Population

This study was performed as a retrospective observational study at a single center.

Between 2021 and 2023, the images of patients aged 0–17 years referred to the radiology clinic for brain MRI with a prediagnosis of PVL by the pediatric neurology clinic were accessed using hospital automation (Octomed) and the archive system (Infinitt). The images were retrospectively evaluated by the consensus of two radiologists with at least 5 years of experience in neuroradiology. As a control group, images of age and sex-matched healthy children who presented to our clinic for different reasons and underwent cranial MRI were evaluated. Patients with MRI findings in favor of PVL (T2W high signal areas, cavitations, periventricular cysts, ventriculomegaly with ventricle wall irregularities, WM volume loss, CC thinning) and optimal imaging quality were included in the study (Fig. 1). The control group included children with no pathology detected on brain MRI and no clinical and laboratory abnormalities that could affect neurological status in the hospital system. Patients with pathology detected on MRI, a current or past history of hemorrhagic stroke, parenchymal hematoma, a history of malignancy/cranial surgery/trauma, known metabolic diseases, artifacts in MRI images, or acute diseases that may affect neurological status were excluded from the study.

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the hospital ethics committee (27.09.2023).

MRI technique and analysis method

Imaging was performed with a 1.5 Tesla (T) MRI device (Philips Ingenia, The Netherlands). The sequences used in imaging are: axial spin echo T1W (TR/TE: 470-570/12-30ms), axial and sagittal T2W (TR/TE: 4500-6000/90-110ms), axial and coronal FLAIR (TR/TE: 6000-9000/100-120ms), and diffusion weighted imaging (DWI) (b = 0,500,1000). WM and GM T1W, T2W, FLAIR signal changes, FLAIR signal ratio, CC morphology and surface area, and the and the presence of the thalamus L sign were evaluated in MRI. To calculate the FLAIR signal ratio in PVL cases, we measured the signal intensity in the periventricular region where white matter signal abnormalities peak and in the adjacent normal-appearing cerebral parenchyma by verifying these signal intensities on T2W sequences. Similarly, we measured the FLAIR signal intensity of periventricular white matter and adjacent subcortical white matter in the control group. We determined the FLAIR signal ratio by proportioning these signal intensities for each hemisphere (Fig. 2). To minimize the margin of error, the measurements were taken three consecutive times, averaged, and recorded. We identified the FLAIR signal ratios measured in the right and left cerebral hemispheres and compared their averages with each other in the groups. We used a circular 5mm-diameter region of interest (ROI) in signal measurements.

We evaluated the presence of the thalamus L sign on axial T2W and FLAIR images as defined by Misser et al. (7) (Fig. 3).

Brain MRI volumetric analysis was conducted using Volbrain, a free, automated online platform designed for research. MR images were anonymized, optimized for quality, and converted to NIFTI format. The platform employs machine learning for automatic segmentation of brain regions, applying normalization and standardization for comparison. Volumetric data, calculated in cubic millimeters, is generated using multi-atlas label fusion techniques and compared against a normative database (8, 9). In our study, we measured various brain volumes using Volbrain analysis, including total WM, normal and abnormally signaled WM, total GM, subcortical and cortical GM, cerebrospinal fluid (CSF), and total brain volume (encompassing both WM and GM). In addition, intracranial cavity, total cerebrum, cerebrum WM, cerebrum GM, total cerebellum (excluding vermis), cerebellum WM and cerebellum GM volumes were measured (Fig.4).

We evaluated the MRI findings comparatively between PVL cases and an age- and sex-matched healthy group.

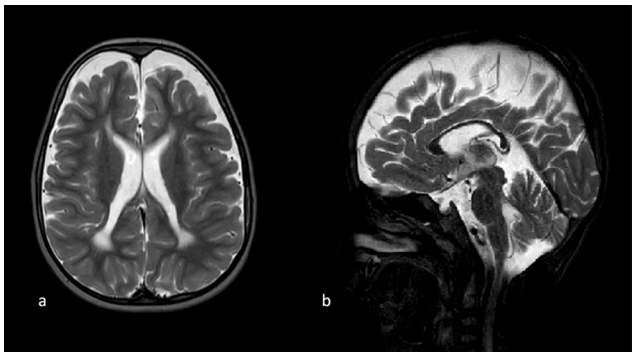

Fig. 1 T2W MRI images in the axial and sagittal planes in a PVL case show periventricular abnormal high signal areas, increased peripheral CSF distance anteriorly, ventricular wall irregularities, mild ventriculomegaly, white matter volume loss, and corpus callosum thinning

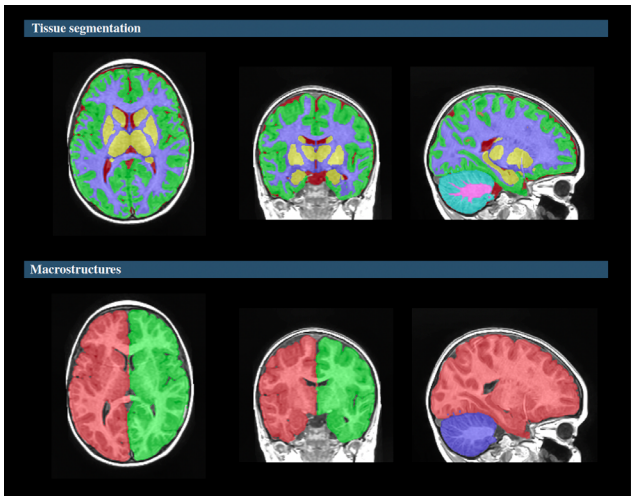

Fig. 4 Brain MRI volumetric analysis of cases with the Volbrain program

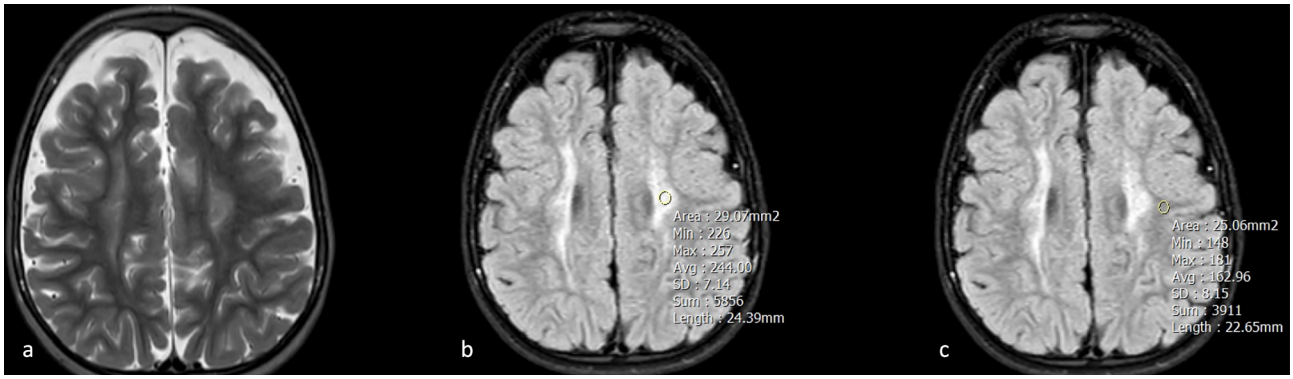

Fig. 2 The FLAIR signal ratio measurement in a PVL case: Signal intensity measurement method with ROI from periventicular abnormally high signaled white matter (b) and adjacent normal signaled white matter (c) in axial FLAIR images

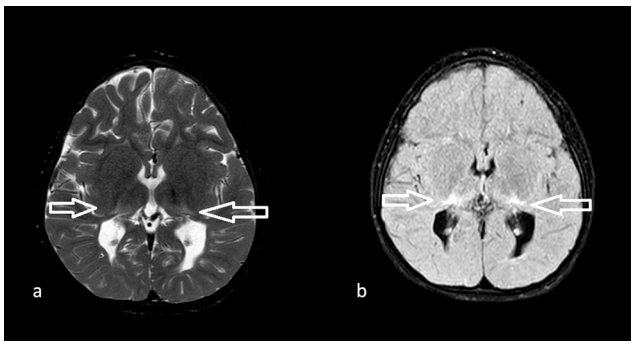

Fig. 3 Thalamus L sign in a case of PVL: Abnormal signal increases in posterolateral extension in both thalamus on T2W (a) and FLAIR (b) MR images in the axial plane (arrows)

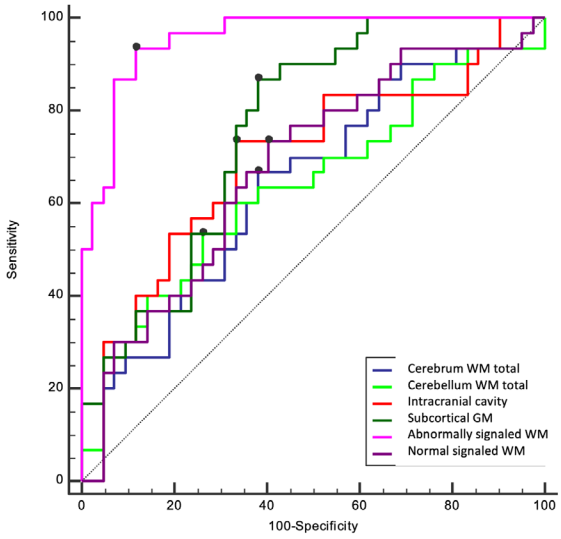

Fig. 5 ROC curves of variables that can be used to diagnose PVL

Table 1. Descriptive statistics and comparison results for PVL and control groups

	Control (n=42)	PVL (n=30)	Z / t	p
Total WM	390.67±103.87	348.03±105.09	1.709	0.092
Normally signaled WM	386.03±105.03	324.49±100.01	2.500	0.015
Abnormally signaled WM	3.15 (1.46-5.87)	22.72 (14.04-27.17)	-6.545	<0.001
Total GM	702.87 (494.36-779.73)	629.11 (492.15-708.98)	-1.416	0.157
Subcortical GM	40.94 (32.23-45.34)	32.57 (21.23-37.38)	-3.735	<0.001
Cortical GM	568.79 (396.45-629.25)	508.24 (398.71-574.24)	-1.371	0.170
Brain total (WM+GM)	1127.91 (826.32-1243.57)	928.69 (822.38-1047.32)	-1.885	0.059
Cerebrum total	1013.95 (736.69-1101.61)	827.80 (725.27-919.81)	-1.953	0.051
Cerebrum WM	369±97.26	328.32±94.77	1.768	0.081
Cerebrum GM	609.05 (425.36-673.26)	542 (419.68-609.99)	-1.588	0.112
Cerebellum total	114.42 (82.35-122.24)	98.38 (91.28-118.14)	-0.845	0.398
Cerebellum WM	21.39 (16.05-26.26)	17.21 (12.58-24.11)	-2.010	0.044
Cerebellum GM	97.71 (69.95-107.25)	87.81 (69.31-102.44)	-0.880	0.379
CSF	103.15 (69.82-301.73)	125.83 (95-150.40)	-0.628	0.530
Intracranial cavity	1232.36±212.91	1108.01±97.26	2.511	0.014

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Table 2. The correlation analysis findings between the mean FLAIR signal ratio and volumetric measurements in the PVL group

		Mean FLAIR signal ratio
Total WM	r=	-0.083
	p=	0.662
Normally signaled WM	r=	-0.070
	p=	0.715
Abnormally signaled WM	r=	-0.034
	p=	0.857
Total GM	r=	0.406
	p=	0.026
Cortical GM	r=	0.369
	p=	0.045
Subcortical GM	r=	0.520
	p=	0.003
Brain total (WM+GM)	r=	0.331
	p=	0.074
Cerebrum total	r=	0.316
	p=	0.089
Cerebrum WM	r=	-0.064
	p=	0.738
Cerebrum GM	r=	0.382
Cerebellum total	r=	0.399
	p=	0.029
Cerebellar GM	r=	0.536
	p=	0.002
Cerebellum WM	r=	0.034
	p=	0.856
CSF	r=	0.399
	p=	0.029
Intracranial cavity	r=	0.427
	p=	0.019

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Statistical Analysis

Statistical analyses of the study were performed using SPSS software (IBM SPSS Statistics for Windows, Version 27.0). Armonk, NY: IBM Corp. Whether the quantitative variables are suitable for a normal distribution was analyzed by the Kolmogorov-Smirnov test. Independent groups were compared with an independent sample t test for normally distributed variables and a Mann-Whitney U test for non-normally distributed variables. The relationship between qualitative variables was analyzed by chi-square analysis. Pearson or Spearman correlation analysis was applied to examine the relationship between quantitative variables. Variables that can be used as markers for the diagnosis of PVL were analyzed by ROC analysis. Descriptive statistics of quantitative variables that conform to normal distribution are shown as mean±standard deviation, and descriptive statistics of quantitative variables that are not normally distributed are shown as median (25th–75th percentile). Descriptive statistics for qualitative variables were expressed as frequency (%). Statistical significance was defined as $p<0.05$ values.

Results

Considering the inclusion and exclusion criteria, 30 patients (16 girls, 14 boys) aged 0–18 years (3 (1.50–6.25)) diagnosed with PVL were included as the patient group, and 42 healthy children (23 girls, 19 boys) aged 0–18 years (3 (1.58–7)) were included as the control group, resulting in a total of 72 individuals.

Descriptive statistics and comparison results for PVL and control groups are given in Table 1. Normal signaled WM, subcortical GM, intracranial cavity, and cerebellum WM volumes were significantly greater in the control group ($p=0.015$, $p<0.001$, $p=0.014$, and $p=0.044$, respectively), while abnormally signaled WM volume was significantly higher in the PVL group ($p<0.001$) compared to controls.

Table 2 shows the correlation analysis findings between the mean FLAIR signal ratio and volumetric measurements in the PVL group. The mean FLAIR signal ratio showed a weak positive correlation with total GM, cortical GM, intracranial cavity, CSF, and total cerebellum volume ($r=0.406$, $p=0.026$; $r=0.369$, $p=0.045$; $r=0.427$, $p=0.019$; $r=0.399$, $p=0.029$; and $r=0.399$, $p=0.029$, respectively). A moderate positive correlation was observed with subcortical GM and cerebellar GM volumes ($r=0.520$, $p=0.003$ and $r=0.536$, $p=0.002$, respectively).

Table 3. Descriptive statistics and comparison results of the PVL group with and without the thalamus L sign

	TALAMUS L SIGN		Z / t	p
	(+) (n=16)	**(-)** (n=14)		
Age	15.25±9.40	12.64±9.35	0.760	0.454
Right FLAIR signal ratio	1.53±0.19	1.56±0.19	-0.515	0.611
Left FLAIR signal ratio	1.56±0.21	1.64±0.30	-0.892	0.382
Mean FLAIR signal ratio	1.54±0.19	1.60±0.24	-0.768	0.449
Corpus callosum surface area	237.81±53.96	147.29±51.75	4.672	**<0.001**
Total WM	313.45±71.28	387.55±124.97	-2.028	0.052
Normally signaled WM	297.27±74.86	355.61±117.86	-1.640	0.112
Abnormally signaled WM	16.18±7.66	31.91±15.23	-3.644	**0.001**
Gray matter	634.23±121.53	574.02±205.10	0.993	0.329
Subcortical GM	32.92±6.69	27.41±11.16	1.611	0.122
Cortical GM	512.78±105.79	457.87±169.82	1.078	0.290
Brain total (WM+GM)	947.68±170.94	961.57±189.67	-0.211	0.834
Cerebrum total	843±154.96	849.04±154.96	-0.102	0.919
Cerebrum WM	297.31±66.59	363.77±111.27	-2.015	0.054
Cerebrum GM	545.70±108.50	485.27±180.30	1.129	0.269
Cerebellum total	96.93 (86.36-117.20)	99.94 (93.39-120.72)	0.480	0.498
Cerebellum WM	15.78±5.47	23.78±14.89	-2.004	0.055
Cerebellum GM	85.52±19.40	88.75±25.96	-0.389	0.700
CSF	112.63 (74.96-185.62)	132.34 (96.14-143.10)	0.678	0.697
Intracranial cavity	1109.17±182.64	1106.69±222.85	0.033	0.974

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Tablo 4. The ROC analysis findings regarding the volume variables that can be used to diagnose PVL

	AUC	SH_{AUC}	p	% 95 CI		Sensitivity (%)	Specificity (%)	Cut-off point
				Lower	Upper			
Abnormally signaled WM	0.955	0.021	<0.001	0.878	0.990	93.33	88.10	>7.23
Subcortical GM	0.760	0.056	<0.001	0.644	0.852	86.67	61.90	≤39.11
Intracranial cavity	0.690	0.065	0.004	0.571	0.794	73.33	66.67	≤1190.37
Normal WM	0.678	0.064	0.006	0.557	0.783	73.33	59.52	≤370.89
Cerebrum WM	0.640	0.066	0.036	0.518	0.750	66.67	61.90	≤351.07
Cerebellum WM	0.640	0.068	0.041	0.518	0.750	53.33	73.81	≤17.38
Total WM	0.638	0.067	0.039	0.516	0.748	66.67	61.90	≤372.91
Cerebrum total	0.636	0.069	0.048	0.514	0.746	83.33	61.90	≤956.82

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

There is also a negative, moderate correlation between FLAIR signal ratio and CC surface area (r=-0.585, p<0.001).

The mean CC surface area was significantly larger in patients without thalamus L sign compared to those with thalamus L sign (p<0.001), and abnormally signaled white matter volume was significantly higher in patients with thalamus L sign (p=0.001). No significant difference was found between the groups in other variables (p>0.05).

Table 4 shows the ROC analysis findings regarding the volume variables that can be used to diagnose PVL. In the analysis performed to determine which variables were more important in diagnosing PVL, the AUC value of the abnormally signaled WM volume variable was significantly greater than the AUC values of the cerebrum WM, cerebellum WM, intracranial cavity, subcortical GM, and normally signaled WM volume variables (p<0.001 for all comparisons) (Fig. 5). Accordingly, the most important variable that can be used to diagnose PVL is the abnormally signaled WM volume (AUC = 0.955, p<0.001).

Discussion

MRI is a neuroradiological marker for the detection of the presence of PVL. Any positive findings on the MRI are valuable for early diagnosis and the immediate initiation of rehabilitation measures. To the best of our knowledge, our study is unique and valuable as it is the first study to evaluate conventional MRI findings, FLAIR signal ratio, the presence of the thalamus L sign, and brain volumetric analysis together in PVL cases.

In children with PVL, MRI studies have revealed changes in both WM and GM volumes. In our study, there was an increase in the abnormally signaled WM volume and a decrease in the normal signaled WM volume in our PVL cases (p<0.001). In our study of PVL cases, volumes of normal signaled WM, intracranial cavity, and cerebellum WM were significantly reduced compared to the healthy control group (p = 0.015, p = 0.014, and p = 0.044, respectively), whereas CSF volume was notably higher (125.83 vs. 103.15). In PVL, which is characterized by a decrease in WM volume, an accompanying increase in CSF volume indicates loss of brain tissue in these regions (1, 10).

This reduction in WM correlates with the motor and cognitive deficits observed in affected children (10). Simultaneously, it has been reported that changes in GM volume are also observed in PVL, but these are more complex and region-specific. Some studies have reported decreased GM volume in areas associated with cognition and memory such as the hippocampus, amygdala and frontal lobes (2). This reduction in GM volume in specific regions may contribute to the cognitive impairments seen in children with PVL (2, 11, 12). In our study, subcortical GM volumes were significantly lower in PVL cases than in the healthy control group ($p<0.001$). A decrease in subcortical GM volume may reflect secondary degeneration resulting from disruption of the white matter pathways connecting these regions (12).

There are also studies in the literature that found that GM volume increased in certain regions of the putamen, thalamus, globus pallidus, and temporal, parietal, and occipital lobes (1, 2). In our study, we discovered a positive relationship between the average FLAIR signal ratio variable, total GM, cortical GM and subcortical GM volume. We believe that brain plasticity mechanisms like axonal sprouting, neuronal hypertrophy and neurogenesis, which may represent the brain's attempt to compensate for damage are associated with increases in GM volume (1). Our findings showing GM volume increases correlated with increased WM involvement are consistent with the idea that brain plasticity may lead to regional GM volume increases in response to WM damage (13). However, the clinical significance of these changes remains to be fully elucidated. Additionally, in our study, we observed a positive correlation between the increase in FLAIR signal ratio and cerebellar GM volume as well as cerebellar subcortical GM volume. This could potentially be explained by compensatory mechanisms or brain plasticity, as suggested by the increased GM volume observed in certain regions in preterm children with PVL (13). In addition to motor coordination, the role of the cerebellum in cognitive functions may also be reflected in these volumetric changes (14). Furthermore, the resistance of the cerebellum to WM damage may be attributed to distinct developmental and cellular states that may provide some degree of protection against the widespread WM damage observed in conditions such as PVL (14). Further research is needed to understand the effects of these volumetric changes on the long-term neurodevelopmental outcomes of pediatric patients with PVL. Our study underscores the importance of MRI techniques in elucidating the complex relationships between structural brain changes and clinical manifestations in pediatric neurology.

It is reported in the literature that the presence of GM damage in PVL is not limited to the cerebral cortex, and that subcortical structures such as the thalamus, basal ganglia, and cerebellar dentate nucleus are affected (15, 16). For this reason, it has been stated that white matter damage in PVL does not occur alone and that it may be appropriate to define the neuropathology as "perinatal panencephalopathy" (15). Thalamic involvement is particularly important as it plays a role in the cognitive and motor dysfunctions observed in children with PVL. As reported in the literature, the bilateral decrease in thalamic volume may be related to the presence of the thalamic L sign on MRI in our cases. In our study, the presence of lower CC surface area ($p<0.001$) and higher abnormally signaled WM ($p = 0.001$) in PVL cases with a positive thalamic L sign suggests that the thalamic L sign is a potential biomarker for the extent of neural damage in PVL, as stated in the literature (16).

In our study, the most important variable that can be used to diagnose PVL was the abnormally signaled WM volume (AUC=0.955, $p<0.001$). This highlights the critical role of abnormally signaled WM volume on MR imaging as an important diagnostic variable for PVL in children. Diffuse WM signal intensity abnormalities have been shown to be associated with PVL (5). The increased signal on MRI is thought to correspond neuropathologically to regions containing increased reactive astrocytes and microglia, decreased oligodendroglial cells, and a striking reduction in axon number (17). The intensity of the abnormal WM signal on MRI reflects underlying microstructural tissue damage. MRI of premature white matter disorders, including PVL, highlights the widespread excessively high signal intensity and its potential association with cognitive and behavioral disorders (18).

The negative relationship we found between FLAIR signal ratio and CC surface area is consistent with previous research showing that WM changes are associated with reductions in WM volume, as well as motor and cognitive deficits. There is also a study suggesting that there is a positive correlation between the thickness of the CC and the volume of cerebral WM in children with cerebral palsy and developmental delay and that damage to the corpus callosum may reflect the extent of white matter loss (19). The literature specifically reports a significant reduction in CC size associated with the severity of motor and cognitive impairments in PVL (1). Our results confirm the idea that the structural integrity of the CC is impaired in PVL, which may contribute to the functional deficits observed in PVL. We contribute to this understanding by highlighting the specific effect of PVL on the corpus callosum. Furthermore, the negative correlation between FLAIR signal ratio and CC surface area suggests that it may be useful in follow-up as a potential indicator of the disease severity.

The underlying neuropathology of PVL includes both WM damage and secondary GM changes (1, 2, 11, 15). As a basic diagnostic tool, MRI is extremely sensitive in detecting the characteristic findings of PVL, especially WM damage and changes in the periventricular area, by providing detailed images of brain tissue. In addition to the decrease in WM volume on MRI, both decreased and increased GM volumes in various regions indicate a complex interaction between the adaptive responses of the brain (2, 12, 15). The

relationship between structural and volumetric brain changes in PVL and functional outcomes highlights the importance of early diagnosis and intervention to reduce potentially its long-term neurodevelopmental impact.

Limitations

Our study had some limitations. Among these was the lack of follow-up data of the patients and the lack of correlation with the clinical severity score due to its retrospective nature. These parameters could be the focus of another study. Additionally, our relatively small sample size and the fact that the cases were not divided into etiological subgroups may also be a limitation. Since there were no 3D thin-section T1 sequences in the volumetric evaluation of the brain, we could not perform detailed microstructural analysis of the subanatomical regions of the brain. Therefore, we can consider our inability to detect specific regions of GM changes as a limitation. Another limitation is the inclusion of patients with chronic, long-term effects of PVL in this study. Another study can examine the effects in the early or subacute phase.

Conclusion

In conclusion, the use of MRI in the early diagnosis of PVL allows for more effective management of the disease and the early initiation of necessary treatment strategies. In addition to white matter involvement, regional GM volumetric changes, morphological changes in the corpus callosum, and their relationship with the increase in abnormal white matter signal intensity may be valuable for the development of targeted treatment strategies aimed at reducing cognitive and motor disorders in PVL.

Statements and Declerations

Conflict of interest: The authors declare that they have no conflict of interest.

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Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors. This study was approved by the local medical ethical committee (2023/514/258/25), and all data was processed anonymously, according to the privacy legislation.

Authorship Contribution Statement

Conception: H.G.D., E.C., Design: H.G.D., E.C., T.B., Supervision: H.G.D., E.C., Materials: E.C., İ.S., S.G.S., Data Collection and/or Processing: H.G.D., E.C., S.G.S., İ.S., Analysis and/or Interpretation: F.C.T., Literature Review: H.G.D., E.C., T.B., Writer: H.G.D., E.C., Critical Review: H.G.D., E.C., S.G.S., İ.S., F.C.T., T.B.

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