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RESEARCH

Comparison of magnetic resonance imaging, clinical, and laboratory findings in atypical and typical posterior reversible encephalopathy syndrome

Atipik ve tipik posterior reversibl ensefalopati sendromunda manyetik rezonans görüntüleme, klinik ve laboratuvar bulgularının karşılaştırılması

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Abstract

Purpose: The aim of the study is to compare cases defined as typical and atypical Posterior Reversible Encephalopathy Syndrome (PRES) based on the regions of involvement and imaging features in terms of clinical findings and laboratory values.

Materials and Methods: The study included 79 patients who were evaluated as PRES according to imaging and clinical findings between January 2012 and March 2022, had sufficient clinical and laboratory data, and had optimal magnetic resonance (MR) images. Thirty-two of the patients were male, 47 were female, and 61 patients were in the pediatric age group. All patients had non-contrast FLAIR, T1 and T2-weighted images, 24 patients had diffusion-weighted images, and 43 patients had contrast-enhanced T1-weighted images. Patients were divided into typical and atypical groups according to MR imaging findings. Each group was compared independently according to clinical and laboratory data.

Results: Hemorrhage was detected in 2, diffusion restriction in 16, enhancement in 13, and lesions located in deep white and gray matter in 10 patients. According to the areas of involvement, parietooccipital was detected in 11 patients, posterior frontotemporal in 28 patients, cerebellar in 29 patients, brainstem in 5 patients, and thalamus in 6 patients. According to the localization, while the change in consciousness was observed in 41% of the typical group, this was more in the atypical group (72%). In addition, inorganic phosphorus and potassium values were lower in the atypical group. Change in consciousness was detected more in patients with enhancement compared to patients without enhancement. Alanine aminotransferase (ALT) and Aspartate aminotransferase

Öz

Amaç: Çalışmanın amacı, tutulum bölgeleri ve görüntüleme özelliklerini baz alınarak tipik ve atipik Posterior Reversibl Ensefalopati Sendromu (PRES) olarak tanımlanan olguları klinik bulgular ve laboratuvar özellikleri açısından karşılaştırmaktır.

Gereç ve Yöntem: Çalışmaya Ocak 2012-Mart 2022 tarihleri arasında görüntüleme ve klinik bulgulara göre PRES olarak değerlendirilen, yeterli klinik ve laboratuvar verileri bulunan, manyetik rezonans (MR) görüntüleri optimal olan 79 hasta dahil edilmiştir. Hastaların 32'si erkek, 47'si kadın olup 61 hasta pediatrik yaş grubundaydı. Hastaların tamamında kontrastsız FLAIR, T1 ve T2 ağırlıklı görüntüler, 24 hastada difüzyon ağırlıklı görüntüler ve 43 hastada kontrastlı T1 ağırlıklı görüntüler mevcuttu. MR görüntüleme bulgularına göre hastalar tipik ve atipik gruplara ayrıldı. Her grup birbirinden bağımsız olarak klinik ve laboratuvar verilerine göre karşılaştırıldı.

Bulgular: Kanama 2, difüzyon kısıtlılığı 16, kontrastlanma 13 ve derin beyaz ve gri cevherde yerleşimli lezyonlar 10 hastada saptandı. Tutulum alanlarına göre paryetooksipital 11, posterior frontotemporal 28, serebellar 29, beyin sapı 5, talamus 6 hastada saptandı. Lokalizasyona göre tipik grupta bilinç değişikliği 41% oranda izlenirken, atipik grupta bu daha fazlaydı (72%). Ayrıca inorganik fosfor ve potasyum değerleri atipik grupta daha düşüktü. Kontrastlanma saptanmayan hastalara göre kontrastlanma görülen hastalarda bilinç değişikliği daha fazla saptandı. Alanin aminotransferaz (ALT) ve Aspartat aminotransferaz (AST) değerleri atipik grupta kantitaf olarak yüksek saptandı. Diğer verilerde anlamlı farklılık saptanmadı.

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(AST) values were significantly higher in the atypical group. No significant difference was detected in other data.
Conclusion: Atypical localization and MR imaging features in PRES cases may lead to potential diagnostic difficulties and traps for radiologists evaluating these scans in emergency situations. In addition, some clinical and laboratory findings may be worse in atypical cases, and early and correct diagnosis is very important for treatment management.
Keywords: Posterior Reversible Encephalopathy Syndrome (PRES), MRI, atypical features

Sonuç: PRES olgularında atipik lokalizasyon ve MR görüntüleme özellikleri acil durumlarda bu taramaları değerlendiren radyologlar için potansiyel tanısal zorluklara ve tuzaklara yol açabilir. Ayrıca atipik olgularda bazı klinik ve laboratuvar bulgular daha kötü seyredebilmekte olup erken ve doğru tanı tedavi yönetimi için çok önemlidir.

Anahtar kelimeler: Posterior Reversibl Ensefalopati Sendromu (PRES), MRG, atipik özellikler

INTRODUCTION

Posterior Reversible Encephalopathy Syndrome (PRES) is a potentially life-threatening neurotoxic condition characterized by a wide range of clinical manifestations, including headache, visual disturbances, seizures, focal neurological deficits, and altered consciousness. It is recognized by its distinct clinical and laboratory features, along with imaging findings particularly on computed tomography (CT) and magnetic resonance imaging (MRI) that suggest cerebral vasogenic edema[1,2].

The underlying pathophysiology of PRES involves impaired cerebrovascular autoregulation and endothelial dysfunction. A state of hyperperfusion with disruption of the blood-brain barrier leads to the extravasation of plasma and macromolecules, resulting in cortical and/or subcortical vasogenic edema. Some researchers have proposed that reversible edema may progress to cytotoxic edema due to vasospasm if left untreated[3,4]. Common precipitating factors include hypertensive crises, preeclampsia/eclampsia, renal failure, solid organ transplantation, sepsis, cytotoxic drug use, infections, and autoimmune diseases[3]. Clinical symptoms typically develop acutely; generalized seizures are common, and coma may occur in severe cases[5].

CT/MRI findings usually show symmetrical vasogenic edema involving the parieto-occipital cortical, juxtacortical, and subcortical regions. The parietal and occipital lobes are most frequently affected, followed by the frontal lobes, the temporo-occipital junction, and the cerebellum[6] (Figure 1). Deep brain structures such as the basal ganglia, thalamus, brainstem, and internal/external capsules may also be involved[7] (Figure 2). When these findings accompany typical hemispheric or cerebellar PRES, they are referred to as "companion lesions"[8]. Restricted diffusion areas are rare but may indicate infarction or irreversible cytotoxic edema, often associated with a poorer prognosis[9] (Figure 3). Intracranial hemorrhage including focal hematoma, sulcal/subarachnoid hemorrhage, or proteinaceous fluid components has been reported in approximately 15% of PRES cases[7,10] (Figure 4). Contrast enhancement is uncommon and, when present, usually appears in a gyriform pattern within typical or atypical PRES regions (Figure 5).

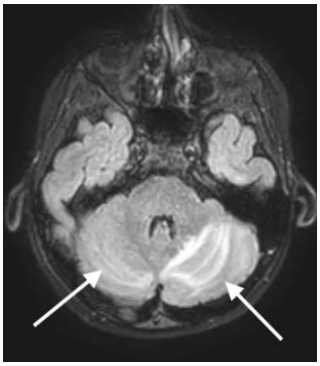

Figure 1. PRES case with cerebellar involvement (arrows) on FLAIR MR image.

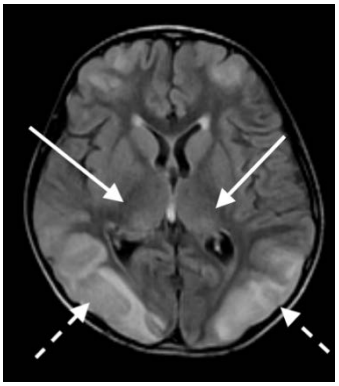

Figure 2. Atypical PRES case. FLAIR MR sequence shows bilateral thalamic hyperintensity (arrows) and bilateral symmetric parietotemporal cortical and subcortical hyperintensity (broken arrows).

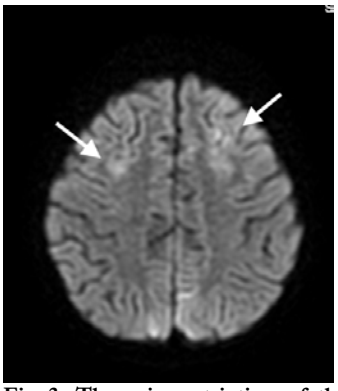

Fig 3. There is restriction of the bilateral frontal gyral pattern (arrows) on diffusion-weighted MR imaging.

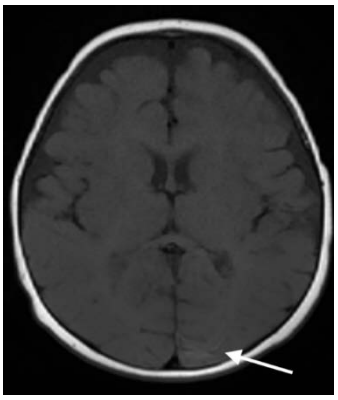

Fig 4. Hyperintensity (arrow) in the left occipital gyral pattern on precontrast T1-weighted MR imaging is consistent with hemorrhage.

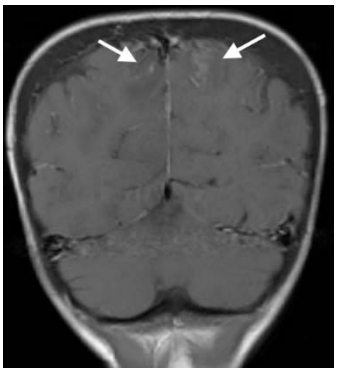

Fig 5. A case of atypical PRES. Contrast enhancement (arrows) in the gyral pattern at the level of bilateral parietal lobe vertex on MRI postcontrast T1-weighted imaging may develop secondary to disruption of the blood-brain barrier.

The syndrome is often reversible with prompt clinical and radiological diagnosis and prompt initiation of treatment. However, it has been reported that irreversible clinical and radiological findings may occur, particularly in atypical cases where diagnosis is delayed[11]. Although PRES is more commonly observed in adults, pediatric cases have also been documented in the literature[12].

In this study, atypical PRES cases with both pediatric age group and atypical radiological findings were examined and the findings were evaluated to contribute to the literature.

MATERIALS AND METHODS

Setting

This study was conducted at the Division of Pediatric Neurology and Department of Neurology, Çukurova University Faculty of Medicine, a prominent institution in the region with over 50 years of experience in undergraduate and specialty medical training. The institution is equipped with advanced applications, secure file storage, and robust radiologic image storage systems, ensuring high-quality data management. Ethical approval for the study was obtained from the Çukurova University Faculty of Medicine Ethics Committee under document number 45, dated April 18, 2025.

Sample

The study population comprised 124 patients diagnosed with posterior reversible encephalopathy syndrome (PRES) based on clinical and magnetic resonance imaging (MRI) findings between January 2012 and March 2022. Patients were identified through a retrospective review of medical records and imaging data from the institution's database. Inclusion criteria required a confirmed PRES diagnosis based on clinical symptoms and characteristic MRI findings, such as hyperintense lesions on fluid-attenuated inversion recovery (FLAIR) sequences. Forty-five patients were excluded due to incomplete clinical or laboratory data, suboptimal MRI quality, or inability to definitively rule out alternative diagnoses (e.g., stroke, demyelinating diseases, or metabolic encephalopathies). The final cohort included 79 patients (32 females, 47 males; 61 pediatric patients, 18 adult patients), with ages ranging from 2 to 65 years.

Imaging procedures

MRI scans were performed using two 3.0 Tesla scanners: Philips Achieva (The Netherlands) and GE Architect (USA). Imaging protocols included non-contrast FLAIR, T1-weighted, and T2-weighted sequences for all 79 patients. Diffusion-weighted imaging (DWI) was available for 24 patients, and contrast-enhanced T1-weighted imaging was performed in 43 patients using gadolinium-based contrast agents. Imaging data were stored in the institution's picture archiving and communication system (PACS) and reviewed using standardized workstations to ensure consistency. Two board-certified radiologists, each with over 10 years of experience in neuroimaging, independently evaluated the MRI scans. Brain regions affected were documented based on FLAIR hyperintensities, with specific attention to the occipital, parietal, frontal, temporal, and cerebellar regions.

Clinical and laboratory data collection

Clinical data were extracted from discharge summaries and electronic medical records by two neurologists with expertise in pediatric and adult neurology. Data included demographic information, clinical symptoms (e.g., seizures, altered consciousness, nausea, vomiting, diarrhea, headache, visual disturbances, fever, hypertension, respiratory distress), and recent surgical history (within 30 days prior to presentation). Laboratory parameters were collected from blood samples obtained at the time of admission or during hospitalization, depending on clinical urgency. These parameters included white blood cell count (WBC), hemoglobin (HGB), platelet count (PLT), albumin, inorganic phosphorus, magnesium (Mg), sodium (Na), potassium (K), chloride (Cl), calcium (Ca), blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, international normalized ratio (INR), and C-reactive protein (CRP). Samples were processed in the institution's central laboratory, adhering to standardized protocols for storage and analysis to ensure data reliability.

Patient categorization

Patients were classified into two groups typical and atypical PRES based on MRI characteristics. Typical PRES was defined by symmetric, bilateral hyperintense lesions predominantly in the parieto-occipital regions on FLAIR sequences, without evidence of diffusion restriction, contrast enhancement, or hemorrhage. Atypical PRES included cases with asymmetric lesions, involvement of non-parieto-occipital regions (e.g., frontal, temporal, or cerebellar), or additional features such as diffusion restriction on DWI, contrast enhancement, or hemorrhage. Discrepancies in categorization were resolved through consensus between the radiologists. The typical and atypical groups were compared for differences in clinical symptoms, surgical history, and laboratory parameters.

Statistical analysis

Statistical analyses were performed using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA). Continuous variables (e.g., laboratory parameters) were assessed for normality using the Shapiro-Wilk test. For non-normally distributed data, the Mann-Whitney U test was used to compare means between the typical and atypical PRES groups. Normally distributed data were analyzed using the Student's t-test to evaluate differences in sample means. Categorical variables (e.g., presence of clinical symptoms) were compared using the Chi-square test or Fisher's exact test when expected cell counts were less than 5. A p-value of less than 0.05 was considered statistically significant. Inter-rater reliability between the radiologists for MRI categorization was assessed using Cohen's kappa coefficient, with a kappa value of 0.8 or higher indicating excellent agreement.

RESULTS

Predisposing factors and associated conditions are presented in Table 1. Due to the small number of patients defined as atypical based on findings of hemorrhage (n=2, subarachnoid hemorrhage), diffusion restriction (n=16), contrast enhancement (n=13), and lesions located in the deep white and gray matter (n=10) group homogeneity could not be achieved, and therefore statistical comparison was not performed.

Based on lesion localization, parieto-occipital involvement (n=11) and additional posterior frontotemporal involvement (n=28) were considered typical. Patients with additional cerebellar (n=29), brainstem (n=5), or thalamic (n=6) involvement were classified as atypical. No basal ganglia involvement was observed. According to lesion localization, altered consciousness was observed in 41% of

patients in the typical group, whereas it was more frequent in the atypical group (72%). No significant differences were found between groups regarding other clinical signs and symptoms. Inorganic phosphorus and potassium levels were found to be lower in the atypical group, while no statistically significant differences were observed in other laboratory parameters. No significant difference was found in the comparison based on lesion symmetry.

Table 1. Accompanying findings in patients

Finding	n (%)
Malignancy; Chemotherapy History	28 (36%)
CRF / HT / Nephrotic Syndrome	20 (25%)
Hematological Disease / BMT / Blood Transfusion	15 (19%)
Pregnancy / Preeclampsia / Eclampsia	7 (9%)
Metabolic and Congenital Diseases	4 (5%)
Sepsis / Shock / Infection / Immunodeficiency	4 (5%)
HELLP	1 (1%)

CRF: chronic renal failure, HT: hypertension, BMT: Bone marrow transfusion, HELLP: Hemolysis, Elevated Liver enzymes and Low Platelets

Table 2. Demographic and clinical characteristics of typical and atypical cases

	Typical PRES (n: 39)	Atypical PRES (n: 40)
Lesion location	Parieto-occipital, posterior frontotemporal	Cerebellum, brainstem, thalamus
Altered consciousness	41%	72%
Other clinical findings	no difference	no difference
Inorganic phosphorus level	Higher	Lower
Potassium level	Higher	Lower
Other laboratory parameters	no difference	no difference
Lesion asymmetry	none	none
Contrast enhancement	none	13 (33%)

Table 3. Comparison of MRI findings in typical and atypical PRES cases is shown in

Feature	Typical PRES	Atypical PRES
Lesion location	Bilateral, symmetrical subcortical and cortical white matter involvement; Parieto-occipital predominance	Brainstem, cerebellum, basal ganglia, thalamus, corpus callosum involvement
Diffusion restriction (DWI/ADC)	Usually no diffusion restriction (High ADC)	Diffusion restriction may be observed
Contrast enhancement	Often absent	Leptomeningeal/gyral/patchy contrast enhancement may occur
Hemorrhage	Often absent	Microhemorrhage or intraparenchymal hematoma more common
Parenchymal involvement symmetry	Usually symmetrical, sometimes slightly asymmetrical	May be asymmetrical or unilateral placement

DWI/ADC: diffusion-weighted imaging/apparent diffusion coefficient,

To ensure group homogeneity, 10 cases were randomly selected from patients without contrast enhancement (n=30) and compared with those showing contrast enhancement (n=13). Altered consciousness was more frequent in the atypical group. ALT and AST levels were quantitatively higher in the atypical group. No statistically significant differences were observed in other

variables. Demographic and clinical characteristics of typical and atypical cases are listed in Table 2.

DISCUSSION

PRES may present with clinical symptoms such as visual disturbances, headache, seizures, and impaired consciousness. While diagnosis can be made based on clinical findings, MRI is crucial in facilitating diagnosis and excluding differential diagnoses. Follow-up MRIs are also important for assessing patients' clinical progress[3]. PRES is typically characterized on MRI by bilateral, symmetrical, vasogenic edema predominantly affecting the white matter in the parieto-occipital regions[10]. These lesions, which appear as marked hyperintensities on FLAIR sequences, often extend into the cortex; however, they usually do not show restricted diffusion on diffusion-weighted imaging, which supports the vasogenic nature of the edema[13]. Nevertheless, PRES imaging findings may not always be confined to this "typical" distribution. In atypical PRES cases, lesions may also be observed in brain regions outside the expected posterior areas[14]. In particular, structures such as the frontal lobes, basal ganglia, thalamus, brainstem, and cerebellum have been reported to be involved[15]. The standard method for evaluating parenchymal involvement is MRI and comparison of MRI findings in typical and atypical PRES cases is shown in Table 3[1,14,15,16,17].

The concept of atypical PRES also includes imaging findings that deviate from the conventional pattern. The presence of hemorrhage and diffusion restriction are important MRI findings that are not typical of PRES but may occur in atypical or complicated cases. In typical PRES lesions, hemorrhage is not expected, and diffusion restriction is generally absent; however, recent studies have demonstrated the presence of small focal hemorrhages (microhemorrhages) or even larger parenchymal bleeds in certain cases[1].

PRES is generally recognized as a distinct clinical and radiological entity; classical MRI findings in an appropriate clinical context are often considered diagnostic[18]. However, when cases present with atypical distribution or unexpected imaging features, diagnosis may become more challenging. These unusual presentations can lead to diagnostic uncertainty and may cause clinicians to overlook PRES as a possible diagnosis[19]. Especially in atypical cases, when diagnosed late, clinical and radiological findings, which are reversible as the name suggests, may become irreversible[11].

PRES is typically a reversible condition when correctly and promptly treated. With the elimination of the underlying cause and supportive treatment, both clinical symptoms and imaging findings show complete or near-complete resolution in most patients within a few weeks[20]. Therefore, early diagnosis of PRES and timely initiation of treatment are critically important[17]. The diversity of MRI findings in PRES cases can directly impact the diagnostic and therapeutic process. While recognizing typical PRES lesions facilitates rapid diagnosis, clinicians must also be aware of atypical patterns and features. When relevant clinical circumstances exist, identifying unexpected MRI findings as manifestations of PRES can provide an opportunity for timely intervention[21]. The contribution of our study to the clinical approach is that it reveals the differences in MRI findings in typical and atypical cases and raises awareness in this regard among clinicians and radiologists.

Limitations of our study include the small number of cases and the fact that all MRI sequences, including SWI and DWI, were not obtained in all patients. Subsequent studies with images including diffusion and SWI MR images, which were not optimized in our study, will increase the diagnostic power.

As a conclusion, in our study, no statistically significant differences were found between the typical and atypical groups in terms of clinical symptoms, conditions, or laboratory findings. However, a wide range of clinical manifestations including encephalopathy, seizures, headache, visual disturbances, and focal neurological deficits were observed in both groups, along with notable laboratory abnormalities. The retrospective and single-center nature of our study, the limited number of patients, and the rarity of atypical cases posed certain challenges in the research process. There is a need for further studies involving larger patient populations and conducted across multiple centers.

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