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ORIGINAL ARTICLE

Evaluation of Clinical Manifestations, Radiological Features, and Outcomes of Posterior Reversible Encephalopathy Syndrome (PRES)

Posterior Reversible Ensefalopati Sendromunda (PRES) Klinik Özellikler, Radyolojik Bulgular ve Hastalığın Sonuçlanmasının Değerlendirilmesi

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ABSTRACT

Introduction: Posterior reversible encephalopathy syndrome (PRES) is a state coupled with a unique clinical and radiological appearance. Various conditions such as preeclampsia/eclampsia, autoimmune diseases, chemotherapy bone marrow and organ transplantation are foreseen and this clinical condition is better illuminated along with imaging, clinical and laboratory features. Therefore, the aim of this study is to describe the clinical and radiological manifestations, diagnosis, and outcome of PRES.
Material and methods: A retrospective review of cases of PRES over five years. Patient characteristics, including demographics, comorbidities, specific therapy, and clinical outcome, were analyzed. Diagnosis was made by clinical examination and imaging techniques.
Results: Fifteen patients detected with PRES between 2015 and 2020 were included. In fifteen patients, the median age was 49.9±17.0 years (25-77 years), 33.3% were men, and 66.7% were women. Two of the patients had active cancer, none had a history of bone marrow or organ transplantation, three had autoimmune disease, four were peripartum, two had chronic renal failure, three had a systemic disease such as hypertension and diabetes, and one had respiratory infection. Patient specific treatment protocols were applied for each patient. MR imaging showed vasogenic edema at 100% and restricted diffusions at 33.3%. CT image showed hemorrhage of 30% additionally. Overall, 86,6% of our patients recovered without sequelae in short term. The rate of individuals aged 50 and over was statistically significantly poor in terms of long-term results compared to the group under 50 years of age individuals (p=0.041).
Conclusion: In this retrospective analysis of PRES patients, the prognosis was good. CT and MRI contribute to the diagnosis, and various imaging findings can be seen. While the patient's age has an important effect in determining the prognosis, other radiological or demographic parameters do not have any effect on short-term or long-term results.

Keywords: computed tomography, magnetic resonance imaging, posterior reversible encephalopathy, syndrome, edema, convulsion, hypertension

ÖZ

Giriş: Posterior reversible ensefalopati sendromu (PRES), kendine özgü klinik bulguları ve radyolojik görünümleri olan bir antitedir. Preeklampsi/eklampsi, otoimmün hastalıklar, kemoterapi, kemik iliği ve organ nakli gibi çeşitli durumlar hastalığa yatkınlık yaratmakta ve bu klinik durum görüntüleme, klinik ve laboratuvar özellikleri ile daha iyi aydınlatılmaktadır. Bu çalışmanın amacı PRES'in klinik ve radyolojik bulgularını, tanı ve hasta sonuçlanmasındaki bulguları tanımlamaktır.
Gereç ve yöntemler: Çalışmamız beş yıllık PRES vakalarının geriye dönük bir incelemesidir. Klinik muayene ve görüntüleme teknikleri ile tanı konulan hastalarda; demografik özellikler, komorbiditeler, spesifik tedavi ve klinik sonuç dahil olmak üzere hasta özellikleri analiz edildi.
Bulgular: Çalışmaya 2015-2020 yılları arasında PRES tespit edilen 15 hasta dahil edildi. On beş hastanın ortanca yaşı 49.9±17.0 (25-77 yıl), %33,3'ü erkek, %66,7'si kadındı. Hastaların ikisinde aktif kanser, üçünde otoimmün hastalık, dördünde peripartum dönem, ikisinde kronik böbrek yetmezliği, üçünde hipertansiyon ve diyabet gibi sistemik bir hastalık ve birinde solunum yolu enfeksiyonu vardı. Hiçbirinde kemik iliği veya organ nakli öyküsü yoktu. MR görüntülemede %100 hastada vazojenik ödem ve %33,3 oranda difüzyon kısıtlaması görüldü. BT'de ek olarak %30 oranda kanama gösterildi. Her hasta için hastaya özel tedavi protokolleri uygulandı. Genel olarak hastalarımızın %86,6'sı erken dönemde sekelsiz iyileşti. 50 yaş ve üstü bireylerin uzun dönem iyi sonuçlanma oranları 50 yaş altı bireylere göre istatistiksel olarak anlamlı derecede düşüktü (p=0,041).
Sonuç: PRES hastalarının retrospektif analizinde genel sağ kalım oranları ve prognoz iyi olarak değerlendirildi. BT ve MRG tanıya katkıda bulunurken çok çeşitli görüntüleme bulguları görülebilir. Prognozu belirlemede hastanın yaşı önemli bir yer tutarken, diğer radyolojik veya demografik parametrelerin kısa veya uzun vadeli sonuçlara etkisi yoktur.

Anahtar Kelimeler: bilgisayarlı tomografi, manyetik rezonans görüntüleme, posterior reversible ensefalopati, sendrom, ödem, konvülsiyon, hipertansiyon

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological entity that affecting predominantly the white matter of the posterior cerebral hemispheres. Syndrome accompanies acute neurological symptoms, including headache, seizures, and visual symptoms (1). PRES is considered to be caused by irregular or unsuccessful autoregulation of the cerebrovascular system caused by uncontrolled hypertension. Also, endothelial dysfunction is discussed in the pathogenesis (2). PRES is usually associated with predisposing factors such as peripartum state, autoimmune disorders, bone marrow, and solid organ transplantation, cancer, sepsis, chronic renal failure, hypertension (HT), and diabetic ketoacidosis (3,4)

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PRES is diagnosed radiologically with a distinctive radiological imaging pattern, which most often includes cortical or subcortical areas of the parietal or occipital lobes (2). Computerized tomography (CT) and magnetic resonance imaging (MRI) typically show vasogenic edema in parenchymal white matter in areas of posterior circulation areas; however, the frontal lobes, basal ganglia, and brain stem involvement has also been reported (5).

Although different imaging characteristics are defined in the literature, factors affecting clinical outcomes in PRES have not been well-characterized (6). Here, we discuss the clinical presentation, associations with radiological features, treatments, and prognosis of PRES. We defined any gender, age, and radiological presentation differences that affect the outcomes.

Materials and Methods

We conducted a retrospective analysis of all cases of PRES admitted to our university-affiliated tertiary hospital between 2015 and 2020. Ethics committee approval has been obtained for the study (No: 118/10).

Brain MRI and CT reports were searched for "PRES" and "Posterior Reversible Encephalopathy Syndrome" from the hospital's electronic data system. The patients were included if typical vasogenic edema on MRI with concomitant neurological symptoms were confirmed by clinical records. The patients were included in the study cohort by a consensus with a radiologist and a neurologist. Patient demographics, comorbidities, symptoms at onset, blood pressure, and clinical PRES characteristics were collected. All patients obtained information concerning the outcome from the medical records and hospital notes. All patients were 18 years of age or older.

A radiologist re-reviewed the initial imaging studies to determine the specific areas with vasogenic edema on MRI and CT. On MRI, vasogenic cerebral edema was defined as hyperintense T2 and FLAIR signals, which do not show restricted diffusion. Also, areas of diffusion restriction were noted. The extent of edema was defined by anatomic locations. The presence of diffusion restriction was recorded using ADC images. Additionally, the presence of hemorrhage was recorded. When available, reversibility was assessed on follow-up imaging. The short-term outcome was defined by the clinical findings at the time of discharge from the hospital. The long-term outcome was defined by the clinical findings in minimum 2 years and over. Good outcome was regarded as complete recovery without residual disability, and poor outcome as persistent neurologic deficits or death.

Statistical Method

Data analysis was performed using IBM SPSS Statistics version 25.0 software (IBM Corporation, Armonk, NY, US). Shapiro Wilk test was used to investigate whether the normal distribution assumption was met. Categorical data were expressed as numbers (n) and percentages (%), while quantitative data were given as mean ± SD. The mean differences in age between groups were compared with Student's t-test. Where applicable, the categorical data were evaluated by Fisher's exact or Fisher Freeman Halton test. A p-value less than 0.05 was considered statistically significant.

Results

Fifteen patients with PRES were documented during the period of the study. Patients were ten women and five men with a mean age of 49.9±17.0 years old. Among them, three of them (20%) were pregnant complicated with hypertension, three of them (20%) had active cancer, three of them (20%) had HT, diabetes mellitus (DM) with chronic obstructive pulmonary disease (COPD), two (13,3%) had autoimmune disease, two (13,3%) had renal failure, one (6,6%) of them was post-partum, one (6,6%) had a respiratory infection and non-had history of bone marrow or organ transplantation. Two cancer patients had been taking chemotherapeutic drugs by the time of diagnosis (carboplatin/paclitaxel and cisplatin). Antiedema therapy was administered to 100% of the patients (Mannitol 20% given intravenously in bolus doses of 0.5-1g/kg over 30 minutes). Anticonvulsant therapy was administered in patients with neurological symptoms. Immediate removal of the triggering factor, such as chemotherapeutics in cancer patients and anti-hypertensive therapy, was administered in patients with high blood pressure. Additional use of magnesium sulfate was used for peripartum patients. Overall, 13 (86.6%) of our patients recovered without sequelae in short-term. A poor long-term outcome was observed in five of 13 patients (38.4%) who had survived PRES. Table 1 summarizes the most relevant clinical findings in these patients.

Table 1. Demographics, clinical manifestations, and outcome of patients with PRES

Age	Sex	Predisposing factors	First symptom	TA	Short-term outcome	2-year survival rate
25	F	preeclamsia	loss of vision	200/110	good	good
30	F	preeclamsia	loss of vision	200/110	good	good
32	F	preeclamsia	decrease of vision	220/114	good	good
33	F	postpartum	decrease of vision	225/114	good	good
38	F	Hypopharynx cancer, under treatment of carboplatin/ paclitaxel	convulsion	150/90	good	poor
39	M	chronic renal failure	loss of vision	200/113	good	good
45	F	SLE	loss of vision	150/90	good	good
51	F	Chronic renal failure	headache	190/111	good	poor
51	F	SLE	loss of vision	150/90	good	good
56	F	Malign mesothelioma, under treatment of cisplatin	loss of vision	150/90	good	poor
64	M	HT, DM, COLD	convulsion	230/112	poor	N/A
65	M	HT, DM, COLD	spasm	220/114	good	poor
71	M	HT, DM, COLD	slip in the mouth	245/110	good	poor
72	M	Prostate adenocancer	blurry vision	220/114	good	good
77	F	SARS virus infection	decrease in fine motor function	180/100	poor	N/A

Abbreviations: F, female; M, male; SLE, systemic lupus erythematosus; HT, hypertension; DM, diabetes mellitus; COLD, chronic obstructive lung disease; TA, tension arteriole; N/A, not acceptable

Table 2. Demographics, detailed CT and MRI finding and outcome of patients with PRES

Age	Sex	CT finding	Affected lobes & structures	DWI	ADC mapping	Short-term outcome	2-year survival rate
25	F	edema	Fr, P, O, CC	isointense	hyperintense	good	good
30	F	edema	Fr, P, O, BG, CC	isointense	hyperintense	good	good
32	F	edema	Fr, P, O	isointense	hyperintense	good	good
33	F	edema	Fr, P, O	isointense	hyperintense	good	good
38	F	none	Fr, P, O	İso/ hyperintense	hypo/hyperintense	good	poor
39	M	none	Fr, P, O	İso/ hyperintense	hypo/hyperintense	good	good
45	F	none	P, O, BG	isointense	hyperintense	good	good
51	F	edema and SAH	Fr, P, O, T	isointense	hyperintense	good	poor
51	F	none	P, O, BG, C	isointense	hyperintense	good	good
56	F	none	P, O	İso/ hyperintense	hypo/hyperintense	good	poor
64	M	cerebellar hematoma	P, O	isointense	hyperintense	poor	N/A
65	M	edema	Fr, P, O	İso/ hyperintense	hypo/hyperintense	good	poor
71	M	none	P, O	isointense	hyperintense	good	poor
72	M	N/A	Fr, P, O	isointense	hyperintense	good	good
77	F	edema	P, O	İso/ hyperintense	hypo/hyperintense	poor	N/A

Abbreviations: F, female; M, male; CT, computerized tomography; SAH, subarachnoid hemorrhage; N/A, not acceptable. Fr, frontal lobe; P, parietal lobe; O, occipital lobe; BG, basal ganglia; T, thalamus; CC, corpus callosum; C, cerebellum

Table 3. Age, gender, radiological characteristics and outcomes of cases

	n=15
Age (years)	49.9±17.0
Range of age (years)	25-77
Age groups	
<50 years	7 (46.7%)
≥50 years	8 (53.3%)
Gender	
Male	5 (33.3%)
Female	10 (66.7%)
Any positive CT finding	
Absent	4 (28.6%)
Exist	10 (71.4%)
Additional MRI finding	
Absent	9 (60.0%)
Exist	6 (40.0%)
Positive diffusion restriction	
Absent	10 (66.7%)
Exist	5 (33.3%)
Short term outcome	
Poor	2 (13.3%)
Good	13 (86.7%)
Long term outcome	
Died (short term)	2 (13.3%)
Poor	5 (33.3%)
Good	8 (53.3%)

Table 4. Demographical and CT and MRI characteristics of cases in terms of long-term outcome

	Poor (n=7)	Good (n=8)	p-value
Age (years)	60.3±13.1	40.9±15.1	**0.021**†
Age groups			**0.041**‡
<50 years	1 (14.3%)	6 (75.0%)	
≥50 years	6 (85.7%)	2 (25.0%)	
Gender			0.608‡
Male	3 (42,9%)	2 (25.0%)	
Female	4 (57.1%)	6 (75.0%)	
Any positive CT finding			N/A
Absent	2 (28.6%)	2 (28.6%)	
Exist	5 (71.4%)	5 (71.4%)	
Additional MRI finding			0.119‡
Absent	6 (85.7%)	3 (37.5%)	
Exist	1 (14.3%)	5 (62.5%)	
Positive diffusion restriction			0.119‡
Absent	3 (42,9%)	7 (87.5%)	
Exist	4 (57.1%)	1 (12.5%)	

† Student's t test, ‡ Fisher's exact test, N/A: Not available

Imaging techniques were performed on all the patients. MRI and CT scans were performed on 15 (100 %) and 14 (93,3 %) patients, respectively. Imaging at clinical presentation showed vasogenic edema in 100% on MRI and nine patients on CT (Figure 1), hemorrhage in two patients (Figure 2), and restricted diffusion in five patients (Figure 3). The most frequently involved lobes are the occipital and parietal lobes equally, and the frontal lobe followed them. Except for

lobar involvement, three patients had basal ganglia, two patients had corpus callosum, one had thalamus, and one had cerebellum involvement (Figure 4). Table 2 and Table 3 present the primary demographic and the radiological findings of these patients.

There was no statistically significant difference between the group with any positive CT findings and the group without any positive CT finding regarding age, gender, early and long-term results (p>0.05). Although the mean age of the group with additional MRI findings other than lobar involvement was lower than the group without additional MRI findings other than lobar involvement, there was no statistically significant difference between the groups (p=0.066). The mean age of the group with diffusion restriction was higher than the group without diffusion restriction, but no statistically significant difference was observed (p=0.434). There was no statistically significant difference between the long-term results of the group with diffusion restriction compared to the group without diffusion restriction (p=0.231).

The mean age of the group with poor long-term results was statistically significantly higher than that of good long-term results (p=0.021). In addition, the individuals under 50 years of age were statistically significantly better long-term outcomes compared to the group with individuals aged 50 and over (p=0.041). Table 4 compares long-term results with patients' age, gender, CT, and MRI findings.

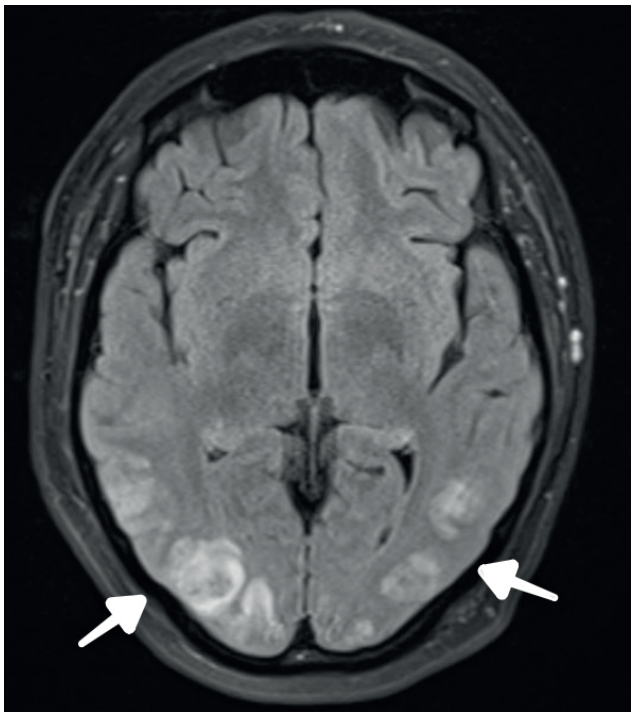

Figure 1: Vasogenic edema on MRI. Axial T2-FLAIR MRI image here demonstrating hyper-intensity foci in the bilateral parietal and occipital lobes, which are characteristic distribution of vasogenic edema in PRES with likely involvement of posterior cerebral artery circulation.

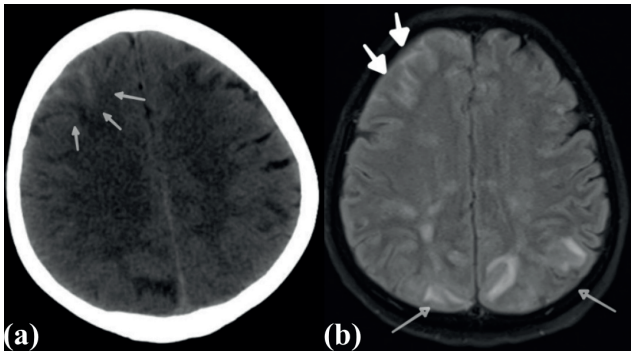

Figure 2. (a) CT scan shows hyperdensity in the right frontal sulci represents hemorrhage (white arrows) (b) Axial FLAIR image of the same patient shows hemorrhage (thick white arrows) and confluent bilateral parietal edema (thin white arrows)

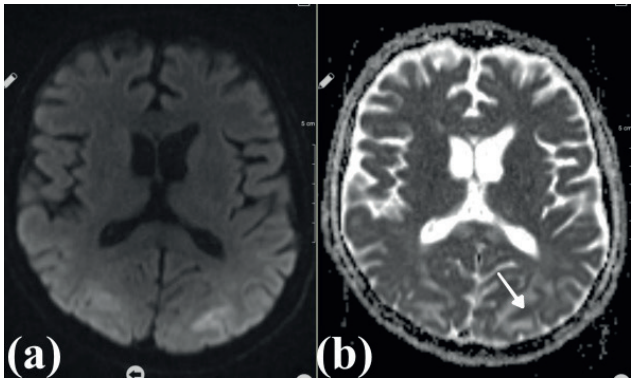

Figure 3. (a) Fifty-five-year-old man with end stage renal disease and severe hypertension. Axial DWI images with ADC inserts show foci of diffusion restriction within left parietal cortex. (b) ADC maps confirm diffusion restriction (White arrow)

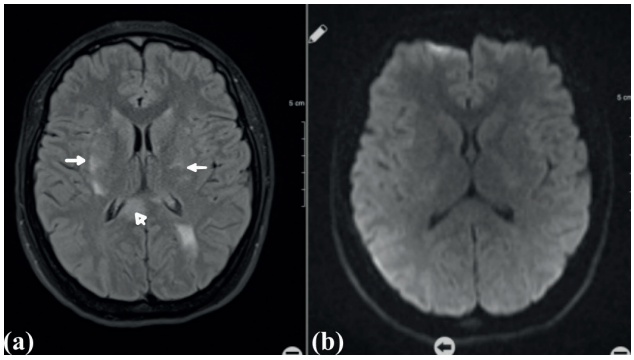

Figure 4: Axial FLAIR images (a) demonstrate central variant PRES with edema involving the splenium of corpus callosum (arrowhead) and basal ganglia (arrows) (b) No diffusion restriction was seen.

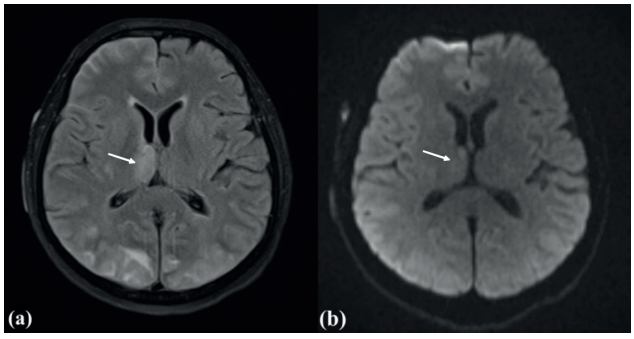

Figure 5. Patient with uncontrolled hypertension presenting with alteration of mental status. T2-FLAIR (a) image demonstrates edema in the right thalamus (arrow). DWI (b) image demonstrates no restricted diffusion (arrow).

Discussion

Since the diagnosis of PRES is widely suspected basing on clinical manifestations and the history of predisposing conditions (7), we tried to evaluate the radiological findings and their relationship to the clinical manifestations of the disease. We found that restricted diffusions were at seen at 33.3% of the patients and CT image showed hemorrhage of 30% additionally. Except for the classically known parietal and occipital lobe involvement; three patients had basal ganglia, two patients had corpus callosum, one had thalamus, and one had cerebellum involvement. Of the patients, 86.6% recovered without sequelae in two-year short-term period. The rate of individuals aged 50 and over was statistically significantly poor in terms of long-term results compared to the group under 50 years of age individuals.

Patients diagnosed with PRES syndrome may have a wide range of symptoms such as headache, seizures, and visual disturbances (8). These symptoms are not always specific for PRES syndrome. These neurological symptoms can also be observed in diseases such as stroke, encephalitis, intracranial hemorrhage (9). Although high blood pressure was recorded in most patients at first admission, it was observed that some patients had only slightly elevated or even normal blood pressure, and such findings were also noted in our study.

Predisposing factors that may cause PRES have been widely discussed and explained in the literature (10). The peripartum period and eclampsia are associated with PRES (11). In our study, 26.6% of the participants were either peripartum or postpartum. Again, chemotherapy is a potential risk factor for PRES (12). In our study, symptomatic patients during chemotherapy showed complete response and resolution in the early period after treatment discontinuation. However, two of these patients died because of other complications and devastating effects of aggressive malignancy, which we thought was unrelated to PRES.

The PRESS is classified as bilateral vasogenic edema, which preferably affects the parieto-occipital lobes bilaterally. It has been suggested that this preferential distribution of posterior circulation is due to the reduced sympathetic innervation of the posterior circulation (13). As shown in our study, posterior circulation such as occipital lobes and posterior areas of parietal lobes, were areas commonly affected. Remarkably, in 40% of the patients, non-lobar involvement was observed on MRI (such as corpus callosum and thalamus). The fact that the arterial vascularization of the splenium part of the corpus callosum was from the pericallosal artery, which is a branch of posterior cerebral artery, supports this theory. However, in our patient with thalamus involvement, the blood supply of the thalamus from both anterior and posterior circulation raises questions about the posterior circulation theory.

In the study by McKinney et al. (5), it was shown that the edema might have a dominant central pattern and can affect the brainstem, basal ganglia, posterior limb of the internal capsule, cerebellum, and periventricular regions without cortical and subcortical involvement. They also state that atypical findings includes restricted diffusion and intracerebral hemorrhage, as in our study. Liman et al. showed that in 30% of patients had restricted diffusion areas (14) Also, Hiremath et al. showed that in 31.7% of patients revealed restricted diffusion areas on MRI (15). These findings are consistent with the 33.3% rate we have shown in our study. Bansal et al. showed recently on a prospective study none of the clinical or imaging features predicted outcome in PRES like our study (16). In the study performed by Wagih et al. with 36 patients, PRES is completely reversible in most patients, even with restricted diffusion (17). Even though Moon et al. (18) showed that the presence of restricted diffusion might be associated with incomplete recovery, our study does not support the idea. Our study, not only supports that diffusion restriction is reversible and that restricted diffusion has no effect on short-term or long-term prognosis. Even the absence of diffusion restriction has often been thought to be related to PRES in previous reports, recent literature clearly emphasizes that diffusion restriction should not be used to exclude PRES (16-18).

Our study confirmed that MRI and CT provided supportive diagnosis of PRES. It should be kept in mind that PRES is usually not restricted to the parietal and occipital lobes despite its name. Short term outcome is generally perfect with medical treatment. Age at the time of diagnosis is an independent risk factor for long term outcome. This might be due to the underlying factors because PRES are more serious in elderly patients or they have more accompanying diseases regardless of PRES. However, due to the small number of patients included in this series, these observations must be taken cautiously and should define this paper's limitation. Further studies, including more significant number of patients are required to determine the outcomes and radiological findings.

Acknowledgments

No potential conflict of interest relevant to this article was reported.

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