Clinical Neurology and Neurosurgery 185 (2019) 105459

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Acute radiological pattern and outcome in posterior reversible encephalopathy syndrome patients

Fabio Pilato[a,*], Rosalinda Calandrelli[b], Marisa Distefano[a], Marco Panfili[b], Giacomo Della Marca[a], Cesare Colosimo[b]

[a] UOC Neurologia, Dipartimento di scienze dell'invecchiamento, neurologiche, ortopediche e della testa-collo, Fondazione Policlinico Universitario A. Gemelli – IRCCS, Roma, Italy
[b] UOC Radiologia e Neuroradiologia, Dipartimento di diagnostica per immagini, radioterapia oncologica ed ematologia, Fondazione Policlinico Universitario A. Gemelli – IRCCS, Roma, Italy

ARTICLE INFO

Keywords:
Posterior reversible encephalopathy syndrome
PRES
MRI
Hypertensive encephalopathy

ABSTRACT

Objective: : Posterior reversible encephalopathy syndrome (PRES) is a neurological disorder of acute or subacute onset characterized by varied neurological symptoms including headache, impaired visual acuity or visual field deficits, confusion, disorders of consciousness, seizures, and motor neurological deficits.

Even if recognition of severe forms of PRES has improved, mainly due to magnetic resonance imaging, pathogenesis is still unclear and management of these patients remains challenging. Moreover, prognosis is unpredictable varying from complete recovery to death and factors related to prognosis are still lacking. We studied early magnetic resonance imaging characteristics and their relationships with prognosis.

Patients and Methods: We performed a retrospective analysis in patients with clinical and neuroradiological charateristics of PRES performing magnetic resonance of the brain within 2 days of symptoms onset.

Results: After reviewing site database of magnetic resonance imaging and clinical records compatible with PRES, 157 patients were selected. After imaging reviewing, 25 patients with clinical and neuroradiological diagnosis of PRES were enrolled, 22 (88%) females. Mean age of enrolled patients at presentation was 44.4±18.4 years (range, 21–84 years). Patients were classified according to neuroradiological characteristics such as ischemic lesions, distribution and severity of edema, hemorrhage and contrast enhancement. In our group 23 patients (92%) showed an almost complete recovery but 2 patients (8%) died during hospitalization. Outcome was significantly related with hypointensity on ADC ($p = 0.002$) and CE ($p < 0.001$).

Conclusion: Early MR features may be helpful in suggesting prognosis. Moreover, neuroimaging at the early stage of PRES may give new insights in pathophysiological mechanisms underlying brain damage and neurological impairment.

1. Introduction

The posterior reversible encephalopathy syndrome (PRES) is a neurological disorder of acute or subacute onset characterized by varied neurological symptoms, which may include headache, impaired visual acuity or visual field deficits, disorders of consciousness, confusion, seizures, and focal neurological deficits occurring in association with several predisposing conditions. PRES is also known as reversible posterior leukoencephalopathy syndrome but other authors labelled it hyperperfusion encephalopathy, or brain capillary leak syndrome; none of these names is completely satisfactory because the syndrome is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain [1–3]. Since its first description in 1996 [1], risk factors associated with the development of PRES including hypertension, preeclampsia, renal failure, autoimmune disorders, immunosuppression, malignancy, sepsis, transplantation and receipt of chemotherapeutic medications remained unchanged but it may occurs also in healthy subjects [1–3]. PRES is usually reversible and monophasic [4] but recurrence has been described [5]. PRES is becoming increasingly recognised, in large part because of improved

* Corresponding author at: UOC Neurologia, Dipartimento di scienze dell'invecchiamento, neurologiche, ortopediche e della testa-collo; Fondazione Policlinico Universitario A. Gemelli – IRCCS, 00168 Roma, Italy.
E-mail addresses: fabio.pilato@policlinicogemelli.it (F. Pilato), rosalinda.calandrelli@policlinicogemelli.it (R. Calandrelli), marisa.distefano@hotmail.it (M. Distefano), marco.panfili@gmail.com (M. Panfili), giacomo.dellamarca@policlinicogemelli.it (G. Della Marca), cesare.colosimo@policlinicogemelli.it (C. Colosimo).

https://doi.org/10.1016/j.clineuro.2019.105459
Received 20 October 2018; Received in revised form 30 June 2019; Accepted 4 August 2019
Available online 08 August 2019
0303-8467/

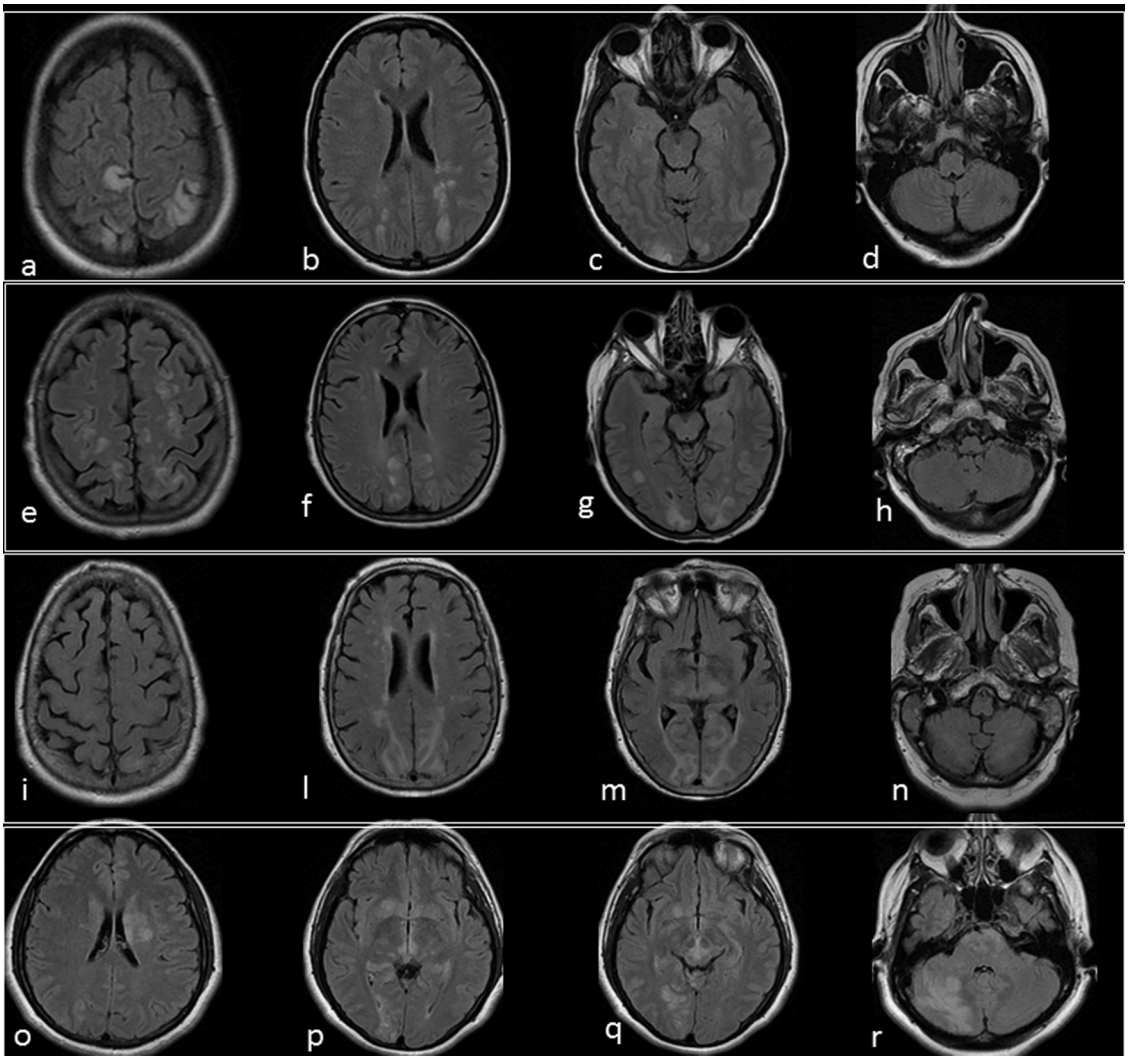

Fig. 1. Distribution Patterns of Edema in patients with PRES.
a-r: FLAIR MRI images
a-d) Holohemispheric watershed pattern: edema is present in a linear pattern spanning the frontal, parietal and occipital lobes with minor involvement of the temporal lobes
e-h) Superior frontal sulcus pattern: similar to the holohemispheric watershed pattern with more pronounced superior frontal sulcal involvement.
i-n) Dominant parietal –occipital pattern: edema involves the parietal and occipital cortex and white matter.
o-r)Atypical pattern: edema involves cerebellar regions and /or basal ganglia, brain stem and deep white matter.

and more readily available brain imaging techniques. Magnetic resonance plays a key role in diagnostic process; frequently it shows a distinctive parieto-occipital pattern with asymmetric distribution of changes reflecting vasogenic edema, but several patterns are described [6,7]. The main finding in neuroimaging is posterior white matter edema, often with symmetrical involvement of the parietal and occipital lobes due to vascular cerebral dysregulation, but hemorrhagic variants were documented [1,8]. PRES is a remarkably heterogeneous group of disorders with patchy areas of edema in the brain [9] but pathophysiological mechanisms underlying PRES development remain unclear [1,10]. Hypertension with failed autoregulation and hyperperfusion was a popular theory for the developing brain edema [1,11] but the theory of vasoconstriction, hypoperfusion and ischemia more easily explains most of the observations in PRES, lesions and edema localization in the brain [12,13].

Even if recognition of severe forms of PRES has improved, the management of these patients remains challenging, particularly in patients with the combination of edema and hemorrhage [6,10].

Although the pathophysiological changes underlying PRES are not fully understood, endothelial dysfunction is supposed to be a key factor [10]. Two main hypotheses have been postulated but pathophysiology of PRES remains controversial. One hypothesis involves impaired cerebral autoregulation responsible for an increase in cerebral blood flow, whereas the other incriminates endothelial dysfunction with cerebral hypoperfusion. Latter hypothesis may be most relevant to cases of PRES associated with cytotoxic therapy [10,13,14]. Under both hypotheses, the cerebral blood perfusion abnormalities result in blood-brain barrier dysfunction with cerebral vasogenic edema [10,13,14]. Hypertension has often been emphasized as a common feature of all PRES associated conditions but normo- or hypotensive patients have made possible to hypothesize other pathological mechanisms involving activation of immune system or alteration of brain barrier permeability known as “cytotoxic, immunogenic and vasogenic theories” [15].

Neurological symptoms at the onset may be puzzling making diagnostic pathway challenging, however the overall prognosis is favorable, since clinical symptoms as well as imaging lesions are reversible in most patients. Nevertheless, neurological sequelae including long-term epilepsy and in-hospital death may occur in individual cases reaching 30% of patients with hemorrhagic PRES [9,16] and also other permanent tissue damages have been observed [6].

In patients with PRES several MR patterns have been hypotized to be linked with prognosis but these associations are still debated [6]. Reversibility of MR alterations is usually described in PRES [17] but permanent tissue damages were also observed [6]. PRES has a quite good prognosis and most patients after toxic phase show a complete recovery but other patients show a different evolution showing persistent neurological impairments sometime leading to the in-hospital death and mortality ranges from 3 to 6% [10]; however factors linked with prognosis remain poorly understood [6,18].

PRES preferentially affects women and relatively young individuals with particular co-morbidities or clinical conditions [19]. Moderate to severe hypertension is encountered in 50%–70% of patients with PRES at the onset of symptoms and emergent hypertension treatment is associated with symptoms improvement in hours or days [6,8,13,14,20].

We performed a retrospective analysis in patients with clinical and neuroradiological charateristics of PRES performing MR by 2 days of symptoms onset to evaluate early neuroradiological findings and their relationship on the prognosis.

2. Patients and Methods

Radiological, admission and discharge report databases of the university hospital “Fondazione Policlinico A. Gemelli - IRCCS” were searched for the following items from January 2010 to December 2016: PRES, posterior reversible encephalopathy, posterior reversible leukoencephalopathy, preeclampsia and eclampsia, toxemia of pregnancy, hypertensive encephalopathy and hypertensive crisis.

The following criteria were used in final diagnosis of PRES: typical clinical presentation of PRES, including headaches, visual disturbance, altered mental functioning, and seizures with an underlying etiology such as hypertension and drug toxicity. Other common causes were included, like renal involvement with renal insufficiency and infection. Patients included in this study had a clinical presentations and specific radiological abnormalities consistent with PRES and MR had been performed by 2 days from symptoms onset. Radiological findings were evaluated by two expert neuroradiologists.

Patient records were assessed for demographic data, clinical presentation, peak systolic and diastolic blood pressure measurements. Comorbidity and predisposing conditions, time to neuroimaging, time to follow-up imaging, hospitalization and in-hospital death were acquired and collected for all PRES patients included into this study.

Retrospective review of neuroimages (including brain computed tomographs [CT] and MRIs) was performed by 2 trained neuroradiologists, blinded to clinical data, to evaluate edema, intracranial hemorrhage, the pattern of radiologic severity and the presence and patterns of contrast enhancement (Fig. 1). Analysis of the clinical details of each case was performed separately, but with joint-consensus grading of MR imaging severity.

Only patients underwent MRI within 2 days from symptoms onset were enrolled. MRI was performed with a 1.5-T unit; protocol might vary but all studies included T2 Fluid-Attenuated-Inversion-Recovery (FLAIR), T2 weighted imaging (T2WI), T1 weighted imaging (T1WI), Diffusion-weighted imaging (DWI), susceptibility weighted MRI (echo planar T2* sequence) and contrast enhancement T1WI. T2 FLAIR and T2WI were used to detect the distribution of edema. DWI and ADC values were used to differentiate vasogenic edema from cytotoxic edema. Susceptibility weighted MRI (echo planar T2* sequence) was used to detect intraparenchymal hemorrhage (both microhemorrhages and hematomas with mass effect) and/or subarachnoid hemorrhage (SAH). Vasogenic edema was diagnosed in cases of signal-intensity hyperintensity on FLAIR and T2WI combined with signal-intensity hyperintensity on DWI sequences and high signal intensity on ADC maps. Cytotoxic edema was diagnosed in cases of signal-intensity hyperintensity on FLAIR and T2WI combined with signal-intensity hyperintensity on DWI sequences with hypo- or isointensity on ADC maps [21]. The local ethics committee approved the study. All study procedures have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

3. Statistical analysis

Descriptive statistics were expressed as the means ± SD for continuous variables and as numbers and percentage for qualitative parameters.

We compared MR findings using Chi-square or Fisher's exact test for categorical variables.

Mann–Whitney *U*test was applied for comparison of data with nonparametric distribution in continuous data. Pearson correlation test and z-test was used to study the relation between radiological and clinical data. Statistical significance was determined at α level of 0.05.

All statistical analyses were performed with Stat View version 5.0 (SAS Institute Inc.).

4. Results

We identified 25 patients with PRES, 22 (88%) females, after reviewing 157 records in wich PRES was suspected. Reasons for exclusion were clinical histories and MR findings inconsistent with PRES (n = 51), alternative radiological diagnoses (n = 22), and clinical or MR evaluations performed more than 2 days later from symptoms onset (n = 59). Mean age of enrolled patients at presentation was 44.4±18.4 years (range, 21–84 years).

Clinical and radiological features are reported in Tables 1 and 2.

The most common clinical presentations were decreased cosciusness (n = 18, 72%), seizure (n = 12, 48%), and headache (n = 8, 32%), whereas focal neurological deficits were visual symptoms (n = 7, 28%) and 5 patients (20%) showed motor deficits.

Co-morbidities and clinical conditions that favour the development of PRES included peri-partum conditions (n = 11; 44%), chemotherapy (n = 4; 16%), post-infective disease (n = 3; 12%), autoimmunity (n = 5; 20%) and end-stage renal disease (n = 2; 8%). Malignancy was present in 4 (16%) patients and included uterine cervical cancer, acute monocytic leukemia, endometrial squamous cell carcinoma and clear cell renal carcinoma and all these patients had received chemotherapy.

In post-infective group one patient was on HAART therapy whereas in autoimmune disorders group all patients but one received immunosuppressive therapy.

Hypertension at the onset of symptoms was very common (n = 19; 76%) and mean arterial pressure (MAP) at onset was 124±28 mmHg (range 60–193), but history of hypertension was rare (n = 3; 12%).

4.1. Radiological findings

Patients were classified according to distribution and severity of edema and hemorrhage [3,9].

23 patients (92%) showed edema. Five patients (20%) showed hemorrhage and 4 out of these patients (16%) showed overlapping edema and hemorrhage (Table 2).

Three hemispheric pattern variants were detected (holohemispheric, superior frontal sulcal and dominant parietal-occipital). These demarcate lateral hemispheric blood supply (middle cerebral artery [MCA]) and medial hemispheric supply (anterior cerebral artery [ACA], posterior cerebral artery [PCA]) and further reflect the junctional/watershed nature of PRES accordingly with previous studies [3,7].

In *Holohemispheric watershed pattern*, vasogenic edema is present in a linear pattern spanning the frontal, parietal and occipital lobes with lesser involvement of the temporal lobes. In *Superior frontal sulcus pattern* an involvement of the frontal lobe is associated with varying degrees of parietal and occipital abnormality. In *Dominant parietal–occipital pattern* the region involved were the parietal and occipital cortex and white matter with variable involvement of the temporal

Table 1
Clinical and demographic features of the patients.

Pt.	Sex/Age	Clinical symptoms (at onset)	BP at onset (mmHg)	Comorbidities	Edema pattern	Edema severity	Hemorrhage	CE	Hospitalization (Days)	Prognosis
	F/44	Visual disturbance, focal neurologic deficits	220/114	Hashimoto's Thyroiditis	Holohemispheric	Severe	No	No	20	Recovery
	F/84	SZ, encephalopathy	80/50	Post-infective	Parieto-occipital	Moderate	No	Gyral	70	Death
	F/21	HA/SZ	160/100	Eclampsia	Holohemispheric	Mild	No	No	12	Recovery
	F/38	HA/ visual disturbance	150/80	Peripartum	Partial	Severe	No	No	23	Recovery
	F/25	Encephalopathy	170/110	HELLP syndrome	Partial	Mild	No	No	8	Recovery
	F/26	HA/SZ/ visual disturbance	140/70	Peripartum	Parieto-occipital	Mild	No	No	22	Recovery
	M/55	Encephalopathy	150/90	Post-infective, HAART therapy	Frontal sulcus	Severe	No	No	30	Recovery
	F/40	Visual disturbance	180/115	Uterine carcinoma, Chemotherapy	Partial	Mild	No	No	25	Recovery
	M/70	Encephalopathy	220/140	Post-infective	Partial	Mild	No	Yes	43	Recovery
	F/55	SZ	230/110	MG, immunosuppressive therapy	Frontal sulcus	Mild	No	No	65	Recovery
	F/61	Visual disturbance, encephalopathy	180/100	Acute Myelomonocytic Leukemia, chemotherapy	Frontal sulcus	Mild	No	No	31	Recovery
	F/26	HA/SZ	240/140	Eclampsia	Partial	Mild	No	No	5	Recovery
	F/32	HA	210/100	Peripartum	Frontal sulcus	Mild	No	No	15	Recovery
	F/54	Visual disturbance/SZ	140/80	Clear cell renal carcinoma, chemotherapy	Parieto-occipital	Mild	No	No	23	Recovery
	F/40	SZ/encephalopathy	260/160	CRF, Multiple sclerosis	Partial	Mild	No	No	13	Recovery
	F/40	SZ	160/110	Peripartum	Parieto-occipital	Mild	No	No	7	Recovery
	F/25	SZ	170/100	Eclampsia	Partial	Mild	No	No	5	Recovery
	F/58	Focal neurologic deficits	130/90	Uterine carcinoma, chemotherapy	Partial	Mild	No	No	61	Recovery
	F/29	SZ	180/90	Pre-eclampsia, antiphopsholid syndrome	Frontal sulcus	Mild	No	No	12	Recovery
	F/29	SZ	160/80	CRF, vasculitis, immunosuppressive therapy	Parieto-occipital	Mild	No	No	14	Recovery
	M/68	Encephalopathy	120/80	Psoriasis, steroid therapy	Frontal sulcus	Severe	SAH	Gyral	85	Death
	F/38	Focal neurologic deficits	160/90	Peripartum	Partial	Mild	HE	No	23	Recovery
	F/27	HA/Visual disturbance/ SZ/ focal neurologic deficits	170/100	Peripartum	Parieto-occipital	Moderate	HE	No	16	Recovery
	F/43	HA/focal neurologic deficit	180/90	–	Partial	No	SAH	No	20	Recovery
	F/83	HA/Encephalopathy	200/90	–	Partial	Severe	HE	Gyral	20	Recovery

HA: Headache; SZ: Seizures; CRF: Chronic renal failure; HE: Intraparenchimal Hemorrhage; SAH: Subarachnoid hemorrhage;

Table 2
Radiological findings in PRES patients.

MRI characteristics	No. Pts (%)	MAP Mean±SD	Hospitalization (days) Mean±SD	P value
Edema Pattern				
Holohemispheric watershed	2 (8)	134.7±20.7	16±5.7	> 0.05
Superior frontal sulcus	6 (24)	122.8±19.9	39.7±29.1	> 0.05
Dominant parietal-occipital	6 (24)	101.7±24.2*	25.3±22.6	< 0.05*
Partial and asymmetric	11 (44)	135.5±29.7	22.5±16.8	> 0.05
Severity Edema				
Mild	17 (68)	130.6±27.1	22.6±18.2	> 0.05
Moderate	2 (8)	91.7±44.8	43±38.2	> 0.05
Severe	5 (20)	116.5±22	35.6±27.9	> 0.05
Hemorrhage				
He	3 (12)	121.1±6.9	19.7±3.5	> 0.05
SAH	2 (8)	106.7±18.9	53.5±44.5	> 0.05
No Hemorrhage*	20 (80)	126.5±30.5*	25.2±19.8	< 0.05*
MR signal				
Hyperintensity (FLAIR/T2)	23 (92)	124.9±29.1	27.2±22.4	> 0.05
Hyperintensity DWI/ADC	13 (52)	124.4±24	23.6±16.2	> 0.05
Hyperintensity DWI, isointensity ADC	4 (16)	118.3±10.4	21.3±26.7	> 0.05
Hyperintensity DWI, hypointensity ADC	6 (24)	126.6±46.1	38.8±30.6*	= 0.002*
CE	4 (16)	111.7±45.7	54.5±28.8*	< 0.001*

ADC: apparent diffusion coefficient; CE: Contrast Enhancement; DWI: Diffusion Weighted Imaging; He: Intraparenchimal hemorrhage.
SAH: Subarachnoid Hemorrhage.
* $p < 0.05$.

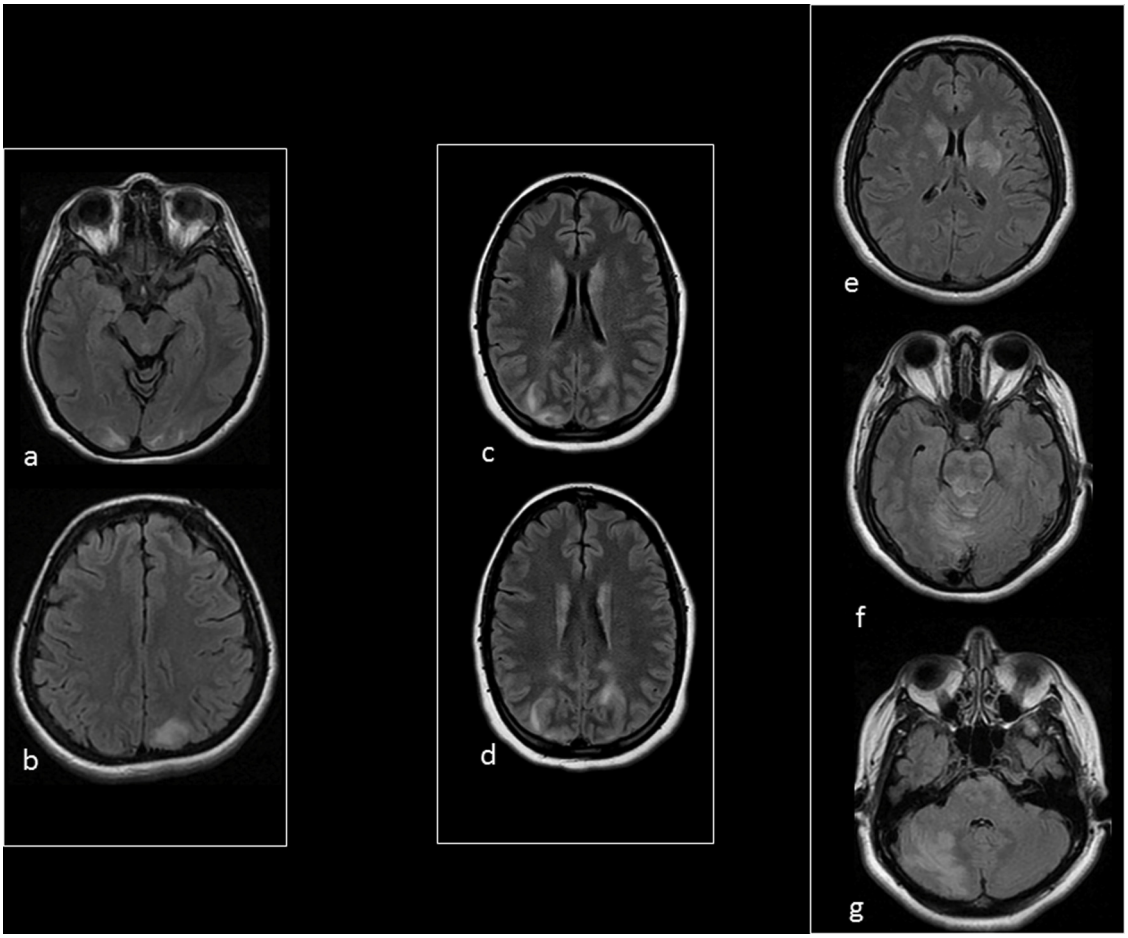

Fig. 2. Edema *in patients with PRES.*
a-g: FLAIR MRI images
a, b) Images show cortical or subcortical white matter edema in parieto-occipital regions
c, d) Images show edema extending from the cortex and subcortical white matter to the deep white matter in parieto-occipital regions without extension to the ventricular margin
e, g) Images show areas of edema involving cerebellum, brainstem, and basal ganglia together

lobes.

Partial or asymmetric expression of these primary patterns was recognized in some patients with incomplete expression of the 3 primary PRES patterns. Moreover the isolated or associated involvement of cerebellar regions and/or basal ganglia, brain stem and deep white matter was detected as atypical lesions [3,7].

Holohemispheric watershed pattern was observed in 2 patients (8%) and 1 of these patients (4%) showed associated talamic involvement. *Superior frontal sulcus pattern* was observed in 6 patients (24%) and 2 patients (8%) showed associated atypical lesions; *Dominant parietal–occipital pattern* was observed in 6 patients (24%) and 3 patients (12%) showed associated atypical lesions; *Partial or asymmetric expression of the primary patterns* was observed in 11 patients (44%) and 7 of these patients (28%) showed associated atypical lesions (Table 2). Patients in dominant parieto-occipital group showed lower MAP values compared with other groups (101.7 ± 24.2; $p < 0.05$).

The extent of vasogenic edema has been classified according to a system of grading that includes mild, moderate, and severe categories [7,22] (Fig. 2). Mild edema was typically classified as cortical or subcortical white matter edema without mass effect, or herniation and minimal involvement of only one of the following structures: cerebellum, brainstem, or basal ganglia. Moderate edema was defined as confluent edema extending from the cortex to the deep white matter without extension to the ventricular margin and mild involvement of two of the following regions: cerebellum, brainstem, or basal ganglia. Mild mass effect may be present but herniation or midline shift is absent, particularly if parenchymal hemorrhage is present. Finally, severe edema was classified as confluent edema extending from the cortex to the ventricle or edema causing midline shift or herniation. Alternatively, involvement of the cerebellum, brainstem, and basal ganglia together constitutes severe edema.

Seventeen patients (68%) showed mild edema, 5 patients (20%) showed severe edema and 2 patients (8%) had moderate edema (Table 2).

FLAIR/T2 hyperintensity in involved subcortical/deep white matter was observed in 23 patients (92%); 13 patients (52%) showed isointensity with/or hyperintensity in DWI associated to hyperintensity in ADC maps; 4 patients (16%) showed areas of hyperintensity in DWI associated to isointensity in ADC maps; 6 patients (24%) showed small, patchy, or punctate hyperintensity in DWI corresponding to hypointensity in ADC maps (Fig. 3); 4 patients (16%) showed gyriform or leptomeningeal enhancement (Table 2).

Intraparenchimal hemorrhage (HE) and subarachnoid hemorrhage (SAH) were detected on the basis of their neuroimaging characteristic such as hyperdensity on CT and hyperintense signal on T1 FSE or hyperintense signal within the sulci on FLAIR images (for SAH) along with corresponding hypointensity on gradient-echo T2-weighted images on MR. Three patients (12%) showed HE, 2 patients (8%) showed SAH and 20 patients (80%) did not show hemorrhage (Table 2). Patients without hemorrhage showed higher MAP values compared with other groups

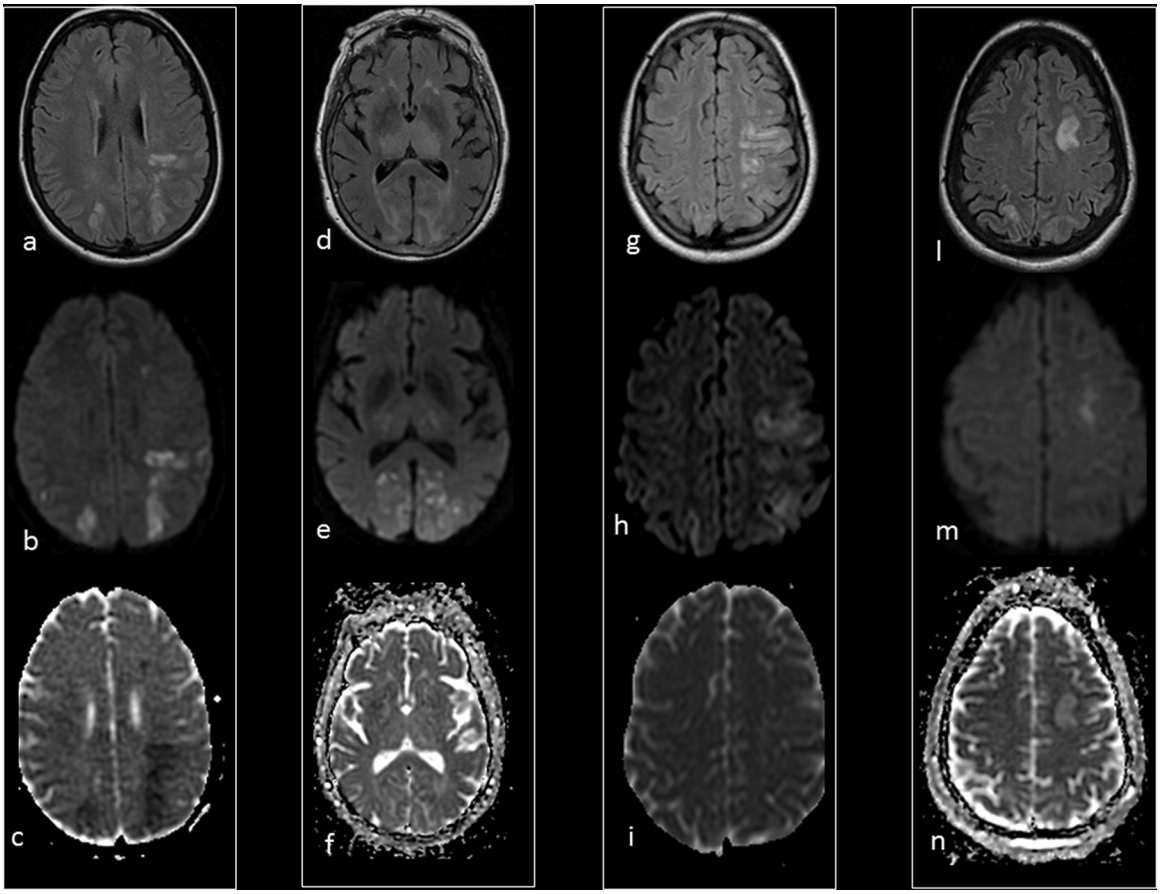

Fig. 3. Variability of *MRI signal of edema in patients with PRES.*
a,d,g,l: FLAIR MRI images; b,e,h,m: DWI MRI images; c,f,i,n: ADC maps.
a-c) Images show hyperintensity of edema signal in FLAIR and DWI corresponding to hypointensity in ADC map.
d-f) Images show hyperintensity of edema signal in FLAIR with small, patchy, or punctate hyperintensity in DWI corresponding to hypointensity in ADC maps.
g-i) Images show hyperintensity of edema signal in FLAIR and DWI corresponding to isointensity in ADC map.
l-n) Images show hyperintensity of edema signal in FLAIR and DWI corresponding to hyperintensity in ADC map.

(126.5±30.5; $p < 0.05$).

4.2. Prognosis and hospitalization

In our group 23 patients (92%) showed an almost complete recovery but 2 patients (8%) died during hospitalization. Outcome was significantly related with hypointensity on ADC ($p = 0.002$) and CE ($p < 0.001$) (Table 2).

5. Discussion

Most of PRES patients show symmetric vasogenic edema in bilateral posterior cerebral circulation territories on MRI imaging but several studies showed that the anterior circulation territory and overlapping watershed territories are frequently present and infratentorial (brainstem, cerebellum) regions may also be involved. Moreover, atypical imaging findings such as hemorrhage, cytotoxic edema/infarction and abnormal enhancement may also occur [23,24].

Acute blood pressure plays a significant role in PRES, whether its role is causative or a compensation mechanism or an epiphenomenon it is still debated [10,12,13]. We found high MAP values in all PRES patients but patients with SAH had lower MAP values then patients with HE or without hemorrhage; moreover we found that acute hypertension was not linked with poor outcome and acute hypertension was not related with hemorrhage rate and hemorrhage type as previously described [6,8]. Some studies highlighted a possible immunological activation in PRES-associated conditions more than an effect of systemic hypertension [12,25]. A recently proposed theory pointed out the importance of endothelial dysfunction due to a multitude of potential causes. Accordingly, recent studies of the effects of immuno-suppressant medications on the endothelium suggest that endothelial cell injury and subsequent blood-brain barrier impairment may cause edema and micro-haemorrhages [19,25,26].

Recent meta-analysis evaluated acute MRI findings in PRES patients and it showed a poor outcome when PRES was associated with haemorrhage and cytotoxic edema [24]. Moreover several studies found haemorrhage as a predictor of poor functional outcome or death [28,29]. We found that MR pattern of hyperintensity on DWI and hypointensity in ADC map and CE are independently linked to a poor prognosis and longer hospitalization periods. A previous study reported the association between radiological severity and clinical outcome but association between CE pattern and prognosis was of uncertain significance [26]. Enhancement is generally considered to represent breakdown or increased permeability of the blood-brain barrier [27] and enhancement could indicate different stages in the integrity of the blood-brain barrier, perhaps even being a temporal phenomenon, with cases lacking enhancement possibly being in a later stage at a point when the barrier has regained impermeability [26]. We enrolled only patients underwent MR within 2 days from the onset of neurological symptoms, at a very early stage of the disease, and this may explain the differences found in previous studies [24,26].

In our group of patients none of the patients with immune-

suppressant medications showed CE but on the other hand it was showed by patients with post-infective co-morbidities and this finding is in accordance with cytotoxic, immunogenic hypothesis [15]. In the majority of patients who develop PRES a complex underlying 'systemic process' is present and hypoperfusion/vasoconstriction and the development of parallel brain and systemic toxicity would more easily explain most of the observations in PRES [15]. Enhanced systemic endothelial activation, leukocyte trafficking, and vasoconstriction, alone or in combination, would result in brain and systemic hypoperfusion and it may explain permanent brain lesions [12]. On the other hand CE may be related to a temporal pattern as previously suggested [24,26] and it may depend on the timing of the examination.

Even if several different mechanisms may promote brain-blood-barrier impairment and endothelial dysfunction these mechanisms may also cause unusual early brain damage such as cytotoxic edema and hemorrhage [10,12,13].

This study demonstrated that very early MR could be an useful tool to evaluate PRES patients and early MR had prognostic significance in studied population. However our study had some limitations. First, because this was a retrospective study and selection bias was present. Second, small sample size and comorbidities, that in these patients are serious, might have influenced prognosis. In addition lack of follow-up MRI has not allowed to evaluate the evolution and the time course of the lesions detected in early MRI.

6. Conclusion

Factors related to clinical onset and outcome in patients with PRES remain not completely understood. However, early MR features may be helpful in suggesting prognosis. Moreover neuroimaging at the early stage of PRES may give new insights in pathophysiological mechanisms underlying brain damage and neurological impairment.

Large-scale studies are needed to confirm whether or not the acute imaging findings such as DWI-hyper/ADC-hypo pattern and or CE on MRI at the onset of the symptoms may be helpful in unveiling specific PRES subtypes of patients in whom personalized treatments, such as aggressive antihypertensive treatment, may be beneficial.

Declaration of Competing Interest

Authors declare no conflict of interest

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