ORIGINAL ARTICLE

Study of Clinicoradiological Profile in Posterior Reversible Encephalopathy Syndrome: An Experience from North India

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Abstract

Background: Posterior reversible encephalopathy syndrome (PRES) is a reversible condition. The Main pathological feature is vasogenic cerebral edema with predominant involvement of posterior part of the cerebrum. Clinical symptoms range from headache, seizure, and vision loss. We evaluated the clinicoradiological features of patients with PRES and their clinical outcome.

Materials and methods: A retrospective study with 30 cases from January 2014 to May 2017.

Results: Of thirty patients, 18 were females and twelve patients were male. The Mean age of the patients was 38.6 years. The most common presentation was seizure (66.6%) followed by altered mental status (53.3%) and headache (40%). The Main comorbid illnesses in our study were renal disease (36.7%), hypertension (23.3%), eclampsia, and postpartum sepsis (26.7%). The Most common site was the occipito-parietal region in the magnetic resonance imaging brain (66%). Atypical presentation involved the temporal lobe (16%), basal ganglia (6%), and microhemorrhage (6%). The Outcome was good with 20% mortalities.

Conclusion: PRES is a reversible condition and has a good outcome in most patients. In our study, seizure was the most common presentation and renal disease is the most common comorbid illness.

Keywords: Hypertension, Neuroimaging, Outcome, PRES.

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Introduction

First described by Hinchey et al. in 1996, posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological syndrome, characterized by headache, visual disturbances, seizures, altered mental status, and occasional focal neurological deficit. In radiological imaging, abnormalities are seen in the posterior region of both cerebral hemispheres.[1] Though the pathophysiology of PRES is not clearly understood, but vasogenic edema secondary to disruption of blood–brain barrier is characteristic of it. There is no specific age group for this condition, but most of the cases occur in the third to fifth decade of life, with predominance in females. Eclampsia is the main comorbidity in PRES.[2–5] Other major comorbidities involved are hypertension (HTN), renal diseases, organ transplantation, autoimmune diseases (systemic lupus erythromatosis and scleroderma), electrolyte imbalance, sepsis, and thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS). The outcome of PRES is good with complete recovery in most of the patients in a period ranging from days to months.[6–9] Several studies were conducted in India on PRES but it has not been extensively studied. The aim of this study was to evaluate the demographics and clinicoradiological profile of patients with PRES and to predict outcome in terms of survival or mortality.

Materials and Methods

A retrospective study was performed in a single center over a period from January 2014 to May 2017. Data was retrieved from the medical records department. Medical records and neuroimages of cases were studied, evaluated, and analyzed to bring out clinical features, etiological factors, imaging findings, and their outcomes. Magnetic resonance imaging (MRI) was prerequisite for inclusion in the study. Patients with clinical and imaging features suggestive of PRES were included. Total number of included patients was 30. Twelve were males and 18 were females. Medical records of all included patients were reviewed. Clinical history and neurological examination at the time of presentation were noted. In addition, clinical information regarding concurrent medical illnesses, immunosuppressive therapy, and other medications was extracted. Laboratory parameters including complete blood count and biochemical parameters such as renal function test, electrolytes, and liver function test were also reviewed. All MRI findings were reviewed. Institutional ethical committee (IEC) approval was taken for the study. Imaging findings were analyzed, including the distribution of lesions, predominant lobe involvement, and presence of restricted diffusion and microhemorrhages. Predictors of outcome were also analyzed.

Statistical Analysis

Numeric values were analyzed as the mean ± standard deviation (SD). Variables of demographic, clinical and radiological parameters among patients with PRESS were shown with numerical variables

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and percentage. Demographic and clinical variables of patients with PRESS with or without survival were compared by using Chi-square contingency analysis to explore the statistically significant difference in predicting outcome. *p*-value of less than 0.05 was considered statistically significant. The epi info-7 statistical software was used for analysis.

Result

The total number of cases was 30. Eighteen cases were females and 12 were males. At the time of presentation, mean age was 38.6 years (range from 13 to 60 years). Main comorbid illnesses associated were renal disease (36.7%), hypertension (23.3%), eclampsia, and postpartum sepsis (26.7%).

Clinical Features

The most common clinical presentation was seizure (66.6%). Most of the seizures were secondary generalized seizure (80%) and only two cases had focal seizure (20%). Other clinical presentations were altered mental status (53.3%), followed by headache (40%), and nausea and vomiting (16.6%). Four patients had postpartum sepsis and two had postpartum sepsis along with eclampsia. Visual symptoms were seen in 20% of the patients. Quadriparesis and hemiparesis were observed in 13.3% of the patients. Of four patients (13.3%), two had quadriparesis and the rest two had hemiparesis. One patient with quadriparesis expired. Other one was dependent for daily activities at the time of discharge. Two patients with hemiparesis were recovered at the time of hospital discharge over a period of 1 week. Mean BP of each patient was calculated, two third of them had hypertension. More than one-third of the patients had main comorbid illness in the kidney. One patient had Guillain-Barre syndrome at admission, developed PRES secondary to hypertension because of dysautonomia. The Outcome was generally favorable with a complete recovery in 80% of the cases. Baseline and demographics characteristics of the patients have been tabulated in Table 1. Clinical and etiological characteristics of the individual patient have been shown in Table 2. Demographic and clinical variables of patients with PRESS with and without survival were compared. No significant difference was noted between both the groups (Table 3).

Neuroimaging

MRI is the key modality of the diagnosis of PRES. It has characteristic hypointense lesions on T1 imaging and hyperintense on T2 and FLAIR images. Most common site was the occipital-parietal lobe (66%) followed by the frontal lobe (46%). Cerebellum was involved in 26% of the patients. Atypical presentations involved temporal lobe (16%), corpus callosum (16%), brainstem (10%), thalamus (6%), and basal ganglia (6%). Least common involvement was seen in internal capsule (4%). Infarct and microhemorrhages were present in 16% of the patients (8% in each). Radiological findings have been tabulated in Table 4. Reversibility of neuroimaging findings has been shown in Figure 1.

Discussion

Posterior reversible encephalopathy syndrome (PRES) is characterized clinically by headache, seizures, visual impairments, and altered mental status. Neuroimaging by MRI is the corner stone of the diagnosis. Main imaging findings are presence of bilateral and symmetric vasogenic cerebral edema, typically seen in subcortical regions of occipital and parietal lobes. Early diagnosis is vital, as timely control of blood pressure helps in early reversal of the condition. It minimizes long-term clinical sequelae.

The pathophysiology of PRES is still unclear. Various theories have been postulated. According to the most widely accepted theory, a rapid rise in blood pressure leads to a breakdown in the cerebral autoregulation, particularly in the posterior cerebral region that lacks sympathetic innervation relatively. Hyperperfusion of the brain leads to protein and fluid extravasation, resulting in focal vasogenic edema.[1,10] An alternative theory emphasizes endothelial dysfunction, which is important in pre-eclampsia, eclampsia, and sepsis. A third theory was also postulated with emphasis on vasospasm. Vasospasm-induced ischemia may be responsible for focal neurological deficit.

Early recognition and timely intervention are important in PRES. Timely institution of therapy includes gradual blood pressure control and withdrawal of potentially offending agents, resulting in early reversal of condition and prevention of long-term clinical sequel. If this condition does not reverse in time, secondary complications, such as status epilepticus, intracranial hemorrhage, and massive ischemic infarction, can cause substantial morbidity and mortality.[11]

In the present study, more than half of the patients were female (60%). This finding is similar to a study by Fugate et al. that showed involvement of 65% of females.[1] In the present study, the mean age of onset is 38.6 years, which is comparable with other studies.[4]

The most common clinical presentation is seizure (66%). Other presentations are altered mental status (53%), followed by

Table 1: Demographics and baseline characteristics of the patients

Variables	*Number of patients*	*Percentage*
Demographics		
Males	12	40
Females	18	60
Mean age	38.6 years	
Clinical profile		
Seizure	20	66.6
Altered mental status	16	53.3
Headache	12	40
Vomiting	5	16.6
Fever	5	16.6
Visual impairments	6	20
Quadriperesis and hemiperesis	4	13.3
Etiology		
Postpartum sepsis	4	13.3
Eclampsia	2	6.7
Postpartum sepsis with Eclampsia	2	6.7
Hypertension	7	23.3
Renal diseases	11	36.7
SLE	1	3.3
Sjögren's syndrome	1	3.3
Poly-trauma	1	3.3
Cardiac disease	1	3.3
Outcome		
Recovered	24	80
Death	6	20

Table 2: Clinical and etiological characteristics of the individual patient

Patient gender/age	*Clinical features*	*Blood pressure (MAP) mm/Hg*	*Comorbidities*	*Outcome*
M/60	Altered mental state (irrelevant talk, confusion), oliguria	170/110	Acute renal failure, hypertension	Recovered
M/20	Headache, seizure, vomiting	166/108	Nephrotic syndrome with hypertension	Recovered
M/17	Headache, blurred vision, altered mental state	160/100	Hypertension with unilateral shrunken kidney	Recovered
F/30	Seizure, fever with chills and altered mental state	144/98	Postpartum septicemia	Recovered
F/40	Backache and quadriparesis	150/100	Guillain-Barre syndrome with hypertension	Recovered
F/22	Fever with chills, seizure and altered medical state	140/96	Postpartum septicemia	Recovered
M/42	Chest pain, left shoulder pain, altered mental state (confusion)	100/60	Ascending aortic aneurysm with severe AR	Recovered
F/22	Fever with chills, altered mental state	116/80	Postpartum sepsis with acute renal failure	Recovered
F/30	Hemiparesis, altered mental state	110/68	RTA with poly-trauma	Recovered
F/28	Seizure, fever with chills, altered mental state	150/90	Lupus nephritis with hypothyroidism with chronic renal failure with postpartum sepsis	Recovered
M/20	Seizure, vomiting	156/100	Nephrotic syndrome with MPGN	Recovered
F/13	Seizure	120/70	PIGN, C3 nephropathy	Recovered
F/22	Seizure, altered mental state	160/100	Eclampsia with intrauterine death with postpartum sepsis with AKI with HELLP	Recovered
M/18	Fever with chills, vomiting, pain abdomen, seizure	110/70	Malaria with acute renal failure with thrombotic thrombocytopenic purpurs-hemolytic uremic syndrome (TTP-HUS)	Recovered
F/52	Seizure, Involuntary movement, drowsy	138/84	Chronic renal failure (stage V) with anemia with uremic encephalopathy	Expired
F/30	Vomiting, seizure, headache	118/64	Postpartum sepsis with acute renal failure	Expired
M/32	Seizures, headache	170/110	Hypertension with coronary artery disease	Recovered
M/28	Altered mental status	190/100	Hypertension, acute febrile illness	Recovered
F/19	Quadriparesis	140/80	Sjögren's syndrome	Expired
F/22	Seizures, altered mental status	140/80	Postpartum sepsis with eclampsia	Expired
M/21	Seizures, headache	190/120	Hypertension	Recovered
M/24	Seizures, headache and vomiting	180/110	Chronic renal failure (stage V), hypertension	Recovered
F/30	Hemiparesis, headache	170/110	Eclampsia	Recovered
M/32	Seizures, altered mental status, headache	160/110	Hypertension, acute febrile illness	Recovered
F/19	Seizures, headache	190/100	Eclampsia	Recovered
F/21	Seizures, altered mental status	190/120	IgA nephropathy/chronic renal failure, hypertension	Expired
M/32	Seizures, headache	190/100	Chronic renal failure (stage V), hypertension	Expired
M/28	Visual impairment altered sensorium	206/110	IgA nephropathy/chronic renal failure, hypertension	Recovered
F/30	Headache, altered sensorium	180/130	Chronic renal failure (stage V), hypertension	Recovered
F/32	Headache, altered mental status	200/110	Obstructive uropathy, chronic renal failure	Recovered
F/35	Seizures, headache	170/140	Hypertension with unilateral shrunken kidney	Recovered

headache (40%). These findings are comparable with other studies in literature.[1]

In a study by Pedraza et al., PRES was most commonly reported with hypertension, preeclampsia and eclampsia, and HELLP syndrome.[12] In the present series, the most common etiologies are underlying kidney disease and eclampsia and postpartum sepsis. In a recently published series from India, the commonest cause of PRES was eclampsia (36.4%). Other common causes were chronic kidney disease and hypertension (22.7% each).[5] Similar results were also shown in other studies.[2–4] In contrary, some studies have shown drugs-toxins and autoimmune disorders as more common underlying etiologies.[13–15] The difference in underlying etiologies of PRES is likely to be related to differences in patient profile of various centers.

In this study, the commonest site of involvement is the occipital-parietal lobe (66%) followed by the frontal lobe (46%) in neuroimaging. Comparable findings have been reported in literature.[1,15]

The Outcome of PRES is determined by the underlying etiology. Death has been reported in 15–19% of cases with PRES in the

Table 3: Predictors of outcome

Variables	*Survived*	*Expired*	*Chi-squre value*	*Likelihood ratio*	*p value*
Age	27.8 ± 9.8	29.3 ± 12.3	—	—	0.83
Female	13	5	1.95	2.14	0.16
SBP (at presentation)	158.3 ± 29.3	152.7 ± 30.1	—	—	0.27
DBP (at presentation)	100.0 ± 18.9	88.0 ± 19.4	—	—	0.21
Altered sensorium	14	3	0.07	0.07	0.79
Seizure	14	5	1.52	1.68	0.22
Focal deficit	3	1	0.09	0.09	0.76
CKD	5	3	2.27	2.07	0.13
Hypertension	14	2	0.99	1.01	0.32
Postpartum sepsis	5	2	0.49	0.46	0.48
Eclampsia	3	1	0.09	0.09	0.76
Autoimmune disorder	6	2	0.22	0.21	0.64

SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease

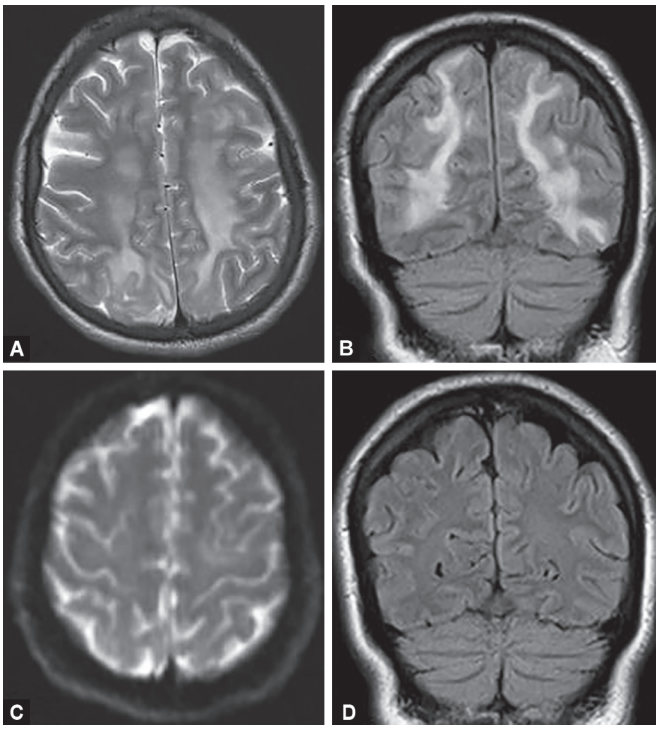
Table 4: Radiological findings of the patients

Lesion distributed	*Number*	*%*
Parieto-occipital lobes	20	66
Frontal lobe	14	46
Cerebellum	8	26
Temporal lobe	5	16
Corpus callosum	4	16
Brainstem	3	10
Thalamus	2	6
Basal ganglia	2	6
Infarct	2	6
Microhemorrhage	2	6
Internal capsule	1	3

literature.[16–19] In a recent retrospective study, 36% out of 100 PRES patients had poor neurological outcome at the time of hospital discharge.[20] Modified Rankin scale score between 2 and 6 was categorized as poor outcome. Singer et al. found 19% mortality rate in their cohort. In our series, mortality is 20%. All patients in the present study were admitted to a critical care setting. Comparatively high mortality in our series can be explained by underlying condition. Two out of six succumbed patients had associated postpartum sepsis and three had underling chronic kidney disease. There was no significant difference among demographic and clinical variables among patients with PRESS with and without survival. The cause may be the small sample size in the present study.

It is probably the largest cohort of PRES patients from the North India. Other strength of the study is the inclusion of the critically ill patients. It emphasizes the role of underlying etiology in outcome of the PRES.

This study has a few limitations. The major limitation is its retrospective nature. It shares all the limitations of a retrospective study. Single-center study is the other limitation. It may cause case selection bias. The transplant and chemotherapy patient population are under-represented in the present study. The present study lacks long-term follow-up of the PRES patients. Analysis by a single radiologist may also cause bias in the interpretation of the neuroimaging findings.



Figs 1A to D: (A) Hyperintense signal intensity in bilateral frontal and parietal regions in axial T2 weighted image; (B) Coronal FLAIR image showed deep white matter hyperintensities in bilateral parietal and occipital region; (C) Diffusion weighted image showed no evidence of diffusion restriction; (D) Follow-up FLAIR scan showed reversal of all abnormalities

Conclusion

Variability of clinical presentations makes the PRES a challenging condition. A high index of clinical suspicion is the key for timely diagnosis of PRES. Literature on outcome and mortality in PRES is scarce. In our study, acute hypertension, preeclampsia-eclampsia, and sepsis were associated with PRES as reported in the literature. The overall outcome for survival and functional independence is better in PRES compared to other neurological conditions.

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