Original Research Article

To study clinical and neuroimaging findings in posterior reversible encephalopathy syndrome (PRES)

M Manjusha[1], Veena Narisetty[2*], Sateesh Kumar Kamera[3], Dhairyawan Pokalkar[4]

[1]Post Graduate, [2]Associate Professor, [3]Assistant Professor, [4]Professor
Department of Neurology, Gandhi Medical College, Secunderabad, Telangana, India
[*]Corresponding author email: **Abilashissac@gmail.com**

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Abstract

Background: Posterior reversible encephalopathy syndrome (PRES) is a clinic-radiological syndrome comprising of seizures, disturbed vision, altered mental function and headache in various combinations developing over hours. The most common risk factor being abrupt or accelerated hypertension, renal failure, immunosuppressive therapy, eclampsia, autoimmune disease and infections. MRI Brain is the gold standard for diagnosis PRES generally has a favorable prognosis, but neurological sequale and even fatalities can occur in some cases.

Aim: The Aim of the study was to Review the clinical and neuroimaging findings in patients diagnosed with Posterior reversible encephalopathy syndrome (PRES).

Material and methods: This was a Prospective study done for duration of 2 years from December 2014 to November 2016 in the Department of Neurology, Gandhi Medical College, Hyderabad, Telangana, a tertiary care teaching hospital in south India. The study group patients were selected from pool of inpatients and out patients from various specialities and subspecialities as neurology, internal medicine, obstetrics and gynecology, pediatrics and nephrology.

Results: A total of 60 PRES patients included in the study. In the present study age group varied from 15 years to 65 years. Majority of cases 50% (30/60) were among 26-35 years age group. This was in accordance with majority of pregnant population in our series. Female to male ratio was 4:1. Highest incidence of cases i.e., 40% (24 /60) was with eclampsia, followed by autoimmune disease in 20% cases (12/60). 90% patients had predominant parieto-occipital hyper intense lesions on MRI.

Conclusion: In the present study the mean age of presentation was 32 years and higher prevalence (85 %) was seen in females. Eclampsia is the commonest cause of PRES. Majority of patients are hypertensive with mean BP being 182/112 mm hg while normotensive PRES seen in sepsis.

Key words

PRES, Eclampsia, Pre- eclmapsia.

Introduction

Posterior reversible encephalopathy syndrome (PRES) also known as reversible posterior leukoencephalopathy syndrome is a condition of acute cerebral dysfunction associated with the presence of vasogenic edema on brain imaging [1]. It is a neurotoxic state coupled with a variety of symptoms and signs and distinct MR imaging appearance [2]. Early Recognition of PRES has been facilitated with increasing availability of MRI. The cerebral white matter is composed of myelinated fiber tracts in a cellular matrix of glial cells, arterioles, and capillaries that makes this region susceptible to the accumulation of fluid in the extracellular spaces vasogenic edema [3].

PRES is caused by endothelial injury related to abrupt blood pressure changes or direct effects of cytokines on the endothelium .The mechanism is related to a hyper perfusion state, with blood–brain barrier breakthrough, extravasation of fluid containing blood or macromolecules, and resulting cortical or subcortical edema. Alternatively, vasospasm may precipitate the reversible edema, leading to cytotoxic edema if left untreated.

Common symptoms include headache, vision change, paresis, nausea, and altered mentation. Generalized seizures are common and may lead to coma. Moderate-to-severe hypertension is present in 70-80% of patients [4].

The typical MRI findings of PRES in the parieto occipital regions is due to sparse sympathetic innervation of posterior circulation making it susceptible. Along with hypertensities in parieto occipital regions, hyperintensities are found a lesser extent in the posterior frontal and temporal lobes, the corona radiata, the pons, the cerebellum, and other locations. The posterior circulation is particularly susceptible because of sparse sympathetic innervation [5]. Resulting in the typical predominant parieto occipital hyper intense lesions on MRI. These findings occur to a lesser degree in the posterior frontal and temporal lobes, the corona radiata, the pons, the cerebellum, and other locations.

Atypical imaging appearances include contrast enhancement, hemorrhage, and restricted diffusion and brainstem involvement on MRI. Several conditions that can present during pregnancy and postpartum, including eclampsia, acute strokes and systemic diseases associated with central nervous system vasculitis (suchas systemic lupus erythematosus), may mimic PRES. Pres can be mimicked by several other conditions occurring during pregnancy and postpartum states like eclampsia, stroke, autoimmune diseases causing cerebral vasculitis [6]. PRES is a misnomer because brain edema is often not isolated posteriorly and the syndrome is not uniformly reversible. The early recognition and treatment of this syndrome is important to prevent permanent neurological sequelae**.** The treatment is based on the management or withdrawal of the triggering factor **.**Atypical regionsof involvement and atypical findings are more common than generally perceivedand may not correlate with the edema severity. An early etiological diagnosis allows prompt correction of the cause of PRES. General measures have to be taken in the setting of complicated PRES such as in cases with seizures or status epilepticus in which airway management ensues, including invasive ventilation and hemodynamic monitoring are needed.

Aim

The Aim of the study was to Review the clinical and neuroimaging findings in patients diagnosed with Posterior reversible encephalopathy syndrome (PRES).

Materials and methods

A Prospective study was done for duration of 2 years i.e., from December 2014 to November 2016 in the Department of Neurology, Gandhi Medical College, Hyderabad, Telangana.

A total of 60 PRES patients included in the study. Patients were selected from pool of inpatients and outpatients from various specialities and subspecialities as neurology, internal medicine, obstetrics and gynecology, pediatrics and nephrology of Gandhi hospital. Ethical clearance and standard protocols for research of the Institute were followed, Ethical permission was taken from concerned institute. Informed consent was taken from all the patients.

Control population was derived from age, and sex matched normal healthy volunteers

Inclusion criteria

- Age groups 15 – 65 years.
- Both males and females were included
- All patients with clinical suspicion of PRES based on history, neurological examination and confirmed by imaging were included.

Exclusion criteria

- Age below 15 years.
- Cases lacking both clinical and imaging follow up were excluded.

Demographic data regarding age, gender, socio economic staus were obtained. Medical History regarding hypertension, diabetes mellitus, cardiac disease, CKD, sepsis, autoimmune diseases, coagulation state, cytotoxic medication and organ transplantation and pre eclampsia or eclampsia was taken in all patient. Detailed clinical history was taken included headache, vomiting, altered sensorium, visual blurring, seizures either generalized or focal and status epilepticus and clinical neurological examination including fundus exam was done in all patients.

Blood Pressure was measured at the time of presentation in all patients. If found to be hypertensive, regular monitoring with treatment including MAP was estimated. MAP=2/3 DBP +1/3 SBP. BP was graded at toxicity as 1) normal (MAP<105 mm Hg), 2) slightly elevated (MAP= 106-115 mm Hg), 3) significant hypertension (MAP>116 mm Hg). Routine biochemical tests like Complete Blood Picture (CBP), Blood sugar, BUN, Serum creatinine, Serum electrolytes, LFTs, Thyroid profile, C reactive protein were done. Further laboratory parameters, that is, Sr. creatinine, C - reactive protein (CRP), liver enzymes, and thrombocytes were acquired.

EEG is done in patients with seizures and in patients with.suspected non convulsive status epilepticus. EEG done in seizures or suspected non convulsive status epilepticus.

Neuroimaging studies were done using either CT or MRI or both in all cases. CT brain findings can be normal or nonspecific. Hypodensities in a suggestive topographic distribution that is posterior parieto occipital regions suggests PRES. MRI brain was done with a 1.5T Siemens scanner, T1, T2 with DWI and ADC, FLAIR sequences were done in all patients MRA, MRV, CTA were done in few suspicious cases.

All neuroimaging findings were reviewed by separately by a neurologist and radiologist.

Follow-up imaging and repeat MRI brain was done around 2 to 6 months in all patients to demonstrate resolution of edematous brain lesions and development of residual structural lesions. Treatment protocols followed for patients in emergency and inpatient department were recorded including mechanical ventilation and management of status epilepticus in ICU and

evaluation of associated organ failures and sepsis. Hypertension management and correction of metabolic disturbances were recorded. Recurrence of PRES was noted when present.

Statistical analysis done using the SPSS software (Statistical Package for Social Science, V 10.5 Package) and results were analyzed and compared with standard studies.

Results

This was a prospective study in which 60 patients of PRES were studied and analyzed.

In the present study, age group varied from 15 years to 65 years .Majority of cases i.e., 50% (30/60) were among 26-35 years age group .The mean age of presentation was 32 years. Next common age group were among 15-25 years i.e., 30% (18/60). 85% (48/60) of cases were females. M: F sex ratio was 1:4.

Among the various etiologies of PRES, Highest incidence of cases i.e., 40% (24 /60) were with eclampsia, followed by autoimmune disease in 20% cases (12/60), sepsis in 15% (9/60), pre-eclampsia in 10% cases (6/60), renal decompensation in 10% (6/60) cases and malignancy in 5% (3/60) cases.

In the present study 85% (51/60) cases presented with seizures, 70% (42/60) cases presented with headache, Blurring of vision in 60% (36/60) cases, nausea and vomiting in 40 %(24 /60) cases and altered sensorium in 20% (12/60) cases. Out of 51 cases who presented with seizures, 34 (66.7%) had generalized tonic clonic type, focal in 6 (11.5%) cases and 12 cases (23.5%) presented with status epilepticus to the emergency department.

Among 60 cases, 57 (95%) were hypertensive at the time of presentation and 3 (5%) had normotensive PRES. The median blood pressure was 182 mm Hg systolic and 112 mm hg diastolic.

90% patients had predominant parieto occipital hyper intense lesions on MRI, 60% had frontal lobe involvement, 50% temporal lobe, 40% cerebellum, basal ganglia in 18% and brain stem in 10% patients.

DWI was done in 42 cases out of which restriction was seen in 6 (10%) cases and iso or hypointense in the rest i.e., 36 (60%).

Lesions were symmetrical in 51(85%) cases, asymmetrical in 8 (13%) cases and unilateral in one case.

MRA revealed vasoconstriction in 3 cases (5%), distal pruning in 2 cases (3.2%) and focal cerebral artery stenosis in 1 case (1.6%). It was unremarkable in 9 cases (15%).

Complications included intracranial hemorrhage in 2 cases (3.3%), infarction in 2 cases (3.3%), fetal demise loss in 6 cases (10%),

Death of 4 cases (6.6%) and Recurrence in 3 cases (5%).

Mean time for resolution was around 6 months in 75 to 80% cases. Residual lesions after 1 year seen in 5 cases out of which 2 had infarction and 2 had intracranial hemorrhage.

Discussion

In the present study mean age of occurrence was 32 years with highest incidence (50%) in 26 to 35 years age group. This is the potential child bearing age group in India where there is a high incidence of pre-eclampsia/ eclampsia .This is on par with a study done by Liman, et al. [7] where the median age was 31 years in PRES with pre-eclampsia/eclampsia and 42 yrs was the median age in patients with other comorbidities.

In the present study Out of 60 patients studied, 48 patients (80%) were females and 12 (20%) were males. This is in accordance with the Bartynski, et al. [2] study that report higher incidence in females. In our study the

commonest association was seen in pregnancy and postpartum period.

Most common comorbidities in our study were eclampsiain (40%) followed by autoimmune disease in (20%), and sepsis (15%), preeclampsia (10%), renal decompensation (10%), and malignancy (5%). Study by Hinchey, et al. [1] showed highest incidence in cytotoxic/chemotherapy, bone marrow or organ transplantation, renal failure, pre-eclampsia/ eclampsia, autoimmune diseases and sepsis. This difference could be due to the fact that more patients in developing India are admitted in government hospital like ours with complicated pregnancies, renal decompensation and autoimmune diseases referred from other primary health centers. Our hospital is a tertiary care referral center and a teaching institute hence, patients with complicated pregnancies, renal decompensation and autoimmune diseases get referred from other primary and secondary health centers.

12 patients (20 %) had auto immune disease, 6 patients had SLE, 2 had systemic sclerosis, 2 patients had hashimoto thyroiditis, and one patient had takayasu arteritis and another had crohns disease in each. Bartynski, et al. [2] reported in his study that 11 – 16% patients on cytotoxic drugs, hypertension in 60 – 72 %, sepsis in 8 – 24 %, pre – eclampsia/ eclampsia in 7 – 20%, auto immune diseases in 8 – 10%. In a study by Bartynski, et al. [2] infections /sepsis were present in 16% to 24% cases. Sepsis in our study was seen in 9 patients (15%).

In our study we had 2 patients with PRES and GBS. A first case was reported by Del Giudice and Aicardi [8], a child presented with a hypertensive encephalopathy and GBS.

In our study the most common cause of hypertension is pre-eclampsia/ eclampsia followed by autoimmune disease. Similar to this acute hypertension was seen in 80% in the study by Hinchey, et al. [1] and 67% in Bartynski, et al. [2] who studied 136 patients, hypertension has been reported in most studies (67 to 80%).

Seizures is the most common manifestation of PRES in our patients seen in 85% cases followed by headache in 70% patients. Seizures were GTCS in 34 out of 51 patients, focal in 6 patients. 11 patients presented with status epilepticus out of which 5 patients needed intubation. In a study by Lee, et al. [5] seizures were seen in 92% patients they occurred in 70% patients. Status epilepticus was described in 5% to 10% in their series. In the study by Koul R, et al. [10] non convulsive status epilepticus was more common than generalized convulsive status.

Headache was seen in 70% in our study ranging from mild to severe throbbing headache. In study by Hinchey, et al. [1] Headaches and nausea/vomiting were reported in 26 % (11) to 53% (3) of patients.

In a study by MC Kinney, et al. [8] myelopathic symptoms and signs caused by spinal cord involvement were documented. This is a rare finding not seen in our study. In our study, 54 patients had parieto occipital hyper intensities, 36 patients frontal lobe involvement, 30 patients had temporal lobe involvement, 24 had cerebellar hyper intensities, 18 patients with basal ganglia involvement and 6 patients had brainstem hyper intensities. This order of involvement is in accordance with the study by Hinchey, et al. [1].

In our study restricted diffusion on MRI was seen in 6 cases which correlated with irreversible infarctions in 3 patients only. In a study by Bartynski, et al. [1] restricted diffusion can be seen on MRI in 15–30% of cases.

In our study intraparenchymal hemorrhage was seen in 2 patients out of which one patient was on warfarin for atrial fibrillation. In a study by Hefzy, et al. [10] intracranial hemorrhage in PRES occurs in 15 to 20% cases. McKinney, et al. [11] higher rates of hemorrhage was reported. In a study by Cruz, et al. [12] ICH occurred in

31% patients most of them on oral anticoagulant therapy. In the study by Fugate[4] a high rate of microhaemorrhages (18 [58%] of 31 patients) has been found using susceptibility-weighted imaging, but the clinical significance of these micro hemorrhages is uncertain.

Death occurred in 4 patients in our study. 1 with underlying malignancy, two with sepsis and 1 with auto immune disease. No deaths occurred in PRES with pre-eclampsia/ eclampsia. In the study by Legriel, et al. [13] substantial mortality in 11 (16%) patients and pronounced disability in 26 (37%) patients with PRES in the intensive care unit; hyperglycemia and longer time to causative-factor control predicted poor outcome.

Fetal loss demise occurred in 6 patients with underlying eclampsia. 4 patients presented with status epilepticus which was uncontrolled needing intubation and anesthetic management. MRI in these patients revealed central PRES that is brain stem involvement in 1 patient and asymmetrical pattern in 1 patient.

Recurrence of PRES in our study was seen in 3 patients, two had autoimmune disease and 1 had renal decompensation. There was no recurrence in other groups. Roth and Ferbert [14] have found recurrence in 8% of 25 patients after complete recovery from their first episode, followed prospectively over a mean follow-up of 4.5 years.

Strength of this study is that it is a prospective study with 6 months follow up whereas most of the previous published studies are retrospective. In India there are only few case reports and case series no major studies and publications. Hence this study serves as a baseline for future work and research in this area.

Limitation of this study is that true etiology of PRES is not known as we don't have a well-established oncology and transplantation center in our hospital.

It overemphasizes pre-eclampsia/eclampsia in the etiopathogenesis and work up.

We don't have much data regarding PRES in cancer, chemotherapy and transplantations.

Conclusion

In the present study highest incidence of PRES is seen in 26-35 years, and higher prevalence (85%) seen in females. Eclampsia is the commonest cause of PRES. Patients presents with seizures predominantly GTCS, headache, visual blurring, nausea and vomiting and encephalopathy.

Majority of patients are hypertensive with mean BP being 182/112 mm hg. MRI shows predominant parieto-occipetal with brainstem involvement in non-eclampsia patients with isointense on DWI. Hemorrhage, infarction, death and fetal demise were common complications.

References

1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior Leuko-encephalopathy syndrome. N Engl Med., 1996; 334: 494–500.
2. Bartynski WS. Posterior reversible encephalopathy syndrome, part 1: fundamental Imaging and clinical features. AJNR Am J Neuroradiology, 2008; 1036–1042.
3. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding patho-physiology of vasogenic edema. AJNR Am J Neuroradiology, 2008; 29: 1043–1049.
4. Jennifer E Fugate, Alejandro A Rabinstein, et al. Posterior reversible encephalopathy syndrome clinical and radiological manifestations and pathophysiology. Lancet Neurol., 2015; 1-12.
5. Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. Clinical spectrum of

reversible posterior leukoencephalopathy syndrome. Arch Neurol., 2008; 65: 205–2108.

6. Marik PE, Varon J. Hypertensive crises: challenges and management. Chest, 2007; 131: 1949-62.
7. Liman ER, Zhang YV, Montell C. Peripheral coding of taste. Neuron, 2014 Mar 5; 81(5): 984-1000.
8. Del Guidice E, Aicardi J. Atypical aspects of hypertensive encephalopathy in childhood. Neuropädiatrie, 1979; 10: 150–157.
9. Koul R, Razdan S, Motta A. Prevalence and pattern of epilepsy in rural Kashmir, India. Epilepsia, 1988; 29: 116–22.
10. H.M. Hefzy, W.S. Bartynski, J.F. Boardman and D. Lacomis. Hemorrhage in Posterior Reversible Encephalopathy Syndrome: Imaging and Clinical Features. American Journal of Neuroradiology, August 2009; 30(7): 1371-1379.
11. McKinney AM, Short J, Truwit CL, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. AJR Am J Roentgenol., 2007; 189: 904–12.
12. Cruz RJ Jr, DiMartini A, Akhavanheidari M, et al. Posterior reversible encephalopathy syndrome in liver transplant patients: clinical presentation, risk factors and initial management. Am J Transplant., 2012; 12: 2228–2236.
13. Legriel S, Schraub O, Azoulay E. Critically III Posterior Reversible Encephalopathy Syndrome Study Group (CYPRESS). Determinants of recovery from severe posterior reversible encephalopathy syndrome. PLoS One, 2012; 7: e44534.
14. Roth, C, Ferbert, A. Posterior reversible encephalopathy syndrome: long-term follow-up. J Neurol Neurosurg Psychiatry, 2010; 81: 773–777.