ORIGINAL ARTICLE

Clinicoradiological Profile and Outcome of Patients with Posterior Reversible Encephalopathy Syndrome

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Abstract

Background: Posterior Reversible Encephalopathy Syndrome (PRES) is a potentially reversible neurologic illness presents with abrupt onset of symptoms of headache, seizures, visual blurring and occasionally altered mentation.

Aims and Objectives: To study Demographic profile, Clinicoradological features, Etiology and Prognosis of patients admitted with a diagnosis of PRES in the department of Neurology at a Tertiary Health care centre in Eastern India.

Materials and Methods: A retrospective-prospective, observational, Non-interventional study. 24 patients admitted in the department of Neuromedicine satisfying the diagnostic criteria of PRES were included in the study during the study period July 2014-June 2017.

Results: Out of 24 patients,19 (79.1%) were females and 5(20.8%) were male. Mean age for females was 28.5 years/S.D of ±13.5.and for males were 42.28 years/S.D± 8.5. Overall mean age was 35.26 (SD±18.34). It was more common in females (Relative risk of 3.8: Odds Ratio: 9.7, p<0.001). Most common symptom was headache in 83.3%. Vomiting (77%), seizures (75%), Cortical Blindness (45.8%) and Altered sensorium (20.88%). In patients having seizures most of them were recurrent (62.12%) and 18.9% had status epilepticus.

Most common precipitating cause was postpartum state (37.5%), Accelerated Hypertension (20.8%), chronic renal failure (16.6%), Pregnancy (12.5%) and chemotherapeutic agents (8.33%). More than 60% of postpartum and pregnant patients had normal blood pressure recordings. MRI scan showed parietoccipital involvement most commonly (62.5%), followed by diffuse involvement (33%), Asymmetric brain involvement (16.6%), Basal ganglia/thalamus and cerebellar involvement in 12.5% each. Haemorrhage and infarcts were seen rarely. Most of the patients improved with no residual imaging findings or neurological deficits.

Conclusion: Early diagnosis with appropriate Imaging is very important to achieve good Neurological outcomes. Post Partum and pregnant patients with PRES may have normal blood pressure measurements.

Introduction

Posterior Reversible Encephalopathy Syndrome (PRES) or Reversible posterior leukoencephalopathy syndrome (RPLS) is a clinical radiographic syndrome of heterogeneous etiologies that are considered together because of similar findings on neuroimaging studies and identical set of clinical features.

As this entity was more studied in details it was found that the syndrome is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain. It is often—but not means always—associated with acute hypertension.[1,2] If promptly recognized and treated, the clinical syndrome usually resolves within a week,[2,3] and the changes seen in magnetic resonance imaging (MRI) resolve over days to weeks.[2–4]

PRES is sporadic and its incidence is unknown but it has been reported worldwide without any gender differences,[5] both children and older people can be affected.[6]

The pathophysiology of PRES is poorly understood. There are several theories.

Breakdown of cerebral autoregulation due to a rapid rise in blood pressure leading to disruption of the blood–brain barrier is the most popular one.[3,10] A second mechanism is endothelial dysfunction due to circulating toxins which is more relevant for triggers such as immunosuppressive therapy, sepsis, autoimmune disease and pre-eclampsia, which all may affect the blood–brain barrier and lead to subsequent vasogenic edema.[11,12] Inherent deficiency of adrenergic innervation which controls cerebral autoregulation in the posterior circulation is the reason behind the posterior prelidiction of Vasogenic edema.

PRES is a syndrome with visual loss, headache, altered mental function, seizures and nausea. The symptoms usually develop quite quickly over a few hours, reaching their worst in 12–48 h. Seizures are the most frequent, in up to 90% of cases and often preceding any of the other manifestations.[5,7,8] Brain CT only shows lesions in PRES in about 50% of cases and brain MRI is not always performed—hence the diagnosis can easily be overlooked unless other symptoms are recognised.

There have been many publications, mostly case reports and imaging studies. Only a few publications have been concerned with the clinical features. In India there has been only one large study looking at the clinical and radiological profile of PRES patients by Patil et al.[9] There are no studies so far from Eastern Part of

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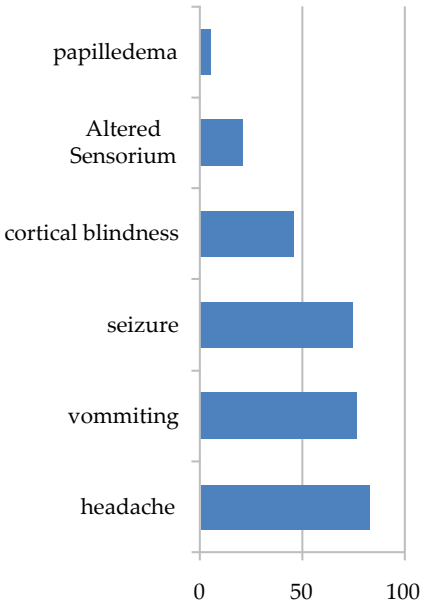

Fig. 1: Percentage of common signs and symptoms of PRES patients

India on PRES. Hence a need for further study into the clinical and radiological picture of PRES was seen and so this study was done.

Aims and Objectives

To study demographic, etiological, and clinic-radiological profile of patients presenting with PRES and their outcome at a tertiary care hospital in Eastern India.

Material and Methods

A retrospective observational and non-interventional study was conducted at a tertiary care Hospital in Durgapur, West Bengal. Patients with diagnosis of PRES admitted in the department of Neurology during the year July 2014 to June 2017 were included in this study. Patient's data were collected from medical records which included patient demographics, Clinical features, blood pressure values, comorbidities, drug history, laboratory investigations and neuroimaging details.

Diagnostic Criteria

The presence of all 3 of the following criteria were mandatory for inclusion: (1) clinical history of acute neurologic change including headache, encephalopathy, seizure, visual disturbance, or focal deficit; (2) brain imaging findings of focal vasogenic edema; and (3) clinical or radiologic proof of reversibility. Hypertension was defined as a systolic blood pressure of 140 mm Hg or greater or a diastolic blood pressure of 90 mm Hg or greater.

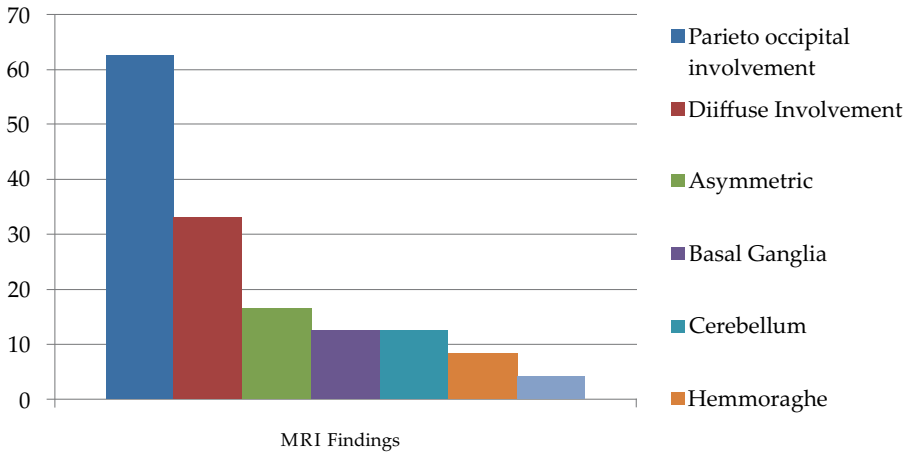

Fig. 2: Distribution of involvement of in MRI brain

The case records were carefully studied and the clinical features at presentation, comorbidities, demographics, neuroimaging findings and other laboratory parameters were collected. The etiology of the PRES was taken as diagnosed by Neurologist.

Exclusion Criteria

Cases lacking both clinical and imaging findings favouring PRES with an alternative diagnosis were excluded from the study.

MRI Brain imaging Standard sequences was unenhanced FLAIR and T1- and T2-weighted images in all patients, with diffusion-weighted imaging in all patients. Contrast Imaging was done in which pathologies like acute disseminated encephalomyelitis or meningoencephalitis was suspected.

Magnetic Resonance Venography was done in suspected patients to rule our cortical or deep venous thrombosis.

Few of patients had a CT Brain done in emergency department or from outside Referring hospitals.

The patient's improvement of symptoms and signs were obtained from case records. Repeat MRI was done in most of the patients to assess the reversibility of lesions. In patients with financial issues in repeating the study total clinical resolution was taken as a marker of reversibility. However patients who had persistent neurodeficits with no follow up imaging were excluded from the study.

Statistical analysis was done by computer software SPSS-11, trial version. Categorical data were analyzed by mean, standard deviation (S.D.), percentage and Chi-square test. The level of significance was set at '*P*' < 0.05, and 95% confidence interval (CI) was used throughout.

Results

Demographic

Out of 24 patients studied 19(79.1%) were females and 5(20.8%) were male. In the female population mean age was 28.5 years and S.D of ± 13.5. In the male population the mean age was 42.28 years and S.D ± 8.5.Overall mean age was 35.26 (SD ± 18.34). It was more common in the female population (Relative risk of 3.8: Odds Ratio: 9.7, p<0.001)

Most common age group involved was 20-30 years (58.3%).

Clinical Features

Most common symptom was headache in 83.3%. Vomiting (77%), seizures (75%), Cortical Blindness (45.8%), altered sensorium (20.88%) and papilledema in (5.5%).

Seizures were generalised tonic clonic seizures in all patients. In patients having seizures most of them were recurrent (62.12%) and 18.9% had status epilepticus.

Precipitating Cause

Most common precipitating cause was post partum state (37.5%). Out of which 81.81% was after 1 week of delivery. Accelerated Hypertension (20.8%), Chronic renal failure with hypertension (16.6%), Pregnancy (12.5%), Immunosuppressive agents (8.33%) and acute renal failure (4%). In the pregnancy group all the cases

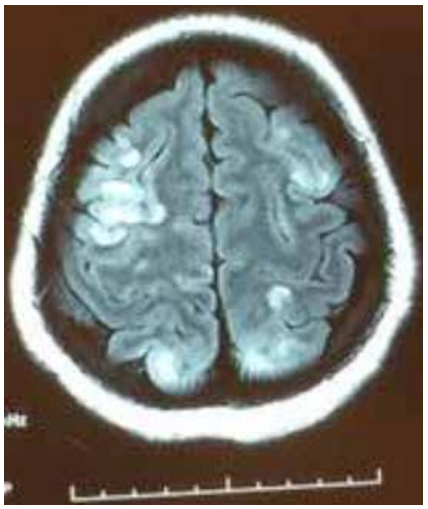

Fig. 3: T2 Flair Axial MRI Image showing diffuse involvement of cortex

were in the 2nd trimester. In the Post partum and pregnancy group blood pressure was normal in 63.6%.The Immunosuppressive agent implicated was Tacrolimus in one patient with history of renal transplant one year back. Other patient was on Mycophenolate for idiopathic thrombocytopenic purpura

Symptoms & Signs

Neuroimaging

CT Scan was done in 62.5% of the patients, out of which 80% had normal CT scan which on MRI Imaging showed features of PRES. MRI Showed Parieto-occipital involvement in 62.5%,33% had diffuse involvement, Asymmetric involvement of brain was seen in 16.6%, basal ganglia and cerebellum involvement was seen in 12.5% each. Hemmoraghe was seen in 8.33%. One patient had subarachnoid bleed and one was small frontal parenchymal bleed. Infarct was seen in one patient (4.16%). The infarct was internal posterior watershed infarcts.

Prognosis on follow up and outcome

Overall outcome was good. Headache resolved in 3-4 days. Vision improved in 95% of the patients in 1 week. Patients with bleed and infarct had residual neurological deficits.

Follow up MRI Could be done in 10 patients after 6 weeks and in 80% the findings had resolved after 6 weeks.1 patients had persistent occipital edema with visual field defect. The patient with infarct had residual spasticity and brisk reflexes with mild cognitive impairment at 6 week follow up.

There was no mortality in our study group .One patient with chronic kidney disease and accelerated hypertension had Recurrence of PRES after one year and presented with seizures and fresh parietoccipital edema.

Discussion

After Hinchey et al[3] initial description[1] in 1996, both its clinical spectrum and underlying pathophysiology remain poorly defined. A clinical diagnosis of PRES includes the presence of headache, seizures, encephalopathy, and visual disturbances, as well as radiologic findings of focal reversible vasogenic edema, best seen on magnetic resonance imaging (MRI) of the brain.

PRES is characterized by headache, seizures, confusion, and visual disturbance. Other focal neurologic deficits are uncommon. Seizures, which might begin focally, are usually generalized tonic-clonic and often multiple. It may be associated with visual loss and hallucinations to suggest occipital lobe onset. Visual abnormalities include cortical blindness field defects like hemianopia, visual neglect, and blurred vision.

The name of PRES may be considered as a misnomer as radiographic lesions in PRES are rarely isolated to the "posterior" parieto-occipital white matter and usually can the cortex, frontal lobes, basal ganglia, and brainstem.[13,14] No clear cut evidence is there showing a clear relationship between clinical patterns and specific imaging findings of extent or location of edema[15] however some studies have suggested more of vasogenic edema in patients with normal blood pressure and more cerebellar and basal ganglia involvement in Pregnancy related cases having high blood pressure.

Abrupt hypertension is seen to be a major mechanism of PRES in substantial number of cases, and hyper perfusion is further validated with the fact that with the adequate control of blood pressure, the clinical signs and symptoms and radiological findings reverse. However, this theory is not fully comprehensive because PRES may affect normotensive patients[26] and does not occur uniformly and predictively in patients with hypertensive surges above the normal upper limits of cerebral auto regulation.

The differential diagnosis to be considered are posterior circulation stroke, encephalitis, reversible cerebral vasoconstriction syndrome (RCVS), cerebral venous thrombosis, arterial dissection and primary CNS vasculitis.

MR Venography and MR Angiography should be done to rule out venous thrombosis and RCVS or Arterial dissection.

In posterior circulation stroke altered sensorium, focal defcitis, visual loss and high blood pressure may be seen. However seizures would be rare and Diffusion restriction in MRI scans would be seen in posterior circulation stroke. The calcarine and paramedian occipital lobe structures are usually spared in posterior leukoencephalopathy syndrome, the differentiation is crucial as aggressive blood pressure control is desirable in PRES, in contrast to the management recommendations for acute stroke, which permit mild to moderate hypertension.

More than 70% of patients with PRES are hypertensive, though a significant proportion has normal or only mildly raised blood pressure.[3,4]

Our study was planned mainly to study the Clinicoradiological profile of patients with PRES and the outcome of these patients. The clinical spectrum of findings and the etiological causes were similar to most of the studies conducted in India and worldwide.[5-9,17,18]

The important differences were Pregnancy and postpartum states were the most important etiological factor (37.5%). In this group of patients one noteworthy point was that more than 60% of the patients had normal or minimally raised blood pressure values. Most of the studies showed blood pressure to be elevated in this group of patients (50-60%).[9,19]

PRES was most common in postpartum period after 1 week in our series. It is in contrast to other Indian study which showed it to be common in the antenatal period.[19] Mean age of pregnant and postpartum females were 28.5 yrs and 90% of them were primigravida.

Our study as in contrast to few large studies[16] did not show high prevalence of autoimmune disorders in patients with PRES.

Radiological findings when compared to other studies,[7,9,20] all

showed a similar pattern of involvement. However the important difference was lack of brain stem involvement in our study and comparatively less cerebellar involvement. The lack of autoimmune disorders in our study population could be one reason for this finding as it is more seen with such disorders. CT scan was normal in 80% of the cases in the initial presentation thus pointing that PRES cases would be missed if we rely on Normal CT scans in ruling out a diagnosis of PRES.

Outcome of patients with PRES was excellent. There was no mortality in our series.

The Limitation of our study was follow up imaging could not be performed in all the patients due to financial constraints. Seriously ill patients with underlying Sepsis, multiorgan dysfunction and autoimmune disorders were not there in the study group. Treatment of PRES, the types of antiepileptic drugs used and its duration have not been studied.

Conclusion

This study highlights that PRES is reversible mostly, if diagnosed early with high clinical suspicion and appropriate investigations. Atypical imaging patterns are quite common and should be kept in mind before excluding PRES. Usually there are no residual neurological deficits. PRES should be always considered in pregnant and postpartum patients even with normal blood pressure.

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