Original Research Article

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A Study of the Clinical Spectrum of Posterior Reversible Encephalopathy Syndrome

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Abstract

Aim: To study the etiological, clinical and radiological profile of patients diagnosed to have PRES *Methodology:* A descriptive study done by analyzing the medical records of patients diagnosed to having PRES this study was done in a tertiary care medical college hospital between jan 2012 to jan 2014 over a period of 2 years. The study population was the patients who were admitted with the clinical features of suggestive of PRES. The clinical data, etiological and radiological features of these patients were collected for the study purpose. *Results:* There is a varied etiology of PRES ranging from the commonest Pregnancy related PRES to the rare causes such as SLE, porphyria, OPC poisoning and a case of PRES following a blunt injury abdomen. Females in the age group 20 – 40 were commonly affected. Head ache and seizures were the commonest clinical presentation of PRES. Documented hypertension was noted on 50% of the patients in our study. Vasogenic odema involving both the occipital and parietal lobe was the commonest radiological presentation. All the symptoms and signs were completely reversible following prompt and appropriate treatment. *Conclusion:* The commonest cause of PRES is PIH. The other causes include any clinical condition causing an abrupt raise in BP or drugs causing endothelial damage. High index of suspicion to PRES is essential for the early diagnosis. It is a reversible condition if diagnosed and treated early.

Keywords: PRES; Pregnancy Induced Hypertension [PIH]; Varied Etiology; Vasogenic Edema; Headache; Seizures; Papilloedema; Early Diagnosis; Reversible.

Introduction

After evaluating 15 patients from 1988 to 1994, Hinchely and co-workers reported their findings in New England journal of medicine (1996) - a clinical and radiological entity in which the patients presented with sudden onset of head ache, altered sensorium, visual abnormalities and seizures and a vasogenic edema in neuroimaging involving posterior circulation. He called this Reversible Posterior Leukoencephalopathy Syndrome which was later renamed as Posterior reversible encephalopathy syndrome (PRES).

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PRES is a syndrome in which abrupt raise in blood pressure or use of certain drugs or sepsis leads to the sudden onset of head ache, altered sensorium, visual abnormalities and seizures.

These symptoms occur in varying combinations or sometimes in isolation. Having a high index of suspicion often helps to diagnose this syndrome, whenever a clinical setting that can predispose to PRES exists.

Cases of PRES are reported from the age 4 to 90 yrs, however most cases occur in the young and the middle age group [1,3]. There is a high female preponderance for Posterior Reversible Encephalopathy Syndrome as the cause of the disease is often pre eclampsia or eclampsia. Other common co morbidities are renal failure, systemic hypertension presenting as accelerated hypertension, bone marrow transplantation and solid organ transplantation [1,3].

The exact Pathophysiology of Posterior Reversible Encephalopathy Syndrome is still undetermined it is postulated the raise in blood pressure causes vasodilatation, hyperperfusion, blood-brain-barrier

breach and extravasation of intravascular fluid in to the interstitium leading to vasogenic cerebral edema and Posterior Reversible Encephalopathy Syndrome.

PRES: Pathophysiology in patient without hypertension

The First description of this disease entity– Posterior Reversible Encephalopathy Syndrome in 1996 was in a patient being treated with cyclosporine. The drugs implicated in causing pres are mainly the immunosuppressant drugs- like cyclosporine, cisplatin, oxaliplatin, Tacrolimus. Several other drugs like α- interferons and erythropoietin, cytarabine, methotrexate, rituximab, linezolide, high dose corticosteroid therapy etc. are also implicated in causing Posterior Reversible Encephalopathy Syndrome [2].

The Mechanisms by which these drugs cause Posterior Reversible Encephalopathy Syndrome is multi factorial. They either causes drug induced hypertension and or endothelial damage.

PRES and Sepsis – Pathophysiology

Sepsis causes Posterior Reversible Encephalopathy Syndrome by two mechanisms–endothelial dysfunction and microcirculation abnormality. Also infections like retro-viral infection (HIV) per se can precipitate Posterior Reversible Encephalopathy Syndrome, even when sepsis or septic shock has not occurred.

The Radiologic Features of PRES

Vasogenic edema is the classical feature of Posterior Reversible Encephalopathy Syndrome. It commonly presents with bilateral symmetrical vasogenic edema typically involving the sub-cortical white matter, predominantly in the bilateral parietal occipital lobes – this is called the dominant parieto occipital pattern. Diffusion – weighted images (DWI) show typically in iso dense or hypo intense lesions with hyper intensity in ADC due to increase in apparent diffusion coefficient for water, indicative of vasogenic brain edema.

PRES and Its Complication – Pathophysiology

Cerebral infarction, hemorrhage and brain stem herniation are the irreversible complication of Posterior Reversible Encephalopathy Syndrome.

Treatment of PRES

Underlying cause correction-

Etiological diagnosis of pres should be identified early to allow prompt correction of the cause precipitating PRES. Blood pressure reduction, withdrawal of offending drug, termination of pregnancy – cesarean section, dialysis etc., may be required. Prompt treatment of the cause prevents irreversible complications or death.

Aim

To analyse and study the etiological, clinical and radiological profile of patients diagnosed to have PRES.

Materials & Methods

After obtaining ethical committee approval this descriptive study was done in Government Stanley Medical college Hospital between January 2012 and January 2014 and the study population were the patients who presented with clinical features of PRES.

Inclusion Criteria

- Patients having clinical and radiological features consistent with Posterior Reversible Encephalopathy Syndrome.

Exclusion Criteria

- Subcortical white matter lesions other than Posterior Reversible Encephalopathy Syndrome:
- Infection– Progressive Multifocal Leucoencephalopathy.
- Vasacular – Posterior Circulation Stroke/ Superior Sagittal Sinus Thrombosis.
- Neoplasms –Gliomatosiscerebri, Lymphoma, Glioma.
- Demyelination- Acute disseminated encephalomyelitis, Multiple Sclerosis.
- Dysmyelination- Leucodystrophies like Metachromatic leucodystrophy.
- Metabolic- severe hypoglycemia, hypotension.

Consent from the patients to participate in the study was taken. Demographic particulars of the patients were noted. The presenting clinical features of the patients were noted carefully. For all the patients MRI brain imaging was done for all the patients and the radiological presentation was recorded. The etiology of each of the patients diagnosed with PRES was carefully identified and recorded. The treatment ensued and the outcome following treatment was

documented.If any persistent neurological deficit occurred the same was noted.

Statistics

Using Microsoft office excel 2010 data entry was done and the recorded data was analyzed using IBM SPSS 16.0 software.

Results

Females are predominantly affected with F: M ratio = 7:1.

The commonest age group affected in this study is 22 – 39 years.

Headache is the commonest symptom of Posterior Reversible Encephalopathy Syndrome in this study Fig. 1.

Duration of headache ranged from ≤ 1 day up to 14 days, at the time of presentation to the hospital.

The commonest etiology of Posterior Reversible Encephalopathy Syndrome is pregnancy induced hypertension (Fig. 2). 18 patients (58.06%) out of the 31 cases in this study were pregnancy related. All these patients were primigravida except one. Amongst the 18 patients 8 had antepartum eclampsia, 6 had preeclampsia and 4 had postpartum eclampsia.

In the non pregnancy related Posterior Reversible Encephalopathy Syndrome primary hypertension is the commonest cause (16.12% of the cases). The other causes, non pregnancy associated cases were primary

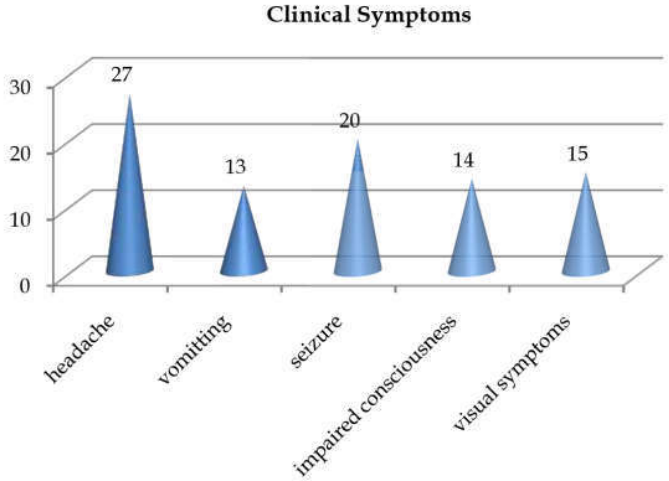

Fig. 1: Presenting symptoms of PRES – headache and seizures were the commonest presenting symptoms in this study

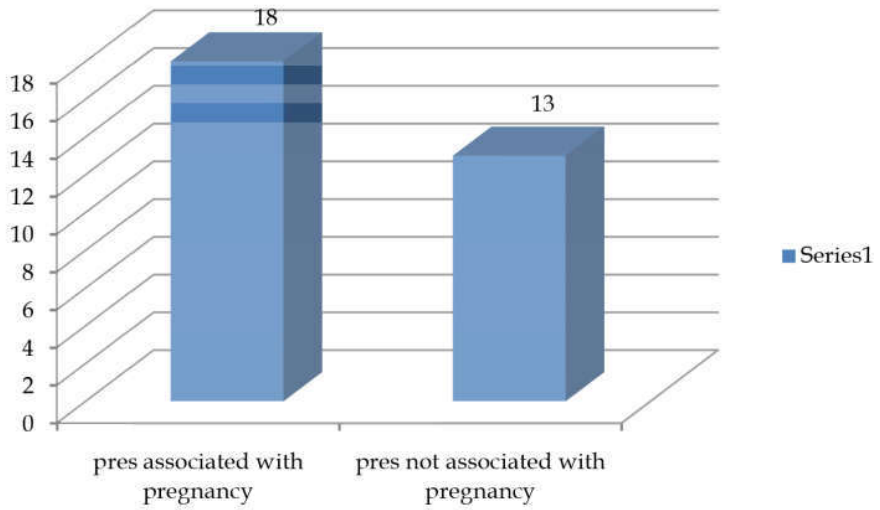

Fig. 2: Distribution of Pregnancy related PRES vs Non Pregnancy related PRES

hypertension in 6 of the 31 cases (16.12% of patients). Others were SLE, PIGN, PAN, ESRD on hemodialysis, OPC poisoning with toxic neuropathy and dysautonomia, porphyria with SIADH and systemic hypertension and Takayasu's arteritis, with Posterior Reversible Encephalopathy Syndrome. All the above aetiology was present in 1 case each (3.225% each) out of the 31 patients.

Hypertension was documented in 21 (67.74%) out of the 31 patients. The range of hypertension varied from 130/96 to as high as 210/140 mmHg (Fig. 3).

With the control of blood pressure symptoms resolved promptly. One of the patient with bilateral cortical blindness regained normal vision within 4 hours after blood pressure control.

On examination papillodema was seen in 7 patients (22.58%) of the patients out of the 31 cases.

The commonest lobes involved was occipital (77.4%) followed by parietal (67.74%), followed by temporal (48.38%), further followed by frontal (19.35%) and other areas including brain stem (6.45%). (Fig. 4).

Vasogenic edema, the prime radiological finding of Posterior Reversible Encephalopathy Syndrome was seen in all the patients in this study.

Symmetrical lesions were found in 21 out of the 31 patients (67.74%). 10 patients had asymmetrical lesions (32.25%).

All had subcortical white matter changes. 48.38% of the patients had both subcortical and cortical involvement.

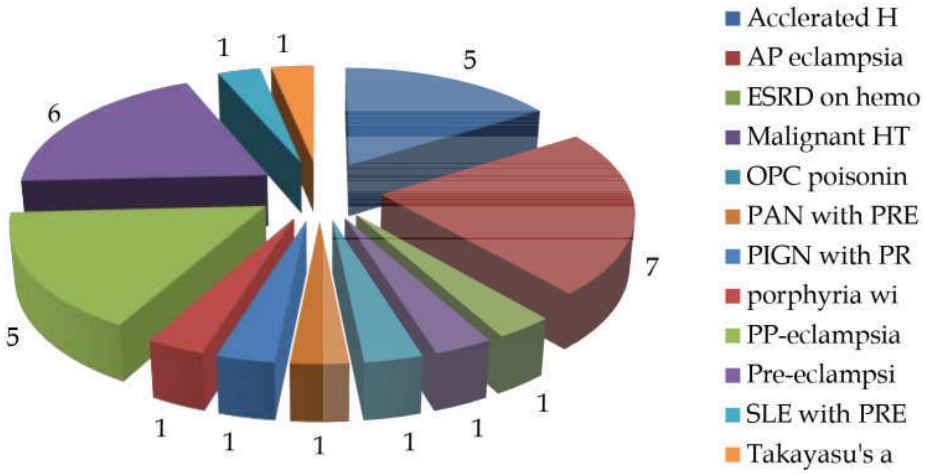

Fig. 3: Distribution of etiologies of PRES in this study

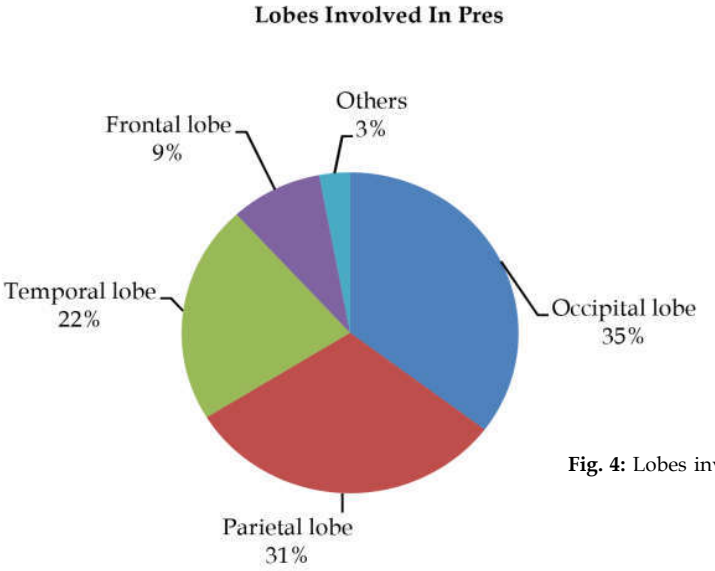

Fig. 4: Lobes involved in PRES

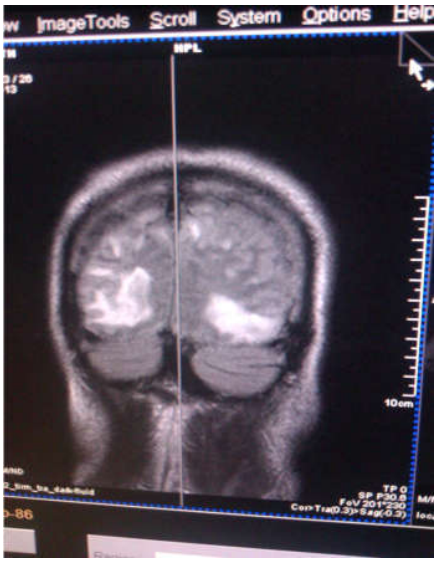

Fig. 5: MRI Brain T2 FLAIR coronal showing bilateral parieto-occipital hyperintensities in a case of PRES

Diffusion restriction was seen in 12.9% of the patients.

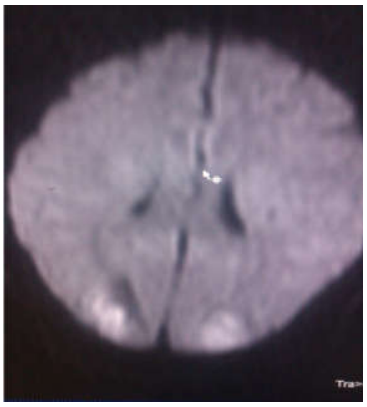

Fig. 6: DWI Brain showing diffusion bright lesion in the bilateral occipital regions –complication of PRES

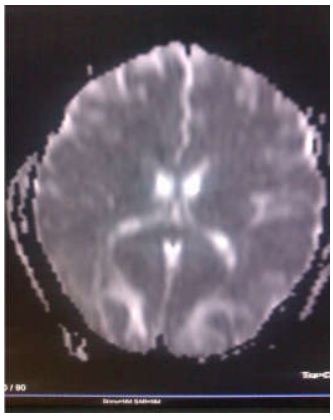

Fig. 7: ADC Brain showing hypointense lesions in the corresponding bilateral occipital region-complication of PRES.

In most of the cases the symptoms were reversible. However irreversible complication (visual defects) was seen in 2 (6%) of the patients. 1 patient died due to worsening of the primary illness.

Discussion

Posterior Reversible Encephalopathy Syndrome is common in females as most of the cases are pregnancy related. In this study also there was a marked female preponderance with 87% of the patients being females and only 13% being males. Posterior Reversible Encephalopathy Syndrome commonly affects young and middle age individuals, the mean age – 39 years to 47years in various studies [1,2,3]. In this study Posterior Reversible Encephalopathy Syndrome was common in the ages 20 – 39 years with the mean of 26.34 years. This finding is consistent with the feature that this disease entity is common in the young and middle age group [1,4]. Also in a case study from India – case series of 20 patients by Praveen Kumar et al. [13], with Posterior Reversible Encephalopathy Syndrome 60 % of the patients were in the age group 20 – 30 years, a finding almost similar to our study. Posterior Reversible Encephalopathy Syndrome has been reported in 4 years old up to 90 years old [1,4].

Hinchey reported that the youngest patient in their case series was 15 years and the oldest was 62 years. In our case study the youngest was 15 years of age and the oldest was 65 years of age.

In most of the studies worldwide, and impaired consciousness were the commonest symptoms of Posterior Reversible Encephalopathy Syndrome [1,2,3,4]. However, in our study headache (87.59%) and seizures (64.51%) were the commonest symptoms of Posterior Reversible Encephalopathy Syndrome. Praveen Kumar et al. [13] reported headache (75%) as the most common symptom of Posterior Reversible Encephalopathy Syndrome followed by seizures, as seen in our study. Abrupt raise in blood pressure of any etiology (as encountered in pregnancy related hypertension) is often the cause of Posterior Reversible Encephalopathy Syndrome. Pregnancy related Posterior Reversible Encephalopathy Syndrome was the commonest cause of Posterior Reversible Encephalopathy Syndrome in our study followed by primary hypertension. Praveen Kumar et al. [13] also reported that pregnancy induced hypertension (55%) of the patients as the commonest etiology of Posterior Reversible Encephalopathy Syndrome followed by primary hypertension. This was consistent with studies that primary hypertension and pregnancy induced hypertension

are the commonest etiology [6,7,8,9,10]. However Hinchey et al. [1], Legriel et al. [2], found immunosuppressive drugs following transplantation was the commonest cause.

Hinchey et al. [1], Burnett et al. [2], Bartynski et al. [11] documented hypertension in 67–80% of the patients; in our study hypertension was noted in 67.74% of the patients.

In the radiological findings, occipital lobe involvement was seen in 93% [1] to 99% [3,9] of the patients followed by parietal 87% [1], 99% [3], 67% [12], 50% [6]. In our study also the commonest lobes affected were occipital 77.41% and parietal 67.74% lobes. Symmetrical lesions were reported in 100% [7] 69% [6] of the patients. In our study the symmetrical pattern was seen in 67.74% of the patients. Asymmetrical pattern was seen in 32.25% of the patients. Subcortical involvement was seen in all the patients. Cortical involvement was seen in 13 out of the 31 patients i.e. 41.93% of the patients had cortical involvement. Also this means that the same 41.93% of the patients had both subcortical and cortical involvement. Vasogenic edema (iso or hypointense in DWI and hyperintense in ADC) pathognomonic of Posterior Reversible Encephalopathy Syndrome was seen in all cases especially in the posterior subcortical regions. Rarely there can be recurrent Posterior Reversible Encephalopathy Syndrome. Recurrent Posterior Reversible Encephalopathy Syndrome had been reported in 6% of the case [12]. In our study one patient (3.22%) had recurrent Posterior Reversible Encephalopathy Syndrome. Legriel et al. [2] reports 15% mortality rate in Posterior Reversible Encephalopathy Syndrome. Lee et al. [4] reported persistent neurological deficit was seen in 26% of the patients. In our study two of the patients had irreversible complications (visual defects) and one patient died of the primary illness. The mortality rate in our study was 3.22%.

Conclusion

In our study Posterior Reversible Encephalopathy Syndrome is common in females. The commonest age groups affected are the young and the middle aged. The commonest cause is Pregnancy related Posterior Reversible Encephalopathy Syndrome with almost all the patients being primigravida. Headache is the commonest symptom of Posterior Reversible Encephalopathy Syndrome. Papillodema is seen in nearly 1/3rd of the patients. Not all patients have documented hypertension. The abrupt rise of blood pressure is more important than the absolute value of blood pressure in causing Posterior Reversible Encephalopathy Syndrome.

There is varied etiology for Posterior Reversible Encephalopathy Syndrome, ranging from the commoner pregnancy related Posterior Reversible Encephalopathy Syndrome to the rare causes like porphyria, Posterior Reversible Encephalopathy Syndrome following blunt injury abdomen, following OPC poisoning etc, as seen in this study. Hence, an high index of suspicion and a thorough knowledge of conditions that could predispose to Posterior Reversible Encephalopathy Syndrome is essential for the early diagnosis.

Prompt control of blood pressure /avoiding any precipitating factors, causing endothelial damage like certain drugs as discussed earlier, prevents irreversible complications.

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