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Original Research Article

Clinical spectrum of patients with posterior reversible encephalopathy syndrome

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ABSTRACT

Background: Posterior reversible encephalopathy syndrome is a neurological disorder which can present with sudden onset headache, visual disturbances, seizures and altered sensorium which is potentially reversible with early detection and treatment of the precipitating factor. The range of presentations is being constantly widened and this endeavour is a step towards understanding the wide array of presentation and primary etiology.
Methods: This is a prospective observational study of 25 patients presenting to a tertiary care hospital with symptoms and imaging features suggestive of PRES. Thorough clinical examination and MRI brain were performed in all patients.
Results: Out of the 25 patients, 18 (72%) were females and 7 (28%) were males. Most common symptom was headache (84%) followed by seizures (56%), nausea (40%), visual blurring (36%) and altered sensorium (20%). In patients presenting with seizure, 28.57% had recurrent seizures.
The most common precipitating cause was postpartum state without hypertension (40%) followed by accelerated hypertension (28%), eclampsia (16%), chronic kidney disease (12%) and one patient of chronic severe anaemia had PRES following blood transfusion (4%). Most of the patients improved with no residual neurological deficit.
Conclusions: Good neurological outcomes can be achieved by early diagnosis and appropriate imaging in patients with PRES. In pregnant and postpartum patients, PRES should be always considered even with normal blood pressure. Rapid correction of chronic severe anaemia is a rare but preventable cause of PRES.

Keywords: Posterior reversible encephalopathy syndrome, Eclampsia, Postpartum, Accelerated hypertension, Chronic kidney disease

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) or Reversible posterior leucoencephalopathy syndrome (RPLS) is a clinicoradiological syndrome, first described by Hinchey et al in 1996, that can be associated with several conditions, including hypertensive encephalopathy, chronic renal insufficiency, blood transfusion, puerperal eclampsia.[1,2] PRES may also develop during treatment with cisplatin, cyclosporin A, tacrolimus, interferon alpha, immunoglobulin, and after liver transplantation or the acute phases of autoimmune diseases.[1,3-7] It is a sporadic disease with unknown incidence, reported worldwide without any gender differences. Both children and older people can be affected.[8] The clinical syndrome can have variable symptoms and typically comprises holocephalic headache, focal neurological deficits such as visual disturbances, dysphasia and paresis, seizures and reduced consciousness. The pathophysiology of PRES is poorly understood. The popular hypothesis is the disrupted autoregulation of cerebral blood flow with abrupt increase in blood pressure[1]. But this does not explain PRES without hypertension. Another theory implicated is

endothelial dysfunction.[8,9] Vasospasm with subsequent ischemia was also proposed as a third possible theory.[10] Although defined as reversible, there may be complications like status epilepticus (SE), intracranial hemorrhage, and massive ischemic infarction leading to morbidity and mortality.[11] The range of presentations is being constantly widened and this endeavour is a step towards understanding the wide array of presentation and primary etiology.

Objective

To study the demographic profile, clinical features and etiological factors of patients admitted to a tertiary health care hospital in South India with a diagnosis of PRES.

METHODS

This is a prospective observational study of 25 consecutive patients presenting to Narayana medical college and hospital, Nellore, Andhra Pradesh, with clinical and radiological features suggestive of PRES. The study period is from July 2018 to June 2020 for duration of 2 years. Patients were included with 3 diagnostic criteria; clinical presentation with acute neurological symptoms such as headache, seizures, visual disturbance or focal neurological deficit, imaging findings suggestive of focal vasogenic edema and clinical or radiological features of reversibility. Clinical features, co morbidities, drug histories were studied with complete neurological examination. MRI Brain without contrast was done for all cases with standard sequences of T1, T2 and FLAIR imaging along with diffusion weighted imaging MR venography was done in suspected patients to rule out cortical vein thrombosis. Cases that favour an alternate diagnosis with similar presentation and imaging features that do not suggest PRES have been excluded. Statistical analysis was done by computer software SPSS, trial version. Data was analysed by mean, standard deviation (SD) and percentage.

RESULTS

Out of the 25 patients, 18 were females and 7 were males. Mean age at presentation was 35.16±12.91. Mean age of females was 31.55±11.33. Mean age of males was 44.42±12.06. The age group of 20-30 years were most commonly affected. Most common symptom was headache (84%) followed by seizures (56%), vomiting (40%), visual disturbances (36%) and altered sensorium (20%) (Figure 1).

Most common precipitating factor was postpartum state without hypertension (40%) followed by accelerated hypertension (28%), eclampsia (16%), CKD with hypertension (12%) and one case of PRES following blood transfusion (Figure 2). There was one case of a 17 year old female presenting with headache and one episode of seizure (generalised tonic-clonic) 4 days following blood transfusions for chronic severe anemia. MRI brain showed diffused T2 and FLAIR hyperintensities without diffusion restriction (Figure 3).

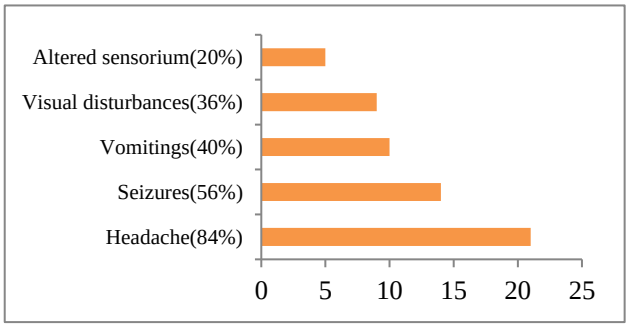

Figure 1: Percentage of common clinical features of PRES patients.

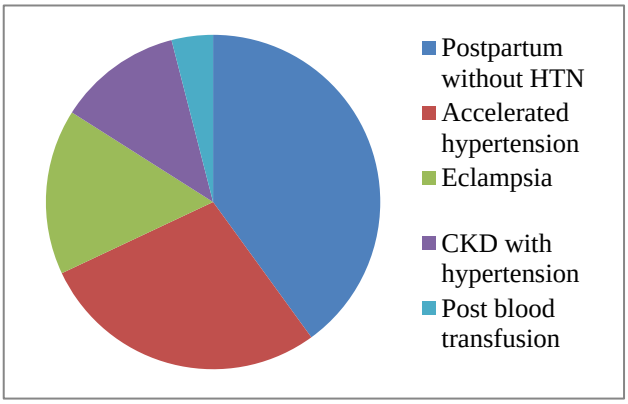

Figure 2: Common precipitating factors of PRES.

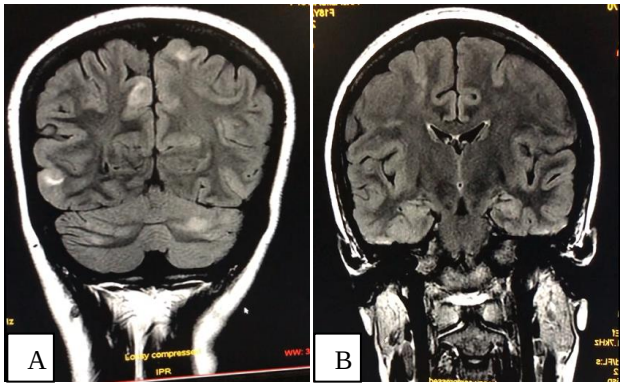

Figure 3: MRI brain FLAIR sequence showing hyperintensities in (A) bilateral fronto-parietal lobes and (B) cerebellar hemispheres.

Follow up MRI could be done in 16 patients after 6 weeks and findings resolved in 93% of the cases. 1 case has developed subsequent infarction and motor deficit. For cases that could not be followed up with MRI, resolution of clinical features was considered. Out of the 9 cases for which follow up imaging could not be done, 8 cases improved symptomatically over 1-2 weeks. 1 case had persistent blurred vision which improved over 6 weeks. There was no mortality.

DISCUSSION

Since the description of PRES by Hinchey et al, the clinical spectrum and its pathophysiology have been unclear and poorly defined.[1] PRES is characterized by headache, seizures, confusion, and visual disturbances such as 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 involve the cortex, frontal lobes, basal ganglia, and brainstem.[8]

In our study females were affected commonly (72%) in comparision with Liman et al (67.7%) and Yadav et al (79%). Only 64.6% were females in a study by Fugate et al.[12,13] Headache was the most common symptom (84%) which is in concurrence with recent study by Yadav et al where it was reported to be 83.3%. Whereas seizures were the most common presentation (67%) in a report by Liman et al.[14]

Abrupt hypertension is a definite contributing factor to the development of PRES, and the frequent presence of substantial hypertension in patients with PRES and subsequent resolution of clinical symptoms and radiologic edema with prompt treatment of hypertension supports the hyperperfusion theory. However this theory does not explain the occurrence of PRES in normotensive patients[5] and does not significantly occur in patients with a surge of hypertension above the normal upper limits of cerebral autoregulation. About 70% of patients with PRES are hypertensive, although a substantial proportion of the cases have normal or mildly elevated blood pressure.[12] In our study, 60% were hypertensives. This is in discordance with Fugate JE et al where hypertension was present in 86% of the patients.[13]

Pregnancy and postpartum state without hypertension were the most common precipitating factors similar to the findings of PK Yadav et al. In this subset, about 60% had normal blood pressures. Most studies show elevated blood pressure in these patients.[15,16] The significant finding in our study is that postpartum state without hypertension was a significant etiological factor than eclampsia. This presentation may be due to endothelial dysfunction leading to disruption of blood brain barrier occurring in postpartum complications like puerperal sepsis, postpartum hemorrhage (PPH).

Another significant finding is a case of PRES which developed after blood transfusions for anemia. It is rare cause as reported by Ito et al.[3] Rapid correction of chronic severe anemia causing PRES may be explained by hyperperfusion theory. Massive blood transfusions can lead to hyperperfusion and disruption of blood brain barrier leading to vasogenic edema. The comparison of the cases of PRES following blood transfusions in literature is shown in (Table 1).

Other differential diagnoses have to considered and ruled out in the setting of PRES like posterior circulation stroke, cerebral venous thrombosis, reversible cerebral vasoconstriction syndrome (RCVS), dialysis disequilibrium syndrome (DDS), cerebral artery dissection and primary CNS vasculitis.

The clinical spectrum and precipitating factors in our study were similar to most of the studies in the literature and a recent study in India by Yadav et al.[12]

Table 1: Comparison of cases of PRES following blood transfusion in literature.

CASE	Ito et al[2]	Boughammoura et al[17]	Heo et al[18]	Huang et al[19]	Sato Y et al[20]	Our case
Age/gender	45/F	48/F	47/F	32/F	43/F	17/F
BT volume of RBC (ml)	800	1000	NA	1600	400	1250
Hb (g/dl) pre/post BT	2.0/10.0	3.0/8.0	1.5/10.9	5.7/12.5	5.7/11.7	2.9/9.3
Period of BT	14 days	7h	4 days	20h	12h	6 days
Symptom onset after BT	2 days	6 days	7 days	5 days	6 days	4 days
Duration of symptom	NA	7 days	NA	5 days	37 days	5 days

The limitation of our study was that the sample size was small and follow up MRI could not be done in all the patients. An overlap of PRES and reversible cerebral vasoconstriction syndrome (RCVS) could not be made as vessel imaging was not done.

CONCLUSION

Good neurological outcomes can be achieved by early diagnosis and appropriate imaging in patients with PRES. In pregnant and postpartum patients, PRES should be always considered even with normal blood pressure.

Rapid correction of chronic severe anaemia is a rare but preventable cause of PRES.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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