Original Article

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Radiology Section

Posterior Reversible Encephalopathy Syndrome: Study of Common Associations and Varying Imaging Features

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ABSTRACT

Introduction: Posterior Reversible Encephalopathy Syndrome (PRES) is a clinically bewildering encephalopathy syndrome which can be encountered in emergency room or in an already hospitalised patient. Its occurrence and mechanisms have been widely published mainly in the population of patients with transplant necessitated immunosuppression and not many studies have been carried out in the setting of many other risk factors.

Aim: To study the frequency of primary clinical conditions causing or associated with PRES in general radiology practice. To study the frequency and distribution of abnormal findings in specific regions of brain.

Materials and Methods: Radiology database of a free-standing imaging center and a multi-specialty hospital was scrutinised for reports citing PRES, hypertensive encephalopathy, eclampsia, renal disorders or any state of neurotoxicity on brain imaging, between July 2011 and June 2015. Reports showing complete or partial PRES pattern on imaging during the clinical neurotoxic syndrome were included in the study.

Results: Total 84 patients were identified with PRES, out of them 80 were adults (mean age- 40.48±13.03 years). Among them 56 were men, 24 were women. There were four children (mean age- 12±2.19 years; with renovascular hypertension due to Takayasu's arteritis). Twenty patients were normotensive and four patients were positive for Human Immunodeficiency Virus (HIV).

Conclusion: There are many causes and associations of PRES but all of them are 'systemic' in nature. Spectrum of these systemic diseases may vary in population/practice. Hypertension is not an absolute requirement for diagnosis of PRES though it is the strongest association. Non posterior (non parieto-occipital) locations being frequent it is advisable to drop 'posterior' component from its name.

Keywords: Eclampsia, Reversible leukoencephalopathy, Seizure

INTRODUCTION

PRES is a clinically bewildering encephalopathy syndrome which can be encountered in emergency room or in an already hospitalised patient. Contrary to its name, it can leave behind irreversible brain damage during the course of recovery. However, its etio pathogenesis has not been completely established [1-5]. Its occurrence and mechanisms have been widely published mainly in the population of patients with transplant necessitated immunosuppression and not many studies have been carried out in the setting of many other risk factors [2,6].There is also limited data on the frequency of occurrence in various clinical risk factors and the pattern of regional distributions of lesions in brain parenchyma in various systemic associations responsible for PRES [7].

MATERIALS AND METHODS

This retrospective study was conducted to identify clinical associations and regional brain parenchyma distribution of imaging findings of PRES in general population.

Radiology database of Departments of Radiology of Medcorre Diagnostics and Trinity Hospital, Bengaluru, India, was scrutinised for reports citing PRES, hypertensive encephalopathy, eclampsia, renal disorders or any state of neurotoxicity on brain imaging, between July 2011 and June 2015. Reports showing complete or partial PRES pattern on imaging during the clinical neurotoxic syndrome were analysed. When more than one clinical association were present, the clinically dominant association was considered. Reports of patients with earlier radiologically established brain

parenchymal changes like ischaemia, dural sinus thrombosis, and traumatic brain parenchymal injury on imaging and deranged coagulation profile were excluded from the study. However, one trauma patient with earlier normal baseline imaging on the day of trauma was also included in the study.

Permission from local ethics committee was obtained and no written consent from the patients were obtained.

Computed Tomography (CT) was obtained when clinical contexts demanded quick imaging diagnosis. Whenever clinical stabilisation was achieved, these patients were subjected to MRI evaluation. Eighteen patients had undergone CT and among eight of them CT was the only imaging modality carried out and the rest 10 underwent MR subsequently.

MRI was performed at 1.5T (Interaand Achieva, Philips, Nether-lands). Although, parameters (TE, TR, flip angle) varied from patient to patient, they were in accordance with standard imaging practice. In all patients T1WI, T2WI, Fluid Attenuated Inversion Recovery (FLAIR), diffusion weighted MR imaging, gradient sequences were employed in transverse plane. In addition to these T2 sagittal, FLAIR coronal images were also obtained. Gadolinium (0.1 mmol/kg) based contrast study was carried out whenever required.

STATISTICAL ANALYSIS

Analysis was done by SPSS Software Version 21.0. Unpaired Student's t-test was used and p-value of <0.05 was considered to be statistically significant.

RESULTS

Total 20 patients had abnormal signal intensities in infratentorial brain parenchyma and in four of them brainstem involvement was noticed while 16 had cerebellar involvement. Four patients had unilateral brain parenchymal abnormalities. Twelve patients had intracranial haemorrhage, which was subarachnoid in location and these patients were normotensives. None of these patients had intraparenchymal haemorrhage [Table/Fig-1].

Among the 20 normotensives, 16 patients had renal disease and four patients had sepsis. Strongest association between the occurrence of PRES and systemic condition was essential hypertension. Twenty patients had renal disease and four patients each had sepsis, HIV, renovascular hypertension,

Locations of Lesions	Number of patients (n=84)	Percentage (%)
Posterior Parieto Occipital	56	66.7
Superior Frontal Sulcus	32	38.1
Temporal	12	14.3
Cerebellum	16	19.1
Brainstem	4	4.8

[Table/Fig-1]: Locations of lesions in the study.

Clinically Dominant Condition	Total No. of Patients (n=84)	No. of Patients with Clinical (n=36)	No. of Patients without Clinical (n=48)	p-value
Essential hypertension	48 (57.1%)	32 (88.9%)	16 (33.3%)	0.024*
Renal disease	20 (23.8%)	0 (0%)	20 (41.7%)	0.045*
Eclampsia	4 (4.8%)	4 (11.1%)	0 (0%)	0.429
Sepsis	4 (4.8%)	0 (0%)	4 (8.3%)	1.000
HIV	4 (4.8%)	0 (0%)	4 (8.3%)	1.000
Reno-vascular	4 (4.8%)	0 (0%)	4 (8.3%)	1.00

[Table/Fig-2]: Clinical dominant condition according to pre imaging suspicion of PRES.
Note: * Signifies statistically significant value.

pregnancy induced hypertension [Table/Fig-2]. In four patients, foci of restricted diffusion were noticed. In 4 patients, signal intensity changes were not appreciated in T1W images.

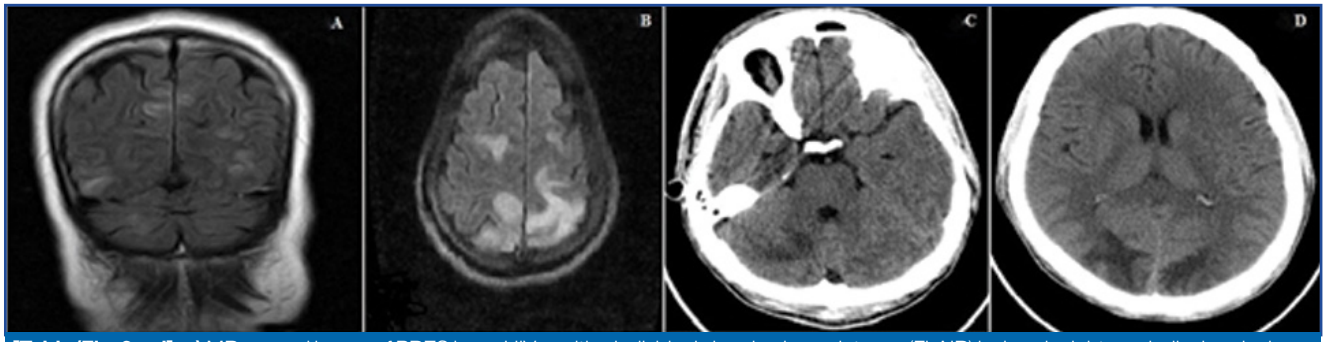
DISCUSSION

The epidemiology of PRES has not been established; however, it has been reported across the age of 4-90. It is predominantly reported in women [2].

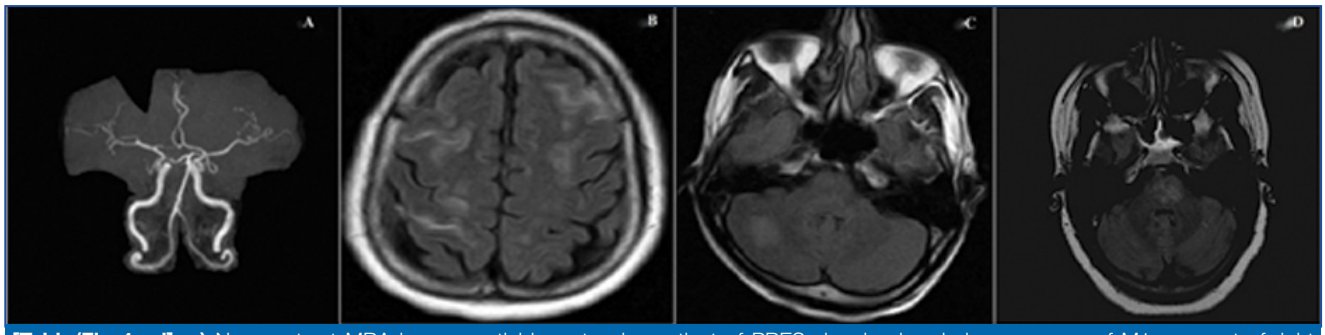
In our study, the mean age was 40.48±13.03 years and females accounted for 33.3% (pregnancy induced hypertension accounted for 4.8%) of the total study population, and this may be due to the nature of our practice which did not include obstetric care. However, earlier studies have revealed female preponderance even after excluding set of pregnancy induced hypertension [1,8]. There were four children (mean age 12± 2.19 years). We employed CT and /or MRI for neuroimaging [9]. In our study, 4 HIV-positive patients who presented with clinical symptoms of headache and visual symptoms showed hyperintense (FLAIR) lesions in right cerebellar hemisphere, posterior aspect of bilateral temporal lobes, and bilateral parieto-occipital regions [10].

In the holo hemispheric [Table/Fig-3a], watershed pattern, vasogenic oedema presents in a linear pattern. This linear edema is seen along the watershed or anastomotic border zone of anterior and posterior cerebral arteries and lateral hemispheric middle cerebral artery branches. In another patient with accelerated hypertension presented with predominant visual disturbances, we observed subtle superior frontal sulcus pattern [Table/Fig-3b]. MRI also showed bilateral strong FLAIR hyperintensities in parieto-occipital region.

CT findings [Table/Fig-3c,d], are often normal and nonspecific [2,11]. CT-scan is best suited for patients who are not either stable enough or not able to co-operate during longer MRI study. It lacks sensitivity in diagnosing PRES [12]. MRI



[Table/Fig-3a-d]: a) MR coronal image of PRES in an HIV positive individual showing hyper intense (FLAIR) lesions in right cerebellar hemisphere, posterior aspect of bilateral temporal lobes, bilateral parieto occipital regions; **b)** MR image in an adult with accelerated hypertension presented showing bilateral strong FLAIR hyper intensities in parieto occipital region and subtle hyper intensities (FLAIR) in bilateral frontal region in relation to superior frontal sulcus suggestive of PRES. Non contrast venogram was normal (not shown in figure); **c,d)** CT images of a patient with essential hypertension showing diffuse hypodensities in right cerebellar hemisphere, bilateral hypo densities in temporal and parieto-occipital regions consistent with PRES.



[Table/Fig-4a-d]: a) Non-contrast MRA in a essential hypertensive patient of PRES showing beaded appearance of M1 segment of right MCA, A1 segment of right ACA. (Patient had mild homo hemispheric pattern, not shown in the image); **b)** MR image in a patient with acute derangement of renal function tests showing FLAIR hyper intensity in frontal sulci (indicating subarachnoid haemorrhage) and adjacent symmetric brain parenchyma in frontal region indicating the diagnosis of PRES; **c)** MR image in a hypertensive with PRES showing hyper intense (FLAIR) foci in right cerebellar hemisphere; **d)** MR image (FLAIR) in an adult with pregnancy induced hypertension and PRES showing heterogeneous hyper intensity in pons.

(particularly T2-FLAIR) is the preferred and correct choice of imaging technique for diagnosing PRES [2,6,13]. Low intensity foci on T1W images were not demonstrated in only four patients, although bright signals were particularly well seen on FLAIR images. MR angiography may show patterns resembling vasculopathy (focal vasoconstriction/vasodilation and diffuse vasoconstriction) [14].

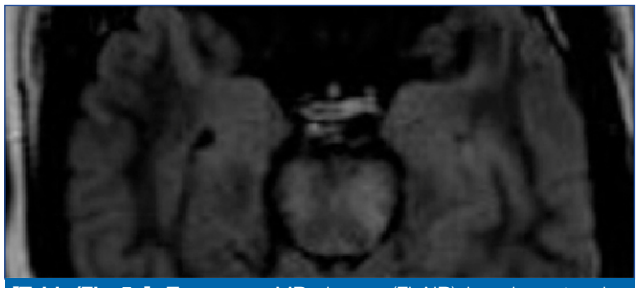
Since, MR angiogram [Table/Fig-4a] was not a part of routine brain imaging protocol, in our study not all the patients were evaluated with the same.

Twelve patients in our study had subarachnoid haemorrhage [Table/Fig-4b] which was mild and predominantly frontal in distribution and bilateral. None of the patients had intrapernchymal haemorrhage. Earlier study has noted increased incidence of parenhymal haematoma in patients with solid organ transplantations and immunosuppression [15].

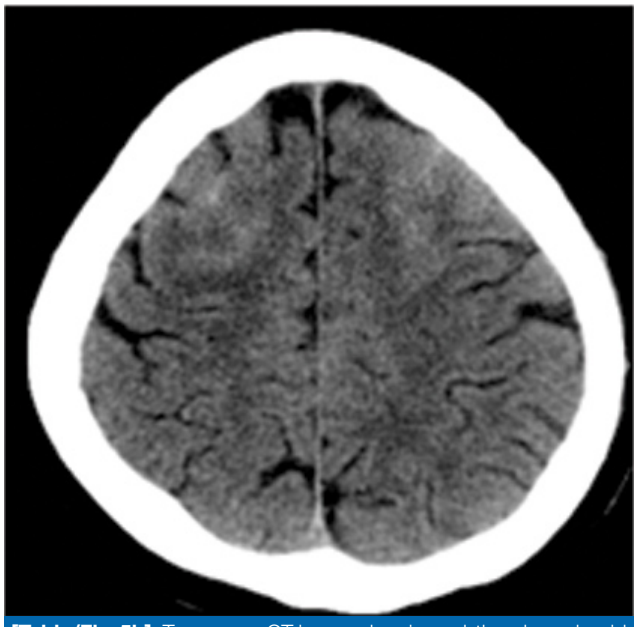
This corresponds well with the fact that none of our patients had any transplantation and subsequent immunosuppression therapy.

In our study, most common pattern was of posterior occipito parietal pattern with 66.7% contribution [Table/Fig-1]. This finding is consistent with the with recent study done in a pediatric population [16]. Next common pattern was of superior frontal sulcus (38.1%), incidence of which was higher compared to earlier cited study. Temporal lobe lesion abnormality accounted for 14.3%. Parieto-occipital region was the most commonly involved region, followed by frontal lobe, temporal lobe and cerebellum [Table/Fig-4c], Involvement of frontal lobe, temporal lobe and cerebellum was relatively common. Isolated involvement of brainstem [Table/Fig-4d,5a], deep white matter, basal ganglia was infrequent. Khan SJ et al., did not observe any central variant of PRES [16]. We derive that less common patterns like superior sulcus and central type are more common with adult risk factors than ones in pediatric population. Partial or asymmetric expressions of the primary patterns are also described in literature [17,18].

In our study, four patients with uncontrolled essential hypertension had unilateral occipital lesion owing to acute fluctuation of blood pressure.



[Table/Fig-5a]: Transverse MR image (FLAIR) in a hypertensive patient with showing subtle pontine hyper intensity.



[Table/Fig-5b]: Transverse CT image showing subtle subarachnoid haemorrhage in bilateral frontal region.

Four of the patients in our study had area of restricted diffusion (of size 10×12 mm) in unilateral occipital region, indicating irreversible cytotoxic oedema [19].

In this study, we found classic clinical scenarios such as hypertension, renal disease, sepsis, and eclampsia [Table/Fig-2], to be associated with PRES [20-23]. Six of the patients who had subarachnoid haemorrhage [Table/Fig-5b], had renal parenchymal disease. Common clinical presentations were seizures, confusion, headache, visual disturbance. Imaging features of intra-cranial hypertension was not observed in any of our patients. Takayasu's arteritis can be a cause of PRES [24]. None of our patients had clinical features of spinal involvement. There was not a single case of transplant related immunomodulation or autoimmune connective tissue disease in the series. HIV was the only immune system related dominant scenario.

LIMITATION

In addition to intrinsic limitation of a retrospective study of limited data set, study was limited by coexisting risk factors and only dominant was considered. Pharmacological agents received during or prior to the diagnosis were not considered. Degree of severity of risk factor (e.g., systemic blood pressure measurements), general wellbeing during the illness were also ignored.

Study is an early attempt to relate various systemic factors with type and locations PRES and this would help radiologist to suspect the systemic cause triggering PRES.

CONCLUSION

There are many causes of PRES but all of them are 'systemic' in nature. Spectrum of these systemic diseases may vary in population and type of clinical practice. Hypertension is not an absolute requirement for diagnosis of PRES though it is the strongest association. Large prospective study involving large set of each risk factor needs to be carried out to determine a possible relation between a particular pattern of PRES and the cause. This would help one understand pathophysiology of this entity, confirm the earlier proposed hypothesis of its development by earlier workers. Non posterior (non parieto-occipital) locations being frequent it is advisable to drop 'posterior' component from its name.

REFERENCES

[1] Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med. 1996;334(8):494-500.

[2] Legriel S, Pico F, Azoulay E. Understanding Posterior Reversible Encephalopathy Syndrome. In: Vincent J-L (ed.). Annual Update in Intensive Care and Emergency Medicine. 2011

[3] Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol. 2008;65(2):205-10.

[4] Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: Associated clinical and radiologic findings. Mayo Clinic Proc. 2010; 85(5):427-32.

[5] Bartynski WS. Posterior reversible encephalopathy syndrome, Part 2: Controversies sur-rounding pathophysiology of vasogenic edema. AJNR Am J Neuroradiol. 2008;29(6):1043-49.

[6] Hedna VS, Stead LG, Bidari S, Patel A, Gottipati A, Favilla CG. Posterior Reversible Encephalopathy Syndrome (PRES) and CT perfusion changes. Int J Emerg Med. 2012;5:12.

[7] Ganesh K, Nair RR, Kurian G, Mathew A, Sreedharan S, Paul Z. Posterior reversible ence-phalopathy syndrome in kidney disease. Kidney Int Reports [Internet]. 2018;3(2):502-07. Available from: https://doi.org/10.1016/j.ekir.2017.10.017

[8] Ay H, Buonanno FS, Schaefer PW, Le DA, Wang B, Gonzalez RG, et al. Posterior leukoen-cephalopathy without severe hypertension. Neurology [Internet]. 1998;51(5):1369 LP-1376. Available from: http://n.neurology.org/content/51/5/1369

[9] Kumar N, Singh R, Sharma N, Jain A. Case Report Atypical presentation of posterior reversible encephalopathy syndrome : two cases case reports. J Anaesthesiol Clin Pharmacol. 2018;34(1):120–22.

[10] Nightingale S, Wood C, Ainsworth J. The posterior reversible encephalopathy syndrome in HIV infection. BMJ Case Rep [Internet]. 2012;2012:bcr0120125647.

[11] Shankar J, Banfield J. Posterior reversible encephalopathy syndrome: A review. Can Assoc Radiol J. 2017;68(2):147-53.
[12] Dandoy CE, Linscott LL, Davies SM, Leach JL, Myers KC, El-Bietar J, et al . Clinical utility of computed tomography and magnetic resonance imaging for diagnosis of posterior reversible encephalopathy syndrome after stem cell transplantation in children and adolescents. Biol Blood Marrow Transplant. 2015;21(11):2028-32.
[13] Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior re-versible encephalopathy syndrome: associated clinical and radiologic findings. Mayo Clin Proc. 2010;85(5):427-32.
[14] Stevens CJ, Heran MK. The many faces of posterior reversible encephalopathy syndrome. Br J Radiol. 2012;85(1020):1566-75.
[15] Hefzy HM, Bartynski WS, Boardman JF, Lacomis D. Haemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features. AJNR Am J Neuroradiol. 2009;30(7):1371-79.
[16] Khan SJ, Arshad AA, Fayyaz MB, ud din Mirza I. Posterior reversible encephalopathy syndrome in pediatric cancer: clinical and radiologic findings. J Glob Oncol [Internet]. 2017;(4):01-08.
[17] Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR Am J Neuroradiol. 2007;28(7):1320-27.
[18] Hugonnet E, Da Ines D, Boby H, Claise B, Petitcolin V, Lannareix V, et al. Posterior reversible encephalopathy syndrome (PRES): Features on CT and MR imaging. Diagn Interv Imaging. 2013;94(1):45-52.
[19] Raman R, Devaramane R, Jagadish GM, Chowdaiah S.Various imaging manifestations of Posterior Reversible Encephalopathy Syndrome (PRES) on Magnetic Resonance Imaging (MRI). Pol J Radiol. 2017;82:64-70.
[20] Shankar J, Banfield J. Posterior reversible encephalopathy syndrome: a review. Can Assoc Radiol J. 2017;68(2):147-53.
[21] Lazo KG, DO, Mandel S, Pramanik B, Lee J, Maria V. Posterior Reversible Encephalopathy Syndrome (PRES): A Case Report and Review of the Literature. Practical Neurology. [Available from]: http://practicalneurology.com/2016/04/posterior-reversible-encephalopathy-syndrome-pres-a-case-report-and-review-of-the-literature&center=181
[22] Brewer J, Owens MY, Wallace K, Reeves AA, Morris R, Khan M, et al. Posterior reversible encephalopathy syndrome in 46 of 47 patients with eclampsia. Am J Obstet Gynecol. 2013;208(6):468.e1-6.
[23] Ibrahim NMA, Badawy ME. MRI imaging of posterior reversible encephalopathy syndrome associated with pregnancy. Egypt J Radiol Nucl Med [Internet]. 2014;45(2):505–10. [Avail-able from]: http://dx.doi.org/10.1016/j.ejrnm.2014.01.002
[24] Camara-Lemarroy CR, Lara-Campos JG, Perez-Contreras E, Rodríguez-Gutiérrez R, Galarza-Delgado DA. Takayasu's arteritis and posterior reversible encephalopathy syndrome: a case-based review. Clin Rheumatol. 2013;32(3):409-15.

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