Posterior Reversible Encephalopathy Syndrome: Our Experience at King Hussein Medical Center

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ABSTRACT

Objective: To describe and determine the frequency of brain Magnetic Resonance Imaging findings for regional involvement of brain lobes in Posterior Reversible Encephalopathy Syndrome.

Methods: This is a descriptive study which was conducted on a total of 13 patients who were diagnosed by Magnetic Resonance Imaging to have Posterior Reversible Encephalopathy Syndrome during the period between July 2009 to September 2011 at King Hussein Medical Center. Criteria for diagnosing Posterior Reversible Encephalopathy Syndrome include partial or complete expression of Posterior Reversible Encephalopathy Syndrome pattern, reversibility of the edema on follow up images, clinical presentation of neurotoxicity and presence of underlying systemic process. Standard Magnetic Resonance Imaging sequences used were unenhanced T1-T2-FLAIR diffusion-weighted and contrast-enhanced T1-weighted imaging

Results: The frequency of regional involvement of brain lobes in Posterior Reversible Encephalopathy Syndrome in this series were as follows; the occipital lobe being affected with reversible vasogenic edema in all 13 patients (100%), followed by the parietal lobe in 10 patients (76.9%), frontal lobe in 8 patients (61.5%), temporal lobe in 2 patients (15.4%) cerebellar in 2 patients (15.4%) and pons in one patient (7.7%). The involvement was almost symmetrical bilateral in 9 patients (75%)

Conclusion: Neuroradiological findings along with clinical signs are consistent enough so that this entity should be readily recognizable which ensures early treatment, also prevention of potential complications as brain hemorrhage and infarction.

Key words: Neuroradiological findings, Posterior Reversible Encephalopathy syndrome, Regional involvement.

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Introduction

Posterior Reversible Encephalopathy Syndrome (PRES) is a proposed clinicoradiological syndrome almost exclusively seen in the setting of a significant complex systemic process characterized by a pattern of clinical and neuroradiological changes. The clinical symptoms are usually subacute and can range from headache, vomiting, visual abnormalities, and cortical blindness to altered mental status, seizures and other focal neurological signs.[1] Seizures are usually recurrent. It has a characteristic CT or MRI imaging features in the form of symmetric vasogenic edema most commonly affecting the parietal and occipital lobes.

PRES is a clinical syndrome that is typically considered in view of clinical course along with imaging findings at presentation and follow up.

These imaging features were originally listed under the category of hypertensive encephalopathy or as separate entities as described in patients with

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preeclampsia/ eclampsia and after transplantation.[2-6] However significant hypertension may be absent in 25%–30% of patients. The wider spectrum of patients who develop this toxicity was highlighted by Hinchey *et al* in 1996,[7] and the term "PRES" was used to characterize the typical and unique imaging appearance,[3,5] and to encompass hypertensive encephalopathy and its related conditions in a single cliniconeuroradiologic syndrome. Similar clinical/imaging presentations are recognized in different etiologies like cyclosporin A or tacrolimus neurotoxicity porphyria and uremia.[8-11] The drugs known to cause toxic encephalopathy include chemotherapeutic agents (methotrexate, interferon alpha, fludarabine, 5-FU, and cyclosporine).[7,12,13] PRES has also been associated with autoimmune diseases (thrombotic thrombocytopenic purpura, SLE and Wegener granulomatosis),[14-17] infection, sepsis and shock,[18] allo-bone marrow transplant and solid organ transplants.[7,16,19-22]

The pathophysiology of PRES has been studied thoroughly but continues to be controversial. Two opposing hypotheses are commonly proposed. The first theory suggests that severe hypertension exceeds the limits of brain auto regulation, leading to hyperperfusion, endothelial injury and breakthrough brain edema.[18,23-27] The second theory suggests that hypertension leads to cerebral auto regulatory vasoconstriction and hypo perfusion, ischemia, and subsequent brain edema.[27-30]

Whatever the exact mechanism behind PRES, it is widely accepted that the edema seen is vasogenic, not cytotoxic, and with early diagnosis and prompt treatment, the syndrome is usually fully reversible.

This study was conducted to describe and determine the frequency of brain Magnetic Resonance Imaging findings for regional involvement of brain lobes in Posterior Reversible Encephalopathy Syndrome.

Methods

This is a descriptive study which was conducted on a total of 13 patients who were diagnosed by MRI to have PRES during the period between July 2009 to September 2011, at King Hussein Medical Center by consensus of two experienced neuroradiologists. Criteria for diagnosing PRES include partial or complete expression of PRES pattern, reversibility of the edema on follow up images, clinical presentation of neurotoxicity and presence of underlying systemic process. The patients age range from 16 to 44 years with a mean age of about 33 years.

The MRI imaging was performed at either 1.5 or 3 T machine.

T1 weighted images TR 500 ms, TE 9 ms slice thickness 5mm flip angle 70

T2 weighted images TR 4000 ms, TE 94 ms, slice thickness 5mm, flip angle 180

T2* TR 620 ms, TE 18 ms, slice thickness 5mm, flip angle 20

Proton density TR 2930 ms, TE 11 ms slice thickness 5mm, flip angle 150

FLAIR TR 9000 ms, TE 93 ms, slice thickness 5mm, flip angle 180

Diffusion Weighted Imaging (DWI) TR 5200 ms, TE 148 ms, slice thickness 4 mm

Contrast enhanced T1 weighted images were obtained using 0.1 mmol/kg gadolinium dimeglumine (magnavist) by using typical T1 weighted parameters as described above.

Results

Nine females and four male patients were radiologically diagnosed of having PRES. Five patients (38.5%) had pre-eclampsia, two (15.4%) had chronic liver disease, two (15.4%) had chronic renal failure, one (7.7%) with hypertension, one (7.7%) with acute lymphocytic leukemia, one (7.7%) receiving chemotherapy, and one (7.7%) had SLE.

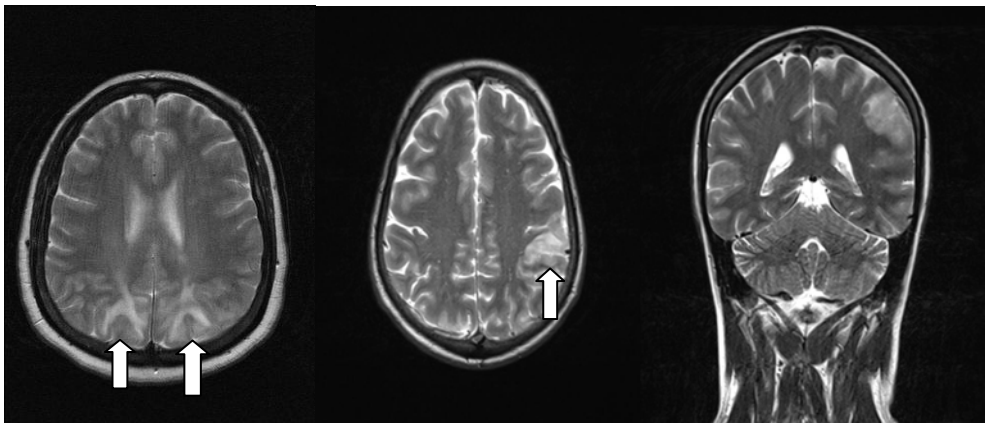
Six patients had mean arterial blood pressure (2/3 diastolic + 1/3 systolic pressure) readings >150-160 mm Hg at time of presentation. Four patients were normotensive and three patients had elevated blood pressure not exceeding the break through point of blood brain barrier (The level at which breakthrough perfusion occurs, which is approximately150-160 mm Hg in humans).

Conventional MRI revealed hyperintensity on T2-weighted and FLAIR images.DWI showed isointensity and increased signal intensity on ADC values, indicating vasogenic edema.

The occipital lobe involvement was noted in all 13 patients (100%), followed by the parietal lobe in 10 patients (76.9%), frontal lobe in 8 (61.5%), temporal lobe in two (15.4%) cerebellar in 2 (15.4%) and pons in one patient (7.7%). Some patients had more than one region involved as shown in Table I, Fig. 1 & 2.

The involvement was almost symmetrical bilateral in 9 patients, while in 3 patients the involvement was more prominent in one side (asymmetrical bilateral).

In all, except one of the patients who had follow-up CT or MRI scans, there was significant improvement or disappearance of white-matter abnormalities, suggesting edema rather than infarction. Another patient had acute cerebellar infarction.



A B C

Fig. 1: Axial (A& B) and coronal T2 MRI images showing hyperintense signal in cortical and subcortical regions of parietal and occipital lobes representing vasogenic edemal. Note the asymmetry in B& C.

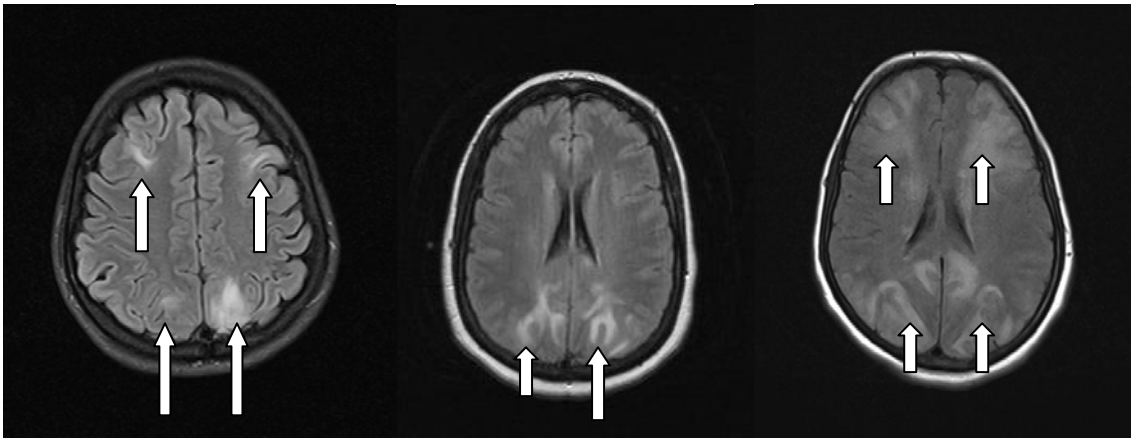


Fig. 2: Axial FLAIR images showing cortical and subcortical hyperintense lesions in frontal, parietal and occipital lobes, representing vasogenic edema.

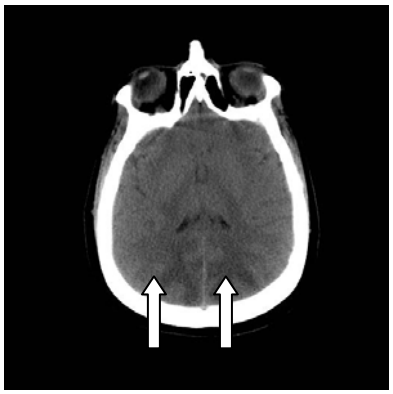


Fig. 3: Axial nonenhanced brain CT scan showing cortical and subcortical hypodensities in parieto-occipital lobes bilaterally representing vasogenic edema.

Table I: Frequency of regional involvement of PRES among the study group

Region	No. of Patients	(%)*
Occipital	13	100
Parietal	10	76.9
Frontal	8	61.5
Temporal	2	15.4
Cerebellum	2	15.4
Pons	1	7.7

*Totals do not add to 100, because some patients had more than one lobe involved

The disappearance of the white matter changes needed 7- 23 days in this study group.

Since the first case was diagnosed in July 2009,[31] recurrence was not noted at King Hussein Medical Center till now.

None of the patients included in this study had brain hemorrhage, and biopsy was not performed for any of them.

All the 13 patients complained of headache (100%), 4 had seizures (30.77%) and 3 had visual disturbances (23%)

Discussion

Recent studies have suggested that lesions of hypertensive encephalopathy and PRES represent vasogenic rather than cytotoxic edema in the majority of cases.[1,7,16,17,22,25,32,33] The basic PRES pattern resembles the brain watershed zones, with the cortex, subcortical and deep white matter involved to varying degrees.[34]

Although the PRES pattern could be identified by CT, the initial findings on CT were usually normal or nonspecific, despite severe clinical symptoms. However, when seen on CT scan, it is bilateral symmetrical white matter low attenuation lesions[35] (Fig. 3). On MRI, T1-weighted images show a hypointense area, and hyperintense onT2-weighted images (Fig. 1).[35]

Fluid attenuated inversion recovery (FLAIR) is a routine sequence in most practices with current MR protocols. FLAIR images are T2-weighted but have nulling of signal from cerebrospinal fluid (CSF) due to the inversion recovery technique. This allows for better detection of T2 hyperintense lesions of the cortex that often are obscured on conventional T2 sequences owing to adjacent hyperintense CSF. So FLAIR should be used in MR protocols for suspected PRES, and may thus lead to prompter diagnosis and more appropriate therapy. The usual imaging findings of PRES are hyperintensity on FLAIR images (Fig. 2).

DWI has been shown to be reliable in distinguishing vasogenic edema in PRES from cytotoxic edema in the setting of cerebral ischemia. It stands to reason that DWI could be used to monitor for ischemia as a complication of PRES.[19,36]

We have used DWI in our series population with similar results but have encountered occasional complicated cases with demonstrable ischemia on ADC maps. Diffusion weighted MRI with ADC mapping shows increased ADC values representing vasogenic edema in these areas, thus differentiating atypical PRES from other brain disorders.[19,36]

Imaging is thus an essential component of the diagnosis of PRES in the presence of the proper clinical context. When typical clinical risk factors are not present, or when the blood pressure is not severely elevated, improvement on follow-up MR images may also be key in the diagnosis.

The regions of predilection are the parieto-occipital and posterior frontal cortical and subcortical white matter, less commonly brain stem, basal ganglia and cerebellum are involved.[7,28,29,37] Follow-up MRI after proper treatment shows resolution of the lesions, unless the condition complicated by hemorrhage 15% or infarction (11%–26%).

In this series, the occipital lobe involvement was noted in 100%, followed by the parietal lobe in 76.9%. According to McKinney[38] larger series of 76 patients having PRES; the incidence of regional involvement was; parietooccipital, 98.7%; posterior frontal, 78.9%; temporal, 68.4%; thalamus, 30.3%; cerebellum, 34.2%; brainstem, 18.4%; and basal ganglia, 11.8%. The incidence of less common findings was enhancement, 37.7%; restricted diffusion, 17.3%; hemorrhage, 17.1%; and a newly described unilateral variant, 2.6%. It also shows that atypical distributions and imaging appearances of PRES have a higher incidence than commonly described and atypical manifestations do not correlate well with the edema severity.

Lesion confluence may develop as the extent of edema increases. The calcarine and paramedian occipital-lobe structures are usually not involved, a fact that distinguishes PRES from infarction of the posterior-cerebral-artery territory bilaterally.

In all, except one of the patients who had follow-up CT or MRI scans, there was significant improvement or disappearance of white-matter abnormalities, suggesting edema rather than infarction.[39] This patient condition was complicated by cerebellar infarction.

The findings in our patients tended to be symmetrical, however the degree of involvement and the clinical manifestations were often asymmetric. Which could have implications related to the mechanism responsible for the development of vasogenic edema in PRES. Variable expression of PRES patterns could be related to differences in vascular anatomy, preexisting diseases, or regional hemispheric involvement in the underlying clinical toxic condition.

PRES is well known to develop after transplantation; Bartynski[40] demonstrate several important features related to PRES in solid organ transplantation (SOT) including:

1. A low incidence of PRES in SOT in particular when compared with allo-BMT.
2. A similar incidence of PRES among the different SOT subtypes.
3. Marked difference in several features of PRES between liver and kidney transplants including time point of onset, extent of brain edema, and blood pressure at presentation.
4. High frequency of bacterial infection, Cytomegalovirus (CMV) expression, and organ rejection in the peripresentation period.

Although none of this study population was complicated by brain hemorrhage, it is a well known complication which is reported in 5-17 % of PRES patients.[41]

Doss-Esper *et al*[41] have proposed 2 theories for brain haemorrhage: 1) nonaneurysmal subarachnoid (sulcal) hemorrhage due to rupture of pial vessels in the face of severe hypertension and impaired cerebral autoregulation, and 2) postischemic reperfusion injury leading to multifocal brain hemorrhages.[42,43]

The results in our patients demonstrated several important observations related to the imaging appearances of PRES: 1- common involvement of "atypical" brain locations other than the parietal or occipital regions 2- partial or asymmetrical expression of the vasogenic edema. These observations are of importance for proper diagnosis of PRES.

Conclusion

The frequency of regional involvement of brain lobes in PRES was consistent with published literature. Reversible vasogenic edema, which is usually symmetrical and bilateral, mainly in the parieto-occipital and posterior frontal lobes are the usual imaging findings in this syndrome. Neuroradiological findings along with clinical signs are consistent enough that this entity should be readily recognizable which ensures early treatment, also prevention of potential complications as brain hemorrhage and infarction.

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