MRI Features of Posterior Reversible Encephalopathy Syndrome
Abdul-Qader Isam Abdul-Hameed, Salwa Taha Ahmed Isma'il, Shaimaa Abdelsattar Mohammad
Radiology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

ABSTRACT
Background and Purpose: Posterior Reversible Encephalopathy Syndrome (PRES) represents a clinico-radiological constellation of neurological symptoms and radiological features. The syndrome tends radiologically to be present with certain features and patterns. Our aim in this study is to investigate the PRES radiological features by which it does present in our community and to correlate the findings clinically. Methods: The MR images obtained for the 17 patients included in the study were analyzed for the PRES features and patterns. Fluid Attenuation Inversion Recovery (FLAIR) sequence was the mainly used sequence for assessment. Diffusion images with their apparent diffusion coefficient maps, T2* images, and Angiography were also utilized for further assessment and characterization. Results: Most of the cases demonstrated a bilateral involvement (94%). The regional distribution supra-tentorially included parietal and occipital affection in 94%, frontal lobe affection in 76%, and a temporal lobe affection in 71%. Infra-tentorial involvement was noted in 41% of the cases. Pattern percentages were slightly different from those available in the literature with the Holohemispheric Watershed pattern being the most common (35%). Conclusion: The originally described PRES features are present in the majority of the studied cases. The identified PRES patterns may reflect underlying clinical or pathological correlations, and hence can vary across communities.

Keywords: Keywords: Posterior Reversible Encephalopathy Syndrome, Reversible Posterior Leukoencephalopathy Syndrome, Brain, Magnetic Resonance Imaging.

INTRODUCTION
Posterior reversible encephalopathy syndrome (PRES) is a syndrome that was originally described in the last decade of the twentieth century by Hinchey and colleagues and was labelled as Reversible Posterior Leukoencephalopathy Syndrome (RPLS). The increasingly recognized syndrome is a clinico-neuro-radiological entity that describes a constellation of headache, vomiting, altered mentality state, blurring of vision, and seizure activities with imaging evidence of brain edema involving gray and white matter with a posterior region predominant fashion.

The syndrome follows a sporadic pattern and its incidence is unknown. The worldwide reports haven’t revealed any gender differences. Both children and adults involvement have been observed. The syndrome is frequently noticed to be associated with acute hypertension. Common associated clinical conditions are Pre-eclampsia/Eclampsia and Hypertensive encephalopathy, however, it has been reported in a wide spectrum of clinical conditions including exposure to toxic agents, sepsis, autoimmune diseases, malignancies and organ transplants.

For the radiological evaluation, MR imaging is considered the gold standard imaging modality, and is recommended to be performed as soon as PRES is suspected. Typical radiological features are usually present in the vast majority of cases especially the parieto-occipital dominance though atypical presentations have also been reported.

According to the topographic distribution of the syndrome, four different radiological patterns were recognized:

1. Dominant parieto-occipital pattern:
   This pattern represents what was thought to be the typical presentation of PRES. The hallmark of this pattern is the predominant parieto-occipital involvement (figure 1). Mild to severe forms of the pattern was recognized. Temporal involvement was variably noted. Though it is described in the literature as the “typical” topography, it was found in 22.1% of patients only.

Figure 1: shows the typical features of the Parieto-occipital pattern of PRES seen by FLAIR; there is a bilateral vasogenic edema affecting the
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occipital (open arrows in A) and parietal (curved arrows in B) regions. The CSF hyperintensity noted is probably related to oxygen administration to the patient\(^\text{10}\).

2. Holo-hemispheric watershed pattern:

This describes the syndrome expression in the watershed area between the medial and lateral arterial territorial hemispheric blood supply, viz. ACA and PCA on a side, and MCA on the other, and hence the pattern name.

The pattern can be described as a confluent strip which involves the frontal, parietal, and occipital regions, with a lesser extent of temporal involvement (figure 2). Mild and severe forms of the pattern were recognized. The pattern was found in 22.8%.

**Figure 2:** shows the typical features of the holo-hemispheric pattern of PRES seen by FLAIR; there is a strip of confluent vasogenic edema extending over the arterial territorial junctions through the frontal (arrows in C and D), parietal (curved arrows in C), and occipital region (open arrows in B). Temporal involvement can also be noted (arrow heads in A). Note that the edema here is extending to the frontal poles\(^\text{10}\).

3. Superior frontal sulcus pattern:

There is a predominant frontal involvement here, the pattern expression is usually linear, involving the middle and posterior portions of the superior frontal sulcus (figure 3). It can be differentiated from the holo-hemispheric pattern by its predominant frontal involvement with a notable frontal pole sparing. A varying degree of involvement of the parietal and occipital regions might be seen. The pattern was reported in 27.2%.

**Figure 3:** shows the typical features of the superior frontal sulcus pattern of PRES seen by FLAIR; the superior frontal sulcus is involved bilaterally in the mid and posterior frontal regions (arrows in C and D). The vasogenic edema can also be seen in the parietal (curved arrows in B) and occipital (open arrows in A) lobes. Note that the extreme frontal poles (A) are intact\(^\text{10}\).

4. Partial or asymmetric pattern:

Generally, there is a lesser brain involvement with PRES here, the pattern in brief constitutes the incomplete expression of the above mentioned forms. It was seen in 27.9% of the patients included.

**Partial expression** describes bilateral sparing of the one of the major sites that are usually affected by PRES, that is to say, bilateral sparing of either occipital or parietal lobes.

**Asymmetrical expression** describes the unilateral sparing of either occipital or parietal lobes.

Lastly, **partial and asymmetrical expression** describes bilateral sparing of either occipital or parietal lobes, with asymmetrical affection of the involved lobe\(^\text{10}\).
Hemorrhage is thought to be related to the hyper / hypoperfusion found in PRES cases. It was found in 3 main patterns; punctate hemorrhagic foci, larger foci (Hematomas), or in the form of subarachnoid hemorrhage. Hemorrhagic events complicate around 15% of PRES cases. Notably, these events were found to be independent of blood pressure level at toxicity.  

METHODS

Study Population and their criteria
This study included patients who were diagnosed with Posterior Reversible Encephalopathy Syndrome (PRES) and had attended the MRI unit of the Radiology Department at El-Demerdash Hospitals, Faculty of Medicine, Ain Shams University in the period from January-2015 to May-2017.

The study inclusion criteria included the expression of the Known PRES imaging MR features with a presentation consistent with clinical neurotoxic syndrome. As the syndrome isn’t confined to a specific age group, no age group to be excluded from the study.

The study was done after approval of ethical board of Ain Shams university and an informed written consent was taken from each participant in the study.

Magnetic Resonance Imaging Settings and Protocol

MR imaging was performed with the 1.5-T ACHIEVA PHILIPS® MR unit using the SENSE NeuroVascular coil (SENSE-NV). With a slice thickness of 5 mm, inter-slice gap of 1 mm and a matrix of 256x256.

The used protocol basically consists of:
- Axial T1- weighted Gradient (GR) image (TR:130-150 ms, TE:1.8 ms with a flip angle of 80°).
- Axial T2- weighted SE image (TR:2500-4500 ms, TE:110 ms with a flip angle of 90°).
- Axial Fluid Attenuation Inversion Recovery (FLAIR) image (TR:6000 ms, TE:120 ms with a flip angle of 90°).
- Axial Diffusion-Weighted (DWI) SE image (TR:3000-3500 ms, TE:90-110 ms with a flip angle of 90°, b values taken at 0 and 1000 s/mm2).

According to the clinical suspicions, Additional sequences including Sagittal T1-weighted GR image, Axial T2*-weighted image, Contrast study, MR Arteriography (MRA) and Venography (MRV) were frequently added.

Image Analysis

All the images were assessed basically by the use of the Fluid Attenuation Inversion Recovery Sequence (FLAIR), this step includes the determination of PRES bilaterality and symmetricity, lobar distribution, and the detection of any basal ganglia or infra-tentorial involvement (brain stem and cerebellum).

White/Gray matter assessment included the detection of the location of the gray and white matter signal abnormalities.

For the sake of better characterization of the syndrome:
-Images were reviewed in conjunction with the diffusion images and its ADC maps; thus, areas of true restrictions can be easily recognized, providing a better characterization of the type of oedema present with PRES; whether vasogenic or cytotoxic.
- The T2* sequence images that are frequently available (12 patients) were used to detect the presence of haemorrhagic foci.
- The obtained MRA-MRV images was also analysed (available in 14 patients) looking for any existing/associated vascular anomalies.

Images were then reassessed for the overall pattern by which the PRES syndrome was expressed. According to the patterns available in the literature, cases were classified into four categories: Dominant parieto-occipital pattern, Holo-hemispheric watershed pattern, Superior frontal sulcus pattern, and Partial or asymmetric expression pattern.

The assessment of syndrome severity was done by using the severity scale adopted by McKinney and his colleagues, which aims to provide an imaging-based severity classification. Accordingly, the syndrome was classified into mild, moderate, and severe forms according to the following criteria:

-Mild PRES: cortical/sub-cortical oedema. Absent herniation, mass effect, and haemorrhage. Absent or minimal involvement of one of the infra-tentorial structures (brain stem or cerebellum) or the basal ganglia.

-Moderate PRES: confluent edema with deep white matter affection not reaching the ventricles. Mild mass effect from Parenchymal haemorrhage or edema without causing herniation or midline shift. Mild involvement of two of the infra-tentorial structures or basal ganglia.

-Severe PRES: confluent oedema reaching the ventricular margins. Parenchymal haemorrhage or edema causing herniation or midline shift. Involvement of the three groups at once (brainstem, cerebellum and basal ganglia).

This study was approved by the Ethics Board of Ain Shams University.
RESULTS

Patients that were diagnosed using MR Imaging as PRES in the years 2015, 2016, and till May 2017 were 17 patients. In most of the included patients, MRI was the only modality used to reach the diagnosis. PRES was identified in both Sexes, with the females constituting the majority of those patients (76%). Patients age was ranging from 52 days of life to 38 years (Mean: 17.4 yrs, SD: 11.4). The various clinical presentations encountered and the recognized associated factors are summarized below in Table 1.

Table 1: demonstrates the frequency of the various clinical presentations and associated/predisposing factors .

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical Presentation</th>
<th>Known Associated/ Predisposing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>F</td>
<td>Convulsions, Hallucinations</td>
<td>Nephrotic Syndrome relapse</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>M</td>
<td>Disturbed consc.</td>
<td>Nephrotic Syndrome, on Steroid, Severe HTN</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>M</td>
<td>Disturbed consc., Convulsions</td>
<td>ALL, on Chemotherapy</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>F</td>
<td>Lt. Side Weakness, Dysarthria, Sudden Blindness (Due to Retinal Detach.)</td>
<td>Known HTN before preg., Eclampsia (Controlled, using MgSO4)</td>
</tr>
<tr>
<td>5</td>
<td>17</td>
<td>F</td>
<td>Disturbed consc., Convulsions</td>
<td>Eclampsia &amp; HELLP Syndrome</td>
</tr>
<tr>
<td>6</td>
<td>37</td>
<td>M</td>
<td>Convulsions, Rt. Facial Palsy</td>
<td>HTN, Chronic Kidney Disease, HCV+ve</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>F</td>
<td>Convulsions, Fever (URT infx), Disorientation</td>
<td>SLE, HTN, DM, Renal Failure (on Dialysis), URT infection</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>F</td>
<td>Disturbed consc., Convulsions, Ascitis</td>
<td>Renal failure in transplanted kidney</td>
</tr>
<tr>
<td>9</td>
<td>21</td>
<td>F</td>
<td>Tonic-Clonic Seizures, Hemptysis and Anemia (from Renal Failure)</td>
<td>Autoimmune Vasculitis, Renal Failure, Plasmapheresis</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>F</td>
<td>Disturbed consc., Convulsions, Resp. Depression</td>
<td>P-E (BP: 150/100), Eclampsia, on Methydopa</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>F</td>
<td>Convulsions and coma for 3wks</td>
<td>Pyonephrosis</td>
</tr>
<tr>
<td>12</td>
<td>6</td>
<td>F</td>
<td>Disturbed consc., Blindness</td>
<td>Acute renal impairment, Hemodialysis (3 times), Hypertensive crisis</td>
</tr>
<tr>
<td>13</td>
<td>52 days</td>
<td>F</td>
<td>apnea and convulsions</td>
<td>Attacks of HTN secondary to steroid therapy (for facial congenital hemangioma)</td>
</tr>
<tr>
<td>14</td>
<td>36</td>
<td>F</td>
<td>Post-Histerectomy Collapse and Convulsion</td>
<td>Ruptured uterus Managed by Histerectomy, on Clixane for hypercoagulable state</td>
</tr>
<tr>
<td>15</td>
<td>11</td>
<td>F</td>
<td>Disturbed consc., Convulsions</td>
<td>Unknwon</td>
</tr>
<tr>
<td>16</td>
<td>8</td>
<td>M</td>
<td>Convulsions</td>
<td>Retro-orbital sarcoma on chemotherapy</td>
</tr>
<tr>
<td>17</td>
<td>25</td>
<td>F</td>
<td>Disturbed consc., Convulsions</td>
<td>P-E (HTN: 200/100), Eclampsia</td>
</tr>
</tbody>
</table>

Abbreviations: HTN, Hypertension; ALL, Acute Lymphocytic Leukemia; HCV, Hepatitis C Virus; SLE, Systemic Lupus Erythematosus; DM, Diabetes Mellitus; URT, Upper Respiratory Infection; P-E, Pre-Eclampsia; BP, Blood Pressure.

MRI features found in the patients were consistent with PRES. All of the patients had a supra-tentorial involvement. Associated infra-tentorial involvement was detected in 7 cases (41%).

For supra-tentorial involvement, almost all the cases were bilateral (94%), the only exception was a patient with a mild unilateral supra-tentorial occipital involvement, with a contralateral cerebellar involvement. In those bilateral cases, lesions were symmetrically distributed in 88% of them. Both parietal and occipital lobes were involved in the majority of cases (16 cases, 94%), however, pure parieto-occipital involvement was seen in one case only, another two cases were having an isolated parieto-occipital affection.
supra-tentorially, but with an additional infra-tentorial affection. A considerable temporal and frontal lobe involvement was recognized (71% and 76% respectively).

For infra-tentorial involvement, 6 patients were having cerebellar affection, one of them had an additional involvement in the pontine region, an additional seventh case was demonstrating a pontine involvement only. There was no recognized Medulla oblongata involvement at all.

The percentages of the patterns identified in this study based on the topographic distribution described above were as following: 35% were of the holo-hemispheric watershed pattern, 29% were of the dominant parieto-occipital pattern, 24% for the superior frontal sulcus pattern, and 22% were having partial or asymmetric expression pattern.

Regarding gray and white matter affection, Sub-cortical involvement was noticed in all of the cases, whereas cortical involvement was recorded in 94% of the cases.

Basal ganglia involvement was noted in 3 cases (18%). One of them demonstrated Globus pallidus involvement, the other showed a Lentiform nucleus involvement, while the third showed involvement of both Globus pallidus and Lentiform nuclei.

According to the extent of edema encountered, 8 cases (47%) had the mild form of PRES, 5 cases (29%) had PRES of moderate severity, while the rest of patients were of the severe type.

The T2* sequence was available in 12 patients (71%) of cases included, from which Micro-haemorrhages were detected in two (17%) of them.

Diffusion imaging and ADC maps revealed a true restriction in 9 patients (53% of the cases).

Angiographic profile was available in the majority of patients studied. Beading of both cerebral circulations was demonstrated in 3 patients of them (18%).

**DISCUSSION**

The intent of our work was to explore and recognize the common MRI features of PRES present in our society by the assessment of affected patients who attended the radiology department at El-Deemash Hospitals, Faculty of Medicine, Ain Shams University during the last two years.

The study included 17 PRES patients in whom a posterior, subcortical, vasogenic edema was the dominant feature. Till now, it is not completely understood why does the syndrome tends to dominate in the posterior regions, however, it is thought that this dominance is related to the presence of a lesser sympathetic supply over the posterior circulation in comparison with the anterior cerebral circulation, thus the regulatory mechanisms that helps preserving the brain tissue in the presence of hypertensive insults are less effective. A posteriorly dominant disease was noted in almost all the cases studied. Similar results have been reported previously.

The frontal lobe involvement documented in our study is similar to that documented previously by many authors. Temporal lobe involvement percentages reported in other studies are much diverse, they have ranged from 33% to total involvement in all the patients.

The patterns of PRES identified in our study were slightly different from those identified before. The predominant pattern seen in our study was the “Holo-hemispheric watershed pattern” which shows a much higher percentage. The least common pattern in our study was the “Partial or asymmetric expression” which was noted in a much lower percentage than result recorded by Bartsynski.

It is not well understood why does PRES present in these different patterns. Probably, being a multi-factorial process is reasonable. Since hypertension is one of the major PRES associations, the presence of an already diseased arteries should be kept in mind in addition to the normal arterial brain anatomic variants, though these factors haven’t yet been studied.

The anterior and posterior dominance which is seen in “superior frontal sulcus” and “dominant parieto-occipital” patterns respectively might be related also to the site of arterial affection, being related to hypo-perfusion with resultant affection of the presumably most vulnerable “distal posterior” circulation arteries, while anterior affection might be the result of proximal arterial affection rather than a distal hypoperfusion.

Regarding the clinical picture impact on these patterns, it is noteworthy that all of the patients who were sustaining an Eclampsic/Pre-eclampsic events were expressing the holohemispheric watershed pattern of PRES, which reflects the presence of generalized arterial changes rather than a posterior or anterior dominance in these patients.

Patients with renal impairment were tending to express either the dominant parieto-occipital or the superior frontal sulcus pattern. Though this category of patients tended to express these two distinct patterns, the correlation here is weak due to the diverse mechanisms that do exist.
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behind the different causes of renal impairment in those patients.

The difference in percentages in “partial or asymmetric” PRES is probably influenced in part by the recognition awareness of such atypical patterns which is sometimes challenging.

Despite the original description of PRES as a leukoencephalopathic disease, that’s to say, a white matter disease; gray matter affection was frequently noted even by the earliest studies. The presence of pure cortical affection may also occur. Although the later finding was considered as an atypical PRES presentation; in fact, studies on animal models have showed an earlier cortical involvement with a later subcortical spread, this was furtherly supported after the introduction and the increased utility of FLAIR which demonstrated a higher cortical involvement percentages among PRES patients. In our study, all the patients had subcortical lesions, that’s to say, no isolated cortical involvement with PRES was documented in our study. However, cortical involvement was recognized in the majority of the cases studied. Though it is easy to explain such a high percentage of cortical involvement theoretically, the finding in fact is much higher than the figures reported in the literature, with no reasonable clinical or radiological explanation yet.

Basal ganglia involvement was seen in three patients, similar results was noted by Casey and his colleagues, who document the affection in 3 cases also. The described pattern above shouldn’t confused with the central PRES-variant of the basal ganglia, as the later devoid of any cortical or sub-cortical affection, which is not the case in our study.

Whether the PRES lesions are symmetrically or asymmetrically distributed over both hemispheres; lesions should be present on both sides in order to fulfill the diagnostic criteria for diagnosing PRES. However, atypical PRES cases with a unilateral distribution was also reported. In our study, unilateral PRES was seen only in a single case in which there is a contralateral infra-tentorial affection, the rest of the cases showed the typical bilateral distribution feature that’s described for the syndrome. The majority of those bilateral cases were also symmetrically distributed, a result which is relevant to the range present in the literature.

Supra-tentorial involvement was recognized in all of the PRES patients included, in other words, no isolated brain stem, pons, spinal cord or cerebellar involvement do present. Nonetheless, associated infra-tentorial involvement was frequently noted in this study, most of which are of cerebellar one. Results are comparable to the results documented in the literature.

The severity of PRES was evaluated with regards to the extent of edema found. The assessment criteria was first used by Mckinney and his colleagues, who have adopted the criteria with respect to the prognostic reviews available. The classification is FLAIR-based, and it does simply classify PRES into a mild, moderate, or severe disease on the basis of edema extension, the presence of hemorrhage, mass effects, or herniation, and the presence of basal ganglia or infra-tentorial involvement. Percentages obtained in our study are relatively similar, and the largest portion of the cases are having a mild disease. Notably, all cases that were reported to have pontine or basal ganglia affection were falling under the “moderate” and “severe” syndrome categories.

Diffusion imaging and ADC maps demonstrated the typical DWI image with the increased ADC value described in the literature in around half of the cases, some of them also showed foci of increased SI in DWI with a low ADC values, which denoted the presence of true restriction in those foci. Overall, true restriction has been documented in more than half of the cases, which is much higher than the percentage found by Mckinney and his colleagues. This seems to be related to the severity of PRES at presentation; with the exception of one case of mild disease, true restriction was noted to occur only in cases under the “moderate” and “severe” syndrome categories.

The angiographic findings reported in the study goes with diagnosis of PRES. Some cases demonstrated beading of both anterior and posterior circulations.

PRES angiographic findings are widely variable, this include focal or generalized vasodilatation, vasoconstriction, or beading. However, other causes of beading like vasculitis should always be sought and excluded.

Regarding the clinical presentations that was commonly encountered, convulsions was the commonest and it was as common as described in the literature. However, visual disturbances were less commonly seen.

To our knowledge, the youngest age reported in the literature was a 10-month-old baby. In our study, the reported age was much younger, PRES was recognized in a 52 days old female baby, who had episodes of apnea and convulsions. Notably, the baby was hypertensive secondary to treatment with steroids, and the edema was of cytotoxic type rather than a vasogenic one. In such cases, hypoxic insults are
important to consider in our differential diagnosis, however, the imaging features goes more with PRES (including the dominant subcortical parieto-occipital affection, bilaterality, symmetry and reversibility).

A potential criticism in our study was the small sample size which could be unrepresentative. Another limitation to be acknowledged also in the study is the lack of documentation of some important notes like the frequently missing numerical documentation of blood pressure, and the absence of clinical data about reversibility. Nevertheless, the study has shed a light on the features of PRES that is present in our community, the patterns by which PRES is manifested, and their clinical correlations with the symptoms and signs that might be faced.

CONCLUSION

PRES is a clinico-radiological syndrome entity which represents a constellation of neurological symptoms with a radiological evidence of vasogenic edema which is predominant posteriorly.

Though many atypical PRES features were identified in the last years, many of the old concepts like posterior dominance, bilaterality and the dominant white matter affection are essentially still accepted for the majority of the cases.

The syndrome tends to be present in four different radiological patterns, namely: the Holohemispheric Watershed pattern, the Dominant Pareto-Occipital pattern, the Superior Frontal Sulcus pattern, and the Partial or Asymmetric pattern. These patterns may in fact reflect the different underlying mechanisms and etiologies by which PRES is mediated.

The radiological severity assessment of the syndrome classifies PRES patients into 3 categories: mild, moderate, and severe types. The assessment which can be easily done might become a good prognostic tool in the future. Further studies are recommended to decide whether the tool do truly have a role in anticipating the occurrence of complications or not.

REFERENCES


