Various Imaging Manifestations of Posterior Reversible Encephalopathy Syndrome (PRES) on Magnetic Resonance Imaging (MRI)

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Summary

Background: Posterior reversible encephalopathy syndrome (PRES), also called the acute hypertensive encephalopathy and reversible posterior leukoencephalopathy syndrome (RPLS), is a neurotoxic syndrome of cerebral vasoregulation classically characterized by bilaterally symmetrical parieto-occipital edema. However, the imaging findings are variable and may occur in other locations such as the frontal lobes, thalami, basal ganglia and brainstem. Most commonly, PRES presents with hyperintense signals on T2 and FLAIR sequences. Restricted diffusion and hemorrhage are rare. This study presents the typical and atypical manifestations of PRES on 3T MR images.

Material/Methods: It is a retrospective study analyzing a radiology report database and MR images of 92 patients with a clinical and radiological diagnosis of PRES. The brain MRI images of these patients were evaluated. The regions involved and the signal intensity of the affected areas on T1, T2, FLAIR and DW sequences were recorded. The location of the abnormal signal intensity as well as the presence or absence of atypical features such as diffusion restriction and hemorrhage were also recorded.

Results: The most commonly affected region was the parieto-occipital lobes (100%), however, other atypical regions involved were the frontal lobes (30.4%), temporal lobes (8.69%), basal ganglia (22%), cerebellum (17.39%), brainstem (9%) and thalamus (4%). Some of the cases showed restricted diffusion (43%) and hemorrhage (9%).

Conclusions: The involvement of the parieto-occipital, frontal and temporal lobes is common in PRES. Occasionally, there may be an involvement of the basal ganglia, cerebellum and brainstem, with or without hemorrhage and restricted diffusion. Radiologists should be aware of the typical and atypical imaging manifestations of PRES in order to make an accurate diagnosis.

MeSH Keywords: Diffusion Magnetic Resonance Imaging • Hypertension • Posterior Leukoencephalopathy Syndrome • Pre-Eclampsia

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hyperperfusion state with a breakdown of the blood-brain barrier leads to extravasation of fluid containing blood or macromolecules, resulting in cortical or subcortical edema [13–15]. Alternatively, some investigators have proposed vasospasm as the cause of reversible edema that progresses to cytotoxic edema if left untreated [16,17].

**Material and Methods**

It is a retrospective study analyzing a report database and MR images of 92 patients with a clinical and radiological diagnosis of PRES, included from September 2014 to February 2016. The brain MRI images of these patients were reviewed. These patients had undergone an MRI study of the brain on the Philips Ingenia 3T MRI scanner. The various regions involved were recorded. The signal intensity of the affected areas on T1, T2, FLAIR and DW sequences was recorded. The presence or absence of atypical features such as diffusion restriction and hemorrhage were also recorded. The data were analyzed and compared with the available literature.

**Technique**

The patients underwent MRI scanning in the Philips Ingenia 3 Tesla MRI scanner with a dedicated head coil. As it is a retrospective study of a radiology database, the patients had already undergone the necessary screening for the contraindications for MRI, and those with contraindications had been excluded.

The pulse sequences used were axial FLAIR (TE/TR =125/10000 msec; TI=2800 msec), T2 (TE/TR=80/3000 msec), T1 (10/2000 msec), DWI (TE/TR=120/3500 msec) and GRE (16/840 msec) sequences.

**Results**

The study population consisted of 92 patients of whom 8 were males and 84 females. The age range of the study population was from below 10 years to 65 years of age. Most of the patients (47.8%) were in the age group of 21 to 30 years followed by the groups of 11–20 years (30.43%) and 31–40 years (13.04%). There were 4 patients younger than 10 years (4.3%) and 4 patients older than 50 years (4.3%).

The presenting complaints of the patients were variable. The majority of the patients in our study (n=46; 50%) presented with peripartum/postpartum eclampsia. The children younger than 10 years had high blood pressure secondary to glomerulonephritis. Two adult patients presented with epilepsy. Nonspecific complaints of headache and blurring of vision were present in the rest of the patients.

The most commonly involved typical locations were the parieto-occipital lobes (n=92; 100%). This was followed by the frontal lobes (n=28; 30.4%), cerebellum (n=16; 17.39%; Figure 1) and temporal lobes (n=8; 8.69%). The other atypical regions involved were the basal ganglia in 22%, brainstem in 9% and thalamus in 4% of the cases, respectively.

Imaging features consisted of bilaterally symmetrical parieto-occipital white matter hyperintensities (Figures 2A, 2B, 3) in all the cases. Some cases showed atypical features such as hemorrhage and restricted diffusion. Hemorrhage was seen in 9% of the cases (Figure 4). Restricted diffusion was seen in 57% of the cases on DW images (Figure 5A). However, corresponding ADC images did not show significant hypointense signals as seen in cerebral infarcts (Pseudo normalization; Figure 5B). Follow-up imaging of 4 patients showed disappearance of restricted diffusion.

The severity of PRES was graded as per the grading system proposed by Mckinney et al. [18]. In our study, mild PRES was seen in 64 cases (69.5%), moderate PRES in 20 cases (21.7%) and severe PRES in 8 cases (8.7%), respectively.

**Discussion**

Posterior reversible encephalopathy syndrome (PRES), first described by Hinchey et al. in 1996 [19], is a neurotoxic syndrome occurring due to the susceptibility of the posterior circulation to variations in blood pressure. It is classically characterized by a symmetric parieto-occipital white matter edema. The imaging manifestations may vary and can include atypical locations and hemorrhage.

Clinical features of PRES range from headache, altered mental status, seizures and loss of vision to even loss of consciousness. The term describes potentially reversible imaging findings and symptomatology that is shared by a diverse group of diseases such as hypertension, glomerulonephritis, eclampsia, preeclampsia and drug intoxication.

**Pathogenesis [20]**

With respect to pathogenesis, the vascular theory of PRES is the most widely acceptable. The posterior circulation has a relatively sparser sympathetic innervation than the
carotid circulation. The cerebral blood flow is regulated by the dilatation and constriction of vessels, which maintains an adequate tissue perfusion. A rapid rise in blood pressure overwhelms the normal autoregulatory mechanisms, which leads to the dilatation and subsequent leakage of cerebral arterioles with resultant vasogenic edema. The breakdown of autoregulatory mechanisms is usually seen when the systolic blood pressure is in the range of 170–190 mmHg. However, it may also be seen at lower levels of the systolic blood pressure. PRES may also occur in chronic/untreated/
inadequately treated essential hypertension. Even though this theory proposes cerebral hyperperfusion as the cause of imaging abnormalities, some PET studies have actually shown cerebral hypoperfusion in PRES [20].

Another theory suggests a systemic inflammatory state causing endothelial dysfunction as the cause of PRES [21]. This theory is supported by the common association between PRES and systemic inflammatory conditions such as sepsis, preeclampsia, transplantation and autoimmune diseases. The occurrence of PRES even in the absence of any systemic inflammation contradicts this theory. Thus, the exact pathogenesis is still not completely understood.

Clinical features

In our study, 100% of the cases had hypertension. Scott W. Atlas [22] says that typical imaging findings should prompt the radiologist to alert the clinician to look for hypertension. Thus, the imaging findings of PRES, when present in classical locations, are diagnostic. Patients may present with headaches, seizures, visual changes, altered mental status and occasionally focal neurologic signs [4].

Age

In our study, most of the patients were in the age group of 21 to 30 years (47.8%). Four patients were in the age group of 10 years or younger. These patients had glomerulonephritis with resultant hypertension.

Pediatric PRES

Due to a low frequency of hypertension in the pediatric population, PRES has rarely been reported in children [23]. There are reports that suggest PRES in pediatric patients with renovascular diseases, immunosuppressive therapy, hematologic malignancies and systemic diseases such as leukemia, aplastic anemia, solid tumors and autoimmune diseases [21]. In our study, four children with the findings of PRES were encountered. All these patients had glomerulonephritis and elevated blood pressure at presentation. There was no malignancy in any of them. PRES should be considered in children presenting with encephalopathy, seizures, raised blood pressure or renal disease as a delay in making the diagnosis and initiating the treatment may result in a permanent neurological deficit [23].

Imaging features

The most commonly described abnormality in PRES consists of symmetrical cortical and subcortical hyperintense signals on T2 and FLAIR-weighted MR images in the parieto-occipital lobes of both hemispheres. These areas are frequently hypointense on corresponding T1-weighted MR images and have a decreased attenuation on CT scans. Similar areas of altered signal intensity can also be seen in other locations such as the frontal lobes, cerebellum, brainstem and basal ganglia [24]. The central variant of PRES with an isolated involvement of the basal ganglia and brainstem with no involvement of the subcortical white matter was seen in 4% of cases in the study by McKinney et al. In our study, the basal ganglia were involved in 22%, the brainstem in 9% and the thalamus in 4% of the cases,
respectively. However, all these cases had changes also in the typical locations such as the parietooccipital subcortical white matter of both brain hemispheres. The isolated central variant of PRES was not encountered in our study.

There may be a mild mass effect with sulcal effacement and mild contrast-enhancement in some cases. In our study, contrast-enhanced MRI was not performed in any of the cases. Patients, with hemorrhage showed a significant mass effect in our study. Mazamaesso et al. [35] have described atypical features of PRES with tumor-like appearance in two of their cases. One of them mimicked a cerebral hemorrhagic metastasis and the other a primary brain tumor. No such tumoral appearance was encountered in our study.

In PRES, magnetic resonance spectroscopy (MRS) may show a reduced NAA peak. The presence of a lactate peak indicates cerebral infarction, i.e. irreversible brain damage and unfavorable prognosis with respect to neurological recovery. However, Evertsen et al. [26] have reported a good outcome in a patient with PRES who had an elevated lactate peak. Similarly, Kwon et al. [27] have described 4 pediatric patients with elevated lactate peaks in the acute phase of PRES who had a complete remission on follow-up. This suggests that the presence of a lactate peak in PRES may represent an acute and reversible form of cerebral ischemia, the duration of which is not long enough to cause permanent cerebral damage. MRS was performed in only 12 cases in our study and none of them showed elevated lactate peaks.

McKinney et al. studied 76 confirmed cases of PRES with an involvement of the typical and atypical regions of the brain (Table 1).

<table>
<thead>
<tr>
<th>Location</th>
<th>McKinney et al. study (%)</th>
<th>Our study (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parieto-occipital</td>
<td>98.7</td>
<td>100.0</td>
</tr>
<tr>
<td>Frontal</td>
<td>78.9</td>
<td>30.4</td>
</tr>
<tr>
<td>Temporal</td>
<td>68.4</td>
<td>8.69</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>34.2</td>
<td>17.39</td>
</tr>
<tr>
<td>Thalamus</td>
<td>30.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Brainstem</td>
<td>18.4</td>
<td>9.0</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>11.8</td>
<td>22.0</td>
</tr>
</tbody>
</table>

Bartynski et al. [28] have described three major patterns of brain involvement in PRES. These include the holohemispheric watershed, the superior frontal sulcal and the dominant parietooccipital variants. Additional types of partial or asymmetric patterns of involvement are also seen [29].

**Diffusion restriction**

The use of diffusion-weighted imaging and ADC maps allows for an earlier and clearer differentiation between cytotoxic and vasogenic edema, which can predict the development of infarction [30].

Potentially reversible restricted diffusion, as an associated finding, has been described in PRES [31]. Benziada-Boudour et al. [32] demonstrated a case of PRES with foci of restricted diffusion that resolved on follow-up imaging with no neurological sequelae.

McKinney et al. [18] studied 76 patients with confirmed PRES, of whom 17.3% had restricted diffusion. Covarrubias et al. studied 22 patients, pf whom 27% showed restricted diffusion [33]. In our study, restricted diffusion was found in 43.4% of the cases. Only four of them underwent follow-up MRI which showed a complete resolution of the findings.

DWI and apparent diffusion coefficient (ADC) have been found to be helpful in differentiating between atypical presentations of PRES and other conditions such as central pontine/extrapontine myelinolysis, non-hemorrhagic infarcts and hypoglycemic or hypoxic encephalopathy. Due to the vasogenic edema in PRES, ADC shows increased values with slightly increased signal intensity on DWI, whereas the other conditions mentioned above show reduced ADC values due to cytotoxic edema [34].

**Hemorrhagic PRES**

The incidence of intracranial hemorrhage in PRES is approximately 15% [35]. The three distinct types of hemorrhage (minute hemorrhage, sulcal subarachnoid hemorrhage, and intraparenchymal hematoma) are identified in PRES with equal frequencies. The pathological mechanism is not well understood. It can be due to hypertension with hyperperfusion or due to vasculopathy with hypoperfusion.

Hefzy et al. studied 151 patients with PRES of whom 15.2% had hemorrhage. In our study, hemorrhage was seen in 9% of the cases and all these patients had preeclampsia.

**Bilateral symmetry**

In our study, 100% of the cases had almost symmetrical lesions in both hemispheres. Atypical unilateral presentations of PRES has also been described in the literature but were not encountered in our study.

**Severity**

Hinchey et al. [4] and McKinney et al. [18] have classified the severity of vasogenic edema in PRES on FLAIR Images. According to these authors, PRES is classified as:
Mild PRES

Defined as cortical or subcortical white matter edema without parenchymal hemorrhage, mass effect, herniation, or a minimal involvement of only one of the following structures – the cerebellum, brainstem or basal ganglia.

Mild PRES was seen in 42.1% of patients in the study by Alexander M. Mckinney et al. [18] and in 69.6% in our study.

Moderate PRES

Defined as confluent edema extending from the cortex to the deep white matter without extension to the ventricular margin, or mild involvement of two of the following structures – the cerebellum, brainstem or basal ganglia. A mild mass effect but no herniation or midline shift, particularly if parenchymal hemorrhage was present, was also classified as moderate.

It was seen in 35.5% of patients in the study by Mckinney et al. [18] and in 21.7% in our study.

Severe PRES

Defined as confluent edema extending from the cortex to the ventricle, or edema or hemorrhage causing midline shift or herniation. Alternatively, an involvement of all three of the following structures – the cerebellum, brainstem, and basal ganglia.

Severe PRES was observed in 22.3% of patients in the study of Mckinney et al. [18] and in 8.7% in our study.

Some conditions such as the cyclosporine and tacrolimus neurotoxic syndrome, SLE, Wegener’s granulomatosis and systemic sclerosis are known to present with a PRES-like appearance on MRI [32]. However in our study, no such specific predilection was found.

Angiography

The findings on cerebral angiography in PRES may vary from a normal appearance to vasospasm [19], dilatation, constriction or a string-of-beads appearance. The findings may be confused with vasculitis. In our study, only three patients underwent cerebral angiography and abnormal findings were not seen in them.

Differential diagnosis

The findings mimicking PRES may be seen in various neurological conditions such as cerebral infarction, cerebral venous sinus thrombosis, demyelinating disorders, metabolic disorders and encephalitis [36].

Infarction

In infarction, a sudden onset of neurological deficit with restricted diffusion on MRI is seen. The ADC values in acute infarction are low. In PRES, restricted diffusion is not very common. Even in those cases where restriction is seen, the ADC values are usually not as low as in infarction (Pseudo normalization).

Encephalitis

Viral encephalitides may present with similar imaging findings as PRES [37]. The involvement of the temporal lobe in PRES requires to be differentiated from HSV encephalitis. Herpes simplex encephalitis typically involves the limbic system – the temporal lobes, insula, subfrontal area and cingulate gyri. It may also involve the cerebral convexity and posterior occipital cortex in some cases. It is usually bilateral but asymmetric, with sparing of the basal ganglia [38]. In PRES, the most common regions involved are the parieto-occipital lobes with an almost symmetrical involvement in both hemispheres. Hemorrhage is common in HSV encephalitis and relatively infrequent in PRES. Follow-up MRI examinations reveal complete resolution of the findings in PRES, whereas there are residual sequelae such as gliosis in HSV encephalitis.

Cerebral venous thrombosis (CVT)

Parenchymal abnormalities in cerebral venous thrombosis resemble closely those of PRES. Venous thrombosis leads to a high venous pressure, which initially results in the vasogenic edema in the white matter of the affected area. When the process continues, it may lead to an infarction and the development of cytotoxic edema in addition to the vasogenic edema. Due to the high venous pressure, hemorrhage is seen more frequently in venous infarction [38].

The differentiation between a venous infarction and PRES is important because both conditions may present with hypertension in the clinical setting of preeclampsia/eclampsia and both have very similar imaging features. The absence of venous thrombosis and an almost symmetrical involvement of both cerebral hemispheres favors PRES [13,38,39].

Acute demyelination

Demyelinating plaques are usually elongated, oval regions with an increased water content, that are oriented perpendicular to the margins of the lateral ventricles. An “incomplete ring” may be seen in post-contrast studies in active demyelination [40,41]. If multiple sclerosis is suspected, MR imaging of the spinal cord may demonstrate additional lesions to help support the diagnosis [38].

As the involvement is symmetrical and subcortical in PRES, with the absence of the different stages of lesions, it can be easily differentiated from demyelination.

Metabolic derangements such as the dialysis disequilibrium syndrome, severe hypoglycemia, hypotension may present with similar imaging findings as PRES. However, history provides diagnostic clues.

Treatment

An adequate control of hypertension and removal of the offending agent is the treatment of choice. Most patients recover completely within 12–24 hours. In some patients, vasogenic edema may progress to cytotoxic edema with resultant infarction.
Conclusions

Posterior reversible encephalopathy syndrome presents with classical imaging manifestations of symmetrical parieto-occipital subcortical white matter hyperintensities in both brain hemispheres. Other locations such as the frontal lobes, basal ganglia, brainstem and cerebellum may also be involved. Radiological findings are typical and support the diagnosis. The radiologists should be aware of the atypical manifestations such as unusual locations, restricted diffusion, hemorrhage and unilateral atrophy.

References: