Imaging PRES syndrome: typical, atypical and follow up findings.

Poster No.: C-2361
Congress: ECR 2013
Type: Educational Exhibit
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Keywords: Neuroradiology brain, Emergency, CT, MR, Diagnostic procedure, Oedema
DOI: 10.1594/ecr2013/C-2361

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Learning objectives

1) Describe the CT and MR imaging findings of patients with typical and atypical PRES syndrome.

2) Review the radiological evolution.

3) Illustrate some differential diagnosis.
Posterior reversible encephalopathy syndrome (PRES) is a clinical radiographic syndrome of heterogeneous etiologies characterized by rapidly progressive signs and symptoms, including headache, seizures, consciousness disturbance, and/or visual disturbances.

Alternative terms such as reversible posterior leukoencephalopathy syndrome, hypertensive encephalopathy or reversible posterior cerebral edema syndrome are also used to describe this syndrome; although as we will see none of these names is completely satisfactory (it is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain).

1.- EPIDEMIOLOGY

Patients in all age groups appear susceptible; reported cases exist in patients as young as two years and as old as 90 years.

Case series suggest that PRES is more common in women, even when patients with eclampsia are excluded.

Hypertensive disorders, renal disease, and immunosuppressive therapies are risk factors for this disorder.

2.- PATHOGENESIS

It remains unclear, but it appears to be related to:

- **Disordered cerebral autoregulation** - normal autoregulation maintains constant cerebral blood flow by arteriolar constriction and dilatation. As the upper limit of cerebral autoregulation is exceeded, arterioles dilate and cerebral blood flow increases. The resulting brain hyperperfusion may lead to breakdown of the blood brain barrier allowing extravasation of fluid and blood products into the brain parenchyma.

- **Endothelial dysfunction** - especially in cases associated with preeclampsia or cytotoxic therapies. The latter may have direct toxicity on vascular endothelium, leading to capillary leakage and blood-brain barrier disruption. In preeclampsia, markers of endothelial cell dysfunction typically arise prior to the clinical syndrome and correlate better with the extent of cerebral edema than do blood pressure changes. Markers of endothelial cell dysfunction have also been reported in patients with PRES in other clinical
settings including chronic renal failure, lupus nephritis, and hemolytic uremic syndrome.

- **Other mechanisms** - uremia, sepsis, hypomagnesemia, and other metabolic disturbances have been implicated. These factors may mediate their effect on the vascular endothelium or other sites of vasogenic control. Fluid overload may also contribute to cerebral edema in some patients.

### 3.- ANATOMIC DISTRIBUTION

The combination of acute hypertension and endothelial damage results in hydrostatic edema which, if severe enough, will be radiographically evident. Unregulated vascular injury to blood-brain barrier endothelium leads to edema, protein extravasation, and fibrinoid necrosis. The cortex, structurally more tightly packed than the white matter, resists accumulation of edema, hence predilection of abnormalities to be seen in the white matter.

The primary involvement of posterior brain regions is not well understood. One possibility involves the regional heterogeneity of the sympathetic innervation of the intracranial arterioles, which is greater in the anterior circulation than posteriorly and has been shown to protect the brain from marked increases in blood pressure.

### 4.- ASSOCIATED CONDITIONS

A wide variety of medical conditions have been implicated as causes of this syndrome (Table 1 on page 6).

The most common are:

- **Hypertensive encephalopathy**: in acute, severe hypertension, PRES results from acute elevation of blood pressure beyond the upper limits of cerebral autoregulation. Rapidly developing, fluctuating, or intermittent hypertension carries a particular risk for hypertensive encephalopathy.

- **Eclampsia**: probably due to similar mechanisms as in hypertensive encephalopathy. Blood pressures in patients with preeclampsia and eclampsia who develop PRES are generally lower than in patients who develop it in other settings.

- **Immunosuppressive therapy**: the neurotoxic effects of these therapies are well known but still poorly understood. Toxic levels of medications are not required for the development of PRES. Patients may be normotensive, but the blood pressure is usually elevated over baseline. Cyclosporine is one of the more common cytotoxic therapies associated with PRES. After renal toxicity, neurotoxicity is the most serious side effect with cyclosporine, affecting 25 percent to 59 percent of transplant patients.

### 5.- CLINICAL MANIFESTATIONS

The clinical syndrome is characterized by:
• **Headaches** -> typically constant, nonlocalized, moderate to severe, and unresponsive to analgesia.

• **Altered consciousness** -> ranging from mild somnolence to confusion and agitation, progressing to stupor or coma in extreme cases.

• **Visual disturbances** -> Hemianopia, visual neglect, auras, visual hallucinations, and cortical blindness may occur. The funduscopic examination is often normal, particularly in eclamptic and chronically hypertensive patients, but papilledema may be present with accompanying flame-shaped retinal hemorrhages and exudates.

• **Seizures** -> are often the presenting manifestation. Seizures are usually generalized tonic clonic; they may begin focally and often recur.
### Medical Conditions Associated with PRES

- Hypertensive encephalopathy
- Eclampsia
- Inmunosppresive, inmunomodulatory and chemoterapic drugs
- Vasculitis
- Acute or chronic renal diseases
- Thrombotic thrombocytopenic purpura
- Hemolytic and uremic syndrome
- Porphyria
- Hypercalcemia, hypomagnesmia
- Blood transfusion
- Contrast media exposure

**Table 1:** Medical conditions associated with PRES.

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IMAGING FEATURES:

Although magnetic resonance (MR) is the best tool for the diagnosis, computed tomography (CT) can also be used satisfactorily.

At CT/MR imaging, the brain typically demonstrates focal regions of symmetric hemispheric edema predominantly of white matter, selectively involving the parieto-occipital regions of the brain (Fig. 1 on page 12, Fig. 2 on page 12 and Fig. 3 on page 13). In patients with extensive involvement other structures such as brain stem, cerebellum, basal ganglia, and frontal lobes can also be affected (Fig. 4 on page 14). Asymmetrical involvement is not unusual and at times the grey matter is also extensively affected.

Fig. 1: Typical PRES findings in a 60 year-old-woman with acute myeloid leukemia in complete remission after autologous stem cell transplantation. On admission she presented with vertigo, ataxia, dysartria and seizures. Non-contrast enhanced brain
CT (A, B) shows bilateral hypodensities in the occipital areas. Axial T2 (C, D) and coronal FLAIR (E, F) MR images show multiple and bilateral areas of white matter hyperintensities in fronto, temporo, parieto, occipital areas. Contrast-enhanced FFE-T1 MR images (G, H) show no pathologic contrast enhancement. DWI and ADC maps (I, J) show no restricted diffusion but T2 shine through effect. Follow up MR (K-N) one month after the initial study demonstrates complete resolution of the lesions.

**References:** Severo Ochoa - Leganes/Madrid/ES

The lesions of posterior encephalopathy are best visualized with magnetic resonance (MR) imaging, which is able to show even small lesions. In a conventional MR study the lesions are usually isointense to hypointense on T1 weighted images, and hyperintense on T2 weighted images. Lesions shown on MR are better demonstrated on fluid attenuated inversion recovery (FLAIR) imaging. In this technique, with nulling of the ventricular and subarachnoid cerebrospinal fluid (CSF) signal, the parenchymal edematous lesions (especially those in the cerebral cortex) show up better than on conventional T2 weighted images.

Echo-planar diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) maps help in differentiating posterior encephalopathy syndrome from ischaemic events such as "top of basilar syndrome" which produces bilateral occipital infarctions (Fig. 5 on page 15 and Fig. 6 on page 16). In acutely infarcted areas of the brain water becomes trapped intracellularly, and its motion is restricted. The decreased water diffusion is characterised by marked hyperintensity on DWI and hypointensity on ADC maps. Conversely, in PRES the regions of vasogenic edema are visualised as a hypointense or isointense signals on DWI and as markedly increased signals on ADC maps compared with normal brain tissue.
**Fig. 5:** Bilateral posterior cerebral artery infarctions. Brain CT scans (A, B) show hypodense lesions in the white matter of the parieto-occipital lobes. Coronal FLAIR (C, D) and axial T2 (E, F) images show hyperintense lesions in the white matter of the parieto occipital areas. DWI and ADC map (E, F) show restricted diffusion.

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Focal areas of restricted diffusion (likely representing infarction or tissue injury with cytotoxic edema) are uncommon and may be associated with an adverse outcome (Fig. 7 on page 17). Hemorrhage (focal hematoma, isolated sulcal/subarachnoid blood, or protein) can be seen in approximately 15% of patients (Fig. 8 on page 18).
Fig. 8: Typical PRES findings with hemorrhage. (A, B) Axial and coronal FLAIR images shows extensive, bilateral, white matter hyperdense lesions in fronto, temoro parietal regions. (C, D) Axial FLAIR and Axial T2 at the level of the protuberance shows diffuse hyperdensity of the pons and a focal lesion in the right pons consistent with hemorrhage. (E-H) Follow up MR shows marked decrease in the extension of the lesions previously described.

References: Hospital Niño Jesus - Madrid/ES

Gyriform signal enhancement, reflecting disruption of the blood-brain barrier, can be present following the administration of gadolinium (Fig. 2 on page 12).

With treatment, resolution of findings on neuroimaging within days to weeks is expected.

The neuroimaging differential diagnosis of PRES include neoplasms (Fig. 9 on page 19), encephalitis, inflammatory and infectious processes, demyelinating pathology (Fig. 10 on page 20) and cerebrovascular accidents.
Fig. 10: Demyelinating disorder. Axial FLAIR (A), CORONAL T2 (B) ADC (C) and DWI (D) MR images. Hyperintense diffuse lesion in the white matter of periventricular and subcortical white matter of posterior regions. No restricted diffusion.

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Fig. 1: Typical PRES findings in a 60 year-old-woman with acute myeloid leukemia in complete remission after autologous stem cell transplantation. On admission she presented with vertigo, ataxia, dysartria and seizures. Non-contrast enhanced brain CT (A, B) shows bilateral hypodensities in the occipital areas. Axial T2 (C, D) and coronal FLAIR (E, F) MR images show multiple and bilateral areas of white matter hyperintensities in fronto,temporo, parieto, occipital areas. Contrast-enhanced FFE-T1 MR images (G, H) show no pathologic contrast enhancement. DWI and ADC maps (I, J) show no restricted diffusion but T2 shine through effect. Follow up MR (K-N) one month after the initial study demonstrates complete resolution of the lesions.

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Fig. 2: 8 year-old-boy. Acute lymphoblastic leukemia and stem cell transplantation. Axial FLAIR (A,B) MR images show marked and diffuse hyperintensity of the left cerebellum and bilateral hyperintensity of parietal and occipital lobes. Coronal FLAIR (C) MR image shows hyperintensity of both parietal lobes, left temporal lobe and left cerebellum. FFE-T2* (D) shows hemosiderin deposit in the left cerebellar hemisphere. Post-contrast FFE-T1 MR image (E) shows mild leptomeningeal enhancement. ADC map (F) shows no restricted diffusion. Follow-up MR two months after admission (G-I) shows complete resolution of the lesions.

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Fig. 3: 7 year-old-girl. Acute lymphoblastic leukemia with stem cell transplantation. Axial FLAIR MR images (A,B) show an area of cortical and subcortical hyperintensity in both occipital lobes that show no restricted diffusion in ADC maps (C,D).

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Fig. 4: PRES. Atypical presentation in a 40 year-old-man with hypertensive emergency. Non-contrast brain CT (A, B) shows swelling and marked hypodensity of the pons. Axial T2 (C, D) and coronal FLAIR images (E, F) show marked hyperintensity of the pons, superior and middle cerebellar peduncles, cerebral peduncles, bilateral diffuse hyperintenssity of the periventricular white matter and external capsules. DWI and ADC maps (G, H) show no restricted diffusion. Follow up study 5 months after the initial one (I-L) demonstrates marked resolution of the lesions.

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Fig. 5: Bilateral posterior cerebral artery infarctions. Brain CT scans (A, B) show hypodense lesions in the white matter of the parieto-occipital lobes. Coronal FLAIR (C, D) and axial T2 (E, F) images show hyperintense lesions in the white matter of the parieto-occipital areas. DWI and ADC map (E, F) show restricted diffusion.

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**Fig. 6:** Basilar top infarction. Non-enhanced brain CT scan on admission (A,B) shows sulcal effacement and bilateral hypodensities in both posterior occipital lobes. Non-enhanced brain CT one day after the previous one (C,D), shows more marked hypodensities and a small area of high attenuation adjacent to the atria of the lateral left ventricle consistent with hemorrhage. Follow up non-enhanced brain CT scan 15 days after admission (E,F) shows frank hemorrhagic transformation in both occipital lobes.

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Fig. 7: PRES with brain ischemia as complication in a 51 year-old woman who presented left hemiparesis and high blood pressure levels. Non-enhanced brain CT scan (A) shows cortico-subcortical hypodensity on the left occipital lobe. Axial FLAIR (B) and axial T2 (C) MR images show cortico-subcortical hyperintensities in the left and right occipital lobes. DWI and ADC (D, E) show restricted diffusion that suggests evolution to brain ischemia.

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**Fig. 8:** Typical PRES findings with hemorrhage. (A, B) Axial and coronal FLAIR images shows extensive, bilateral, white matter hyperdense lesions in fronto, temoro parietal regions. (C, D) Axial FLAIR and Axial T2 at the level of the protuberance shows diffuse hyperdensity of the pons and a focal lesion in the right pons consistent with hemorrhage. (E-H) Follow up MR shows marked decrease in the extension of the lesions previously described.

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**Fig. 9:** Gliomatosis cerebri. Non-enhanced brain CT scan (A-D) shows diffuse hypodensity of the white matter of the cerebellum and temporoparietal lobes. Axial T2 (E, F), axial FLAIR (G, H) and coronal FLAIR (I,J) images show diffuse hyperintensities of the white matter of the posterior fossa, pons, basal ganglia and periventricular white matter. ADC map (K) shows no restricted diffusion.
Fig. 10: Demyelinating disorder. Axial FLAIR (A), CORONAL T2 (B) ADC (C) and DWI (D) MR images. Hyperintense diffuse lesion in the white matter of periventricular and subcortical white matter of posterior regions. No restricted diffusion.

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Conclusion

- Posterior reversible encephalopathy syndrome (PRES) is a neurologic syndrome defined by clinical and radiologic features.

- PRES most often occurs in the setting of hypertensive crisis, preeclampsia, or with cytotoxic immunosuppressive therapy; however, many other clinical settings are described.

- Typical MRI findings are consistent with vasogenic edema and are predominantly localized to the posterior cerebral hemispheres. DWI can be helpful in distinguishing PRES from stroke.
References


