Radiologic Features and Pathophysiology of Posterior Reversible Encephalopathy Syndrome (PRES): Controversy Goes on

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Our Patient: Mrs. A

- This is a 36 y.o. female who presented to the hospital with 4 weeks history of muscle tenderness, weakness and rash. Two days later, she developed seizure; she had nystagmus to left, head deviation to left, and left sided clonic jerking. She became nonresponsive and was intubated.

- PMH: Unremarkable

- FH: Mother rheumatoid arthritis

- Social history: Tobacco, alcohol use: none

- Medication: Azithromycin
Our Patient: Mrs. A (cont’d)

- **PHx:**
  - **Vitals:** BP182/111 was noted on the day of seizure
  - **Skin:** Diffuse maculopapular rash on the dorsum of hands, shoulders, back, chest, buttocks and thighs.
  - **NEURO:** Opens eyes to voice. Agitated and biting tube. Not following any commands. Babinski: extensor on the right side.

- **Labs:**
  - CK 22940, AST 288, ALT 1163, aldolase 76.5, Anti-Jo1 -ve

Further workup plans?
Neuroimaging in Seizure

CT

- Preferred in emergency settings
  - Intracranial mass
  - Hemorrhage
  - Large stroke
- MRI contraindicated (Pacemakers, aneurysm clips)

MRI

- In other settings, MRI is preferred over CT
Recommended Routine MRI Sequences in Epilepsy

- **T1-weighted**
  - Differentiation of gray and white matter

- **T2-weighted**
  - Sensitivity for brain pathology

- **Fluid-attenuated inversion recovery (FLAIR) sequence**
  - Picks up T2-high lesions in areas close to CSF
Our Patient: Head CT

- Axial head CT w/o contrast appeared almost normal
- Slightly hypodense foci in bilateral posterior occipital lobes (arrows)
Our Patient: Brain MRI

- Axial T2-weighted images showed hyperintense foci in bilateral occipital lobes (arrows)
- White matter was predominantly involved
- Cortex was relatively spared
Our Patient: Brain MRI

- Hyperintense lesions were also seen on axial FLAIR, corresponding to T2 high areas (arrows)

- FLAIR suppresses CSF signal – makes it easier to see lesions by the brain surface
Our Patient: Brain MRI

- On axial diffusion weighted imaging (DWI), no restricted diffusion was seen
- No stroke

PACS BIDMC
Our Patient: Summary of Imaging Findings

- Bilateral CT hypodense areas in posterior occipital lobes
- Hyperintense on T2WI, with white matter predominance
- Hyperintense on FLAIR
- No restricted diffusion
Our patient: Differential Diagnosis

- Posterior reversible encephalopathy syndrome (PRES)
- Venous thrombosis
- Encephalitis
- Vasculitis
- Demyelinating diseases
- Stroke

CSF findings:
- WBC 1, RBC 7, TP 36, Glucose 122

MR venography -ve

Could not be ruled out...

Atypical presentation, oligoclonal band, IgG index, HIV, JCV all -ve

No restricted diffusion
Posterior Reversible Encephalopathy Syndrome (PRES)

- A neurological syndrome characterized by radiologic findings of focal vasogenic edema usually in the posterior cerebral hemispheres

- Possibly heterogeneous disorder, associated with a number of conditions such as preeclampsia, hypertension, immunosuppressive therapies and autoimmune diseases

- Clinical manifestations include headache, mental alteration, seizure and visual disturbances
PRES: Underlying Conditions

- Acute hypertension (acute renal failure etc.)
- Preeclampsia
- Immunosuppressive therapies (most commonly cyclosporin or tacrolimus)
- Others
  - Autoimmune disorders
  - Infection
Companion Patient 2: MRI Findings in PRES

- Increased signal on axial T2-weighted images (arrows)

- Water appears bright on T2WI – suggests the presence of edema

- Lesions are typically seen in the white matter of posterior parietal and occipital lobes, but cortex is also affected
Companion Patient 2: MRI Findings in PRES

- Increased signal on axial fluid-attenuated inversion recovery (FLAIR) sequence (arrows)

- FLAIR suppresses CSF signal – lesions can be better defined with FLAIR than with T2WI
Companion Patient 3: MRI Findings in PRES

- Low-normal signal intensity on axial DWI (arrows)

- Increased signal on axial apparent diffusion coefficient (ADC) mapping (circles)

Companion Patient 4 and 5 MRI: Varying Brain Regions Can Be Involved


<table>
<thead>
<tr>
<th>Location</th>
<th>% of cases</th>
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<tbody>
<tr>
<td>Parieto-occipital lobes</td>
<td>94%</td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>77%</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>64%</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>53%</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>34%</td>
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<tr>
<td>Brainstem</td>
<td>27%</td>
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Pathogenesis of PRES

- Vasogenic brain edema (as opposed to cytotoxic edema in stroke)

- The cause of brain edema is still controversial

- Hyperperfusion vs. Hypoperfusion

- Endothelial dysfunction
Cerebral Blood Flow Autoregulation

CBF is kept constant in normal range of BP

Once BP exceeds the limit, CBF begins to rise
Companion Patient 6 MRI: Hypertension-Hyperperfusion

- Hypertension that exceeds the capacity of normal brain autoregulation results in passive dilation of capillary beds, breakdown of blood-brain barrier, and subsequent fluid extravasation.

- Pros:
  - 50-70% of patients with PRES are severely hypertensive.
  - Hyperperfusion was seen on single photon emission computed tomography (SPECT) in some cases.

Axial T2-weighted image (left) and SPECT of the same patient during (middle) and after (right) the disease course, red areas showing increased perfusion.

Mechanism of Parieto-Occipital Predominance

- Sympathetic nervous system is responsible for the cerebral autoregulation by modulating vascular tones

- It was suggested that posterior regions of the brain including occipital lobes have less sympathetic tone than other areas of the brain
Companion Patient 7, 8: MR angiography and SPECT Hypoperfusion- Endothelial Dysfunction

- However, about 20% of patients with PRES are normotensive
- Endothelial dysfunction, and possibly subsequent hypoperfusion might account for these cases
- Autoimmune disorders were found in 45% of patients with PRES in one study (Fugate et al, 2010)
- Vasoconstriction, hypoperfusion and even ischemia were seen in some cases

“Beadling” of vessels (vasoconstriction) Hyperintensities on FLAIR Hypoperfusion shown on SPECT (Dark-blue areas)

3D TOF MRA from companion patient 7 (left), axial FLAIR MRI (middle) and SPECT (right) of companion patient 8. From Bartynski WS. AJNR Am J Neuroradiol. 2008 Jun;29(6):1036-42.
Summary: Pathogenesis of PRES

Underlying conditions (Autoimmune disease, Immunosuppressive agents, infection)

Endothelial damage
T cell activation
Cytokine release

Endothelial damage
T cell activation
Cytokine release

Endothelial activation
Vasoconstriction

Brain Edema

BBB breakdown

Hyperperfusion

Hypoperfusion
VEGF production
Vascular permeability

Acute hypertension
Preeclampsia
PRES: Treatment & Prognosis

- Usually reversible condition if treated promptly

- Correct the underlying conditions: Anti-hypertensive medication such as labetalol, nicardipine and nitroprusside should be given if hypertensive

- In eclampsia, immediate delivery of the fetus and placenta is sufficient

- Seizures usually respond to phenytoin except in eclampsia, in which case magnesium is better
Our Case: Resolution

- Mrs. A was treated with steroid pulse and IVIG, and her rash, weakness and CK subsequently improved.

- Her seizure was treated with phenytoin, which was later switched to levetiracetam. Her blood pressure was managed with labetalol. 5 days after the event, she was able to follow commands and her muscle strength improved.
Companion Patient 9: Mr. B

A 84 y.o. male who suffered subarachnoid hemorrhage 5 days ago
Companion Patient 9 Mr. B: MRI

- Hyperintense foci in bilateral occipital lobes on axial T2WI
- Also hyperintense on axial FLAIR
Companion Patient 9 Mr. B: MRI

- Restricted diffusion on axial DWI (arrows)

- Stroke
Future Directions

- The pathogenesis of PRES is unknown
- Currently multiple mechanisms are suggested, including hypertension-hyperperfusion, hypoperfusion, endothelial dysfunction or possibly all of them
- PRES is associated with aberrant immune activation as well as hypertension, implying that endothelial dysfunction may be the core mechanism rather than hypertension, as classically suggested
- Better clarification of the underlying mechanism and more advanced imaging techniques might be of help in the treatment and assessment of prognosis in PRES
References


- Terry A Neill, J Claude Hemphill, III. Reversible posterior leukoencephalopathy syndrome. UpToDate. Viewed 04/10/2011

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