

## PRES and PLEDs: An Uncommon Association

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### Abstract

Posterior reversible encephalopathy syndrome (PRES) or reversible posterior leucoencephalopathy syndrome is a relatively new entity having been described first in 1996 by Hinchey. The most common manifestations of this syndrome are headache, visual defects, altered sensorium and frequently seizures. EEG in these patients shows a diffuse slowing of waves- theta or delta waves are seen. Focal EEG pathologies may be seen in cases with focal seizures. Seizure activity recorded may also include focal or generalized spikes, spike wave pattern or sharp spikes. We present our case who presented with myoclonic seizures, and not with the usually expected generalized tonic clonic seizures. Besides, the myoclonic jerking persisted beyond 24 hours, and this is usually unexpected. Most patients become seizure free spontaneously or within 24 hours of the onset of antiepileptic medicines. Also, chronic kidney disease is not a commonly considered cause of PRES. Most patients of chronic kidney disease that develop this syndrome are on dialysis. The patients usually do not show periodic lateralized epileptiform discharges. Our patient showed PLEDs in her EEG. And in our review, only one report was found of a patient having developed epilepsy after PRES. That patient however had recurrent PRES, while our patient had the first episode of PRES.

**Keywords:** Encephalopathy; Hyperintensity; Sensorium; Epilepsy

### Introduction

Posterior reversible encephalopathy syndrome (PRES) or reversible posterior leucoencephalopathy syndrome is a relatively new entity having been described first in 1996 by Hinchey. The most common manifestations of this syndrome are headache, visual defects, altered sensorium and frequently seizures. The radiological features like edema occur in many areas like brainstem, cerebellum and other cerebral areas, but almost always in the posterior region [1].

### Case

The patient, a 74 year old female, known case of diabetes, hypertension, coronary artery disease and chronic kidney disease (not initiated on dialysis) presented to the hospital with history of altered sensorium. At presentation, the patient had a high blood pressure of 200/110. The patient, in altered sensorium was initiated on infusion of nitro-glycerine. The biochemical investigations were significant for azotemia. Electrolytes were within normal range. MRI was done that showed T2/FLAIR hyperintensity in central midbrain, pons showing no diffusion restriction/blooming in SWI images. T2/FLAIR hyper intensities were seen in bilateral periventricular, frontal, occipito-parietal cortical and subcortical white matter. Findings were suggestive of hypertensive posterior encephalopathy syndrome. Despite control of blood pressure, the patient continued to be in altered sensorium. A few abnormal jerks were noted. The patient had been found to have non convulsive myoclonic seizures. EEG showed a background activity consisting of bilaterally symmetrical and synchronous 5-7 Hz theta activity intermixed with beta activity. Periodic lateralized high amplitude sharp and slow wave discharges were seen. Sleep and photic stimulation shows continued activity. She was started on injectable antiepileptic drugs (levetiracetam 500 mg twice a day)

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where after her myoclonic jerks settled in 2-3 days and she became better with improved sensorium. On review in OPD, her EEG was normal. However, her antiepileptic needed to be continued to maintain her seizure free.

## Discussion

PRES usually manifests with headaches, altered sensorium, visual disturbances or seizures. The severity of the manifestation of these symptoms can vary. The visual symptoms can range from blurring of vision to cortical blindness. Change in the sensorium may vary from mildly confused or agitated state to comatose state. The seizures may be of the generalized clonic tonic type and often patients have status epileptics. Non convulsive seizures may be known in the form of staring look, eye blinking and head turning and should be suspected if the patient has a prolonged period of psychogenic states [2]. In a series, majority of the patients were found to have grand mal seizures (single, serial or recurrent episodes). In the series the patients were found to have seizures not lasting more than the first day. Seizures are seen soon after the onset of the syndrome. The seizures may terminate spontaneously or under therapy [3]. Other symptoms may be present in the form of nausea, vomiting, paresis and brainstem deficits [2].

The most important predisposing factor is hypertension, but not always. Usually the peak systolic blood pressures may range between 170 to 190 mm Hg. However, PRES is also known in patients with normal or mildly elevated blood pressure [2]. It is often noted in patients with eclampsia, transplantation-solid organ and allogenic bone marrow, autoimmune conditions and thrombotic thrombocytopenic purpura. It has also been noted in patients with chemotherapy (e.g. cyclosporine and tacrolimus), sepsis (multiorgan dysfunction syndrome and systemic inflammatory response syndrome) and shock. Autoimmune conditions (like systemic lupus erythematosus, systemic sclerosis, Wegeners and polyarteritis nodosa) are also known risk factors to PRES. It has been variably involved with various other conditions like Guillain Barre syndrome, dyselectrolytemia (hypomagnesemia, hypercalcemia), dialysis related, erythropoietin related and so on [4].

Recurrent PRES is known in systemic hypertension after bone marrow transplant, sickle cell disease, recurrent sepsis, infections and autoimmune diseases [4].

The neuroradioimaging shows focal symmetric regions of edema in the cerebral hemispheres, most commonly involving the parietal and occipital lobes (94%) but also affecting the other lobes like the frontal lobe [4] (77%), temporal lobe (64%) [1] And even the basal ganglia, brainstem and cerebellum [4] (53%) [1] And deep white matter. These areas are companion lesions. These lesions can lead to hydrocephalus and brainstem compression. As the edema increases, the lesions become confluent. The pattern is similar to the brain watershed area. The cortex, sub cortex, deep white matter may also be affected [4]. The pattern variants encountered are primary parietal-occipital, superior frontal sulcal and holohemispheric [5]. They divide the lateral and the medial hemispheric supply. The expression of PRES may range from diminutive to extensive forms. Patterns that are asymmetric or partial or mixed may also be seen. Hemorrhages may be seen in a few patients [4]. Diffusion weighted MRI shows isointense appearance, not hypointense signals. T2 weighted images reflect vasogenic edema and have increased intensity due to T2 prolongation effect also called T2 "shine though" effect [1].

Cerebellar lesions are commonly seen in patients with autoimmune disorders while in patients afflicted with sepsis, cortical involvement is more commonly seen [1].

EEG in these patients shows a diffuse slowing of waves- theta or delta waves are seen. Focal EEG pathologies may be seen in cases with focal seizures [3]. Seizure activity recorded may also include focal or generalized spikes, spike wave pattern or sharp spikes [6].

The pathophysiology remains elusive. There are several theories proposed. One theory is that development of high blood pressure over a short period of time results in breakdown of the cerebral auto regulation. This is more common in the posterior area due to relative lack of sympathetic innervations. The breakdown of auto regulation results in hyper fusion resulting in extravasation of fluids and proteins. Second theory revolves around endothelial dysfunction that results in conditions like sepsis, pre-eclampsia, and eclampsia. Third theory proposed the possibility of ischemia, secondary to vasospasm as a cause [1].

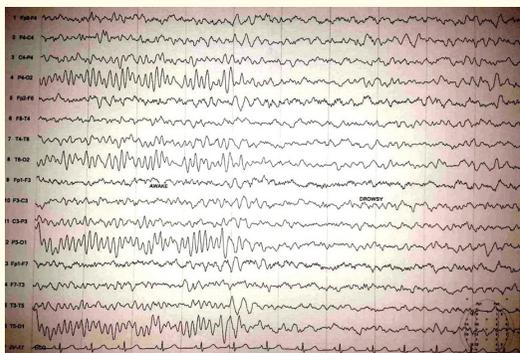
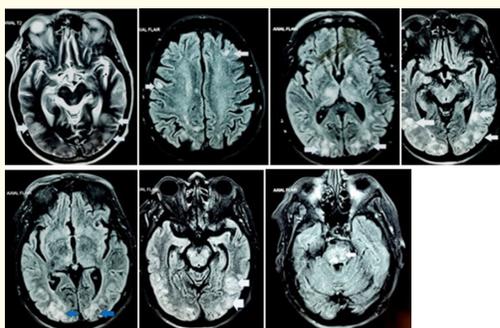
PRES when evaluated early on biopsy or autopsy shows vasogenic edema in areas paralleling MRI findings. Inflammation, neuronal damage or ischemias are not seen. Still, scattered macrophages or lymphocytes and reactive astrocytes are frequently seen. Demyelination and myelin pallor may be seen in late cases along with evidence of white matter ischemia, neuronal damage, or old hemorrhages. Vessel injury has been documented as intimal thickening or dissection, vessel narrowing or thrombus [4].

PRES is a reversible if appropriate therapy is administered at an appropriate time. The syndrome may resolve completely over several days to weeks and the syndrome can be fatal. Treatment with antihypertensives and antiepileptics and withdrawal of any offending agent is the treatment of choice [1]. In a multicentre retrospective cohort study, three independent factors were identified that were associated with 90 day functional outcome assessed by Glasgow outcome scale. Time to control of the causative factor, control of blood pressure and avoidance of hyperglycemia were the associated features detected. However, hyperglycemia may be associated due to the brain injury resulting in hyperglycemia [5]. Corticosteroids should theoretically improve the vasogenic edema, but there is no evidence for their use [1].

**Conclusion**

Our patient had myoclonic seizures beyond 24 hours. She was a case of chronic kidney disease but not on dialysis. And her EEG showed PLEDs. She also needed continued antiepileptic therapy. In our review, only one report was found of a patient having developed epilepsy after PRES. That patient, unlike our patient, had recurrent PRES [7].

Prolonged altered sensorium should be evaluated with an EEG. One should be aware of the possibility of PLEDs and recurrent seizures in PRES needing antiepileptic therapy. Possibility of epilepsy as a long term sequel of PRES needing continued antiepileptic therapy in recovered patients needs to be considered.



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