EDITORIAL

Posterior Reversible Encephalopathy Syndrome: Not Always Posterior, Not always Reversible

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Reversible Posterior Leukoencephalopathy Syndrome (RPLS)[1] is classically characterised by rapid onset of neurological symptoms like headache, altered sensorium, convulsions and visual disturbances coupled with neuro-imaging findings of symmetrical parieto-occipital oedema. Described by Hinchey et al in 1996, (though case reports with features of RPLS were already published),it has been also referred by various other terminologies as Posterior Reversible Encephalopathy Syndrome (PRES), Brain capillary leak syndrome, APPLE (Acute Predominantly Posterior Leuko encephalopathy syndrome), although none of the above names are completely satisfactory. Some cases are not confined to posterior region or white matter of brain, neither it is always reversible.

RPLS is seen in various etiologies like chronic hypertension, chronic and acute renal failure, eclampsia, pre-eclampsia, immunosuppressive drugs use like cyclosporin and tacrolymus, Hemolytic Uremic Syndrome(HUS), Systemic Lupus Erythematosus (SLE). They present with similar clinical and radiological features. Clinical signs may include acute onset of headache, visual disturbances, seizures and altered sensorium.[2] Majority of patients have high blood pressure on presentation although some may have normal or mildly elevated blood pressure.

The patho-physiology of PRES remains unproven and controversial. The most popular hypothesis remains the breakdown of auto-regulation of cerebral blood flow in the event of abrupt increase in blood pressure.[3] Blood flow to brain is regulated by arteriolar constriction and dilatation over a range of blood pressure. Breakdown of auto-regulation occurs above a mean arterial blood pressure of 160 mm hg; it may break down at higher blood pressure in cases of chronic hypertension. The rate of increase in blood pressure also plays an important role. Uncontrolled hypertension leads to hyperperfusion which in turn damages blood brain barrier. It also causes extravasation of fluids and blood products into the brain parenchyma leading to vasogenic brain oedema. However, breakdown of auto-regulation theory cannot explain PRES in the absence of hypertension.

Endothelial dysfunction has also been implicated in causing PRES.[4] Systemic inflammatory state as seen in sepsis, eclampsia, auto-immune diseases causes endothelial dysfunction. When blood pressure increases, it results in arteriolar constriction which increases endothelial dysfunction causing tissue hypoxia and vasogenic oedema. Specially in cases of eclampsia-markers of endothelial dysfunction like lactate dehydogenase and dysmorphic red blood cells are commonly seen. Secretions of trophoblastic cytotoxic factors from poorly perfused fetal unit may provide the initial stimulus. Markers of endothelial cell dysfunction have also been reported in patients with RPLS in other settings like SLE, chronic renal failure, HUS, etc. Both the hypotheses have their drawbacks, hence more research is warranted in understanding of patho-physiology of PRES.

The clinical signs and severity varies and may not necessarily correlate with radiological involvement. Patients may be comatose or just have mild confusion or agitation.[3] Visual disturbances may range from blurred vision to cortical blindness. In seizures, mostly tonic clonic are common. Convulsive and non-convulsive status epilepticus that may be refractory to multiple agents are also encountered. Headache is usually constant, non-localised, moderate to severe and un-responsive to analgesia. A wide variety of etiologies like acute hypertensive episodes, eclampsia, immune suppressive and chemotherapeutic agents, vasculitis, acute or chronic renal failure, porphyria, contrast media exposure has been implicated. Hence increased suspicion of PRES in such cases will be helpful.

Though MRI is the gold standard for diagnosis,[4,5] most patients in emergency department require urgent CT scan of brain to rule out other differentials like central venous thrombosis, intra cranial bleeds and cerebrovascular accidents. Neuro-imaging in majority of cases shows vasogenic oedema in cortical or subcortical white matter of parieto occipital region. Lesions of frontal lobes are seen mostly in superior frontal gyrus along with edema in posterior circulation.

Focal or confluent areas of increased signal on T2 weighted images are most commonly observed.[6] Fluid Attenuated Inversion Recovery (FLAIR) sequences can detect subtle peripheral lesion and increase sensitivity. Gadolinium contrast studies show increased gyri-form signal suggesting blood brain barrier dysfunction.

Based on FLAIR findings some researchers have classified PRES into mild, moderate and severe, depending on extent of hyper intensities and presence of mass effect.[7] Mild PRES was defined as cortical or subcortical white matter edema without parenchymal haemorrhage, mass effect, herniation, or minimal involvement of only one of the group of cerebellum, brainstem, or basal ganglia. Moderate PRES was 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 group of cerebellum, brainstem, or basal ganglia. Mild mass effect with no

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herniation or midline shift, particularly if parenchymal haemorrhage was present, was also classified as moderate. Severe PRES was defined as confluent edema extending from the cortex to the ventricle, or edema/ haemorrhage causing midline shift/ herniation. Alternatively, involvement of all three of the group of cerebellum, brainstem, and basal ganglia was considered severe. As brain cortex is tightly packed than white matter, it usually resists edema. Increased concentration of adrenergic nerves in anterior circulation than posterior, can explain increased finding in posterior circulation.

Follow up studies in majority of cases show partial or complete reversal within few days to weeks after treatment.

Other investigations required to rule out differential diagnosis should be considered, as clinical and radiological findings are not specific. The tests include blood counts, creatinine, electrolytes and other liver function tests. Patients may require EEG monitoring as seizures are common and persistent. Altered sensorium may be due to non-convulsive status epilepticus.

Prompt recognition of PRES with rapid management of trigger leads to hastened recovery. Increased blood pressure should be managed aggressively. In case of malignant hypertension, blood pressure should be reduced to about 100 diastolic. Care should be taken that the blood pressure should not fall by more than 25% of the current reading. Prompt delivery should be done in eclampsia. Withdrawal of offending agent should be considered. Anti epileptics, air way protection and mechanical ventilation with supportive care in intensive care may be required.

In this edition of JAPI, PK Yadav and D Sen have described clinico-pathological profile and outcome of patients with Posterior Reversible Encephalopathy Syndrome. Preponderance of females in the study may be due to high level of suspicion with consequent detection of PRES following eclampsia and pregnancy-induced hypertension. 80% normal CT scan in study also suggest that MRI should be the preferred modality of investigation if other the causes of altered sensorium -especially stroke in golden hour of thrombolysis, is not suspected. MRI changes may not be restricted to posterior area, but may be diffused. Basal ganglia are involved in good number of cases in present study.

Overall mortality rate is good in PRES, with majority gaining full clinical and radiological recovery[8] as seen in this study also, however in some cases mild residual features may persist. Further studies and clinical trials with larger number of patients will help us further understand the disease better and optimize treatment. Early recognition and prompt treatment is the key to a good outcome.

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