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Posterior Reversible Encephalopathy Syndrome

KEYWORDS: Posterior reversible encephalopathy syndrome (PRES), seizures, eclampsia, MRI

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ABSTRACT *Posterior reversible encephalopathy syndrome is a potentially reversible clinico-neuro-radiological syndrome characterized by clinical symptoms of headache, visual perception defects, altered mental status and seizures. It may occur in diverse situations like hypertension, eclampsia, preeclampsia, systemic lupus erythomatosus (SLE), renal failure, sepsis. It involves the brain stem, cerebellum and other cerebral areas. MRI of the brain is an essential tool in diagnosing. The pathophysiology of PRES remains controversial. Early recognition and resolution of the underlying cause is the keystone of management.*

Posterior reversible encephalopathy syndrome (PRES) also known as reversible posterior leuko encephalopathy syndrome (RPLS) was first described by Hinchey in1996.[1]

It is considered to be a potentially reversible clinico-neuro-radiological syndrome characterized by clinical symptoms of headache, visual perception defects, altered mental status and seizures.[2]

Consciousness impairment may range in severity from confusion, somnolence, and lethargy to encephalopathy or coma. Consciousness impairment has been reported in 13 % to 90 % of cases. Seizure activity occurs in upto 92 % of cases. The seizures are rarely isolated (23 %-28 %). Secondary generalized seizures are common (53–62 %).

It may occur in diverse situations, including hypertension, eclampsia, preeclampsia, severe hypercalcaemia thrombocytopenic syndromes, Henoch-Schonlein purpura haemolytic uraemic syndrome, amyloid angiopathy, systemic lupus erythomatosus (SLE), renal failure, post-transplantation, infection, sepsis (gram positive organisms predominate) ,shock , patients on immunosuppressive medications such as cyclosporine, and various anti-neoplastic agents. [3]

It involves the brain stem, cerebellum and other cerebral areas. Parieto-occipital regions were the most commonly involved (94%) followed by the frontal lobe (77%), temporal lobe (64%), and cerebellum (53%). Cerebellar involvement was significantly more frequent in patients with a history of autoimmunity and patients with sepsis were more likely to have cortical involvement .[4]

PRES has been reported in patients aged 4 to 90 years, although most cases occur in young to middle-aged adults, the mean age ranging across case-series from 39 to 47 years with marked female predominance. Many patients with PRES have co-morbidities, which may be severe conditions, such as bone marrow or solid organ transplantation, chronic renal failure, and chronic hypertension.[5]

Hypertension leads to a breakdown in cerebral auto regulation, particularly in the posterior head region (where there is a relative lack of sympathetic innervation). Hyper perfusion ensues with protein and fluid extravasation, producing focal vasogenic oedema. An alternative theory, which has been best characterized in pre-eclampsia, eclampsia, and sepsis, implicates endothelial dysfunction. A third theory proposes that vasospasm with subsequent ischaemia may be responsible[6].

Hypertension is sufficient to trigger severe vasoconstriction . Cerebral hyper perfusion leads to the release of the vasodilators nitric oxide (NO) and prostacyclin under the influence of endothelial agonists such as acetylcholine, Nor epinephrine, and substance P. Concomitantly, there is overproduction of catecholamines, vasopressin ,thromboxane ,and endothelin .These substances increase vaso reactivity and activate the renin-angiotensin-aldosterone system. Angiotensin II activates the gene expression of pro-inflammatory cytokines such as interleukin (IL)-6 and the transcription of nuclear factor-kappa B (NF-.B), leading to direct cytotoxic effects on the blood vessel wall.

The combination of suggestive clinical manifestations and radiological criteria establishes the diagnosis of PRES.

MRI of the brain is an essential tool in diagnosing:-

- Appearance on MRI
- Multifocal T2-hyperintensities
- Favors parietal and occipital cortex, but can involve other cortex, thalamus, basal ganglia, cerebellum and brainstem.
- Can exhibit subcortical "gyral" enhancement secondary to breakdown of the blood-brain barrier.
- Mass effect associated with edema.

Complications diagnosed radio-logically at presentation of PRES:-

Cerebral ischemia: Cerebral infarction is seen as high DWI signal intensity with a decrease in the apparent diffusion coefficient below 20 %. Cerebral infarction is among the early signs of non-reversible damage associated with adverse outcomes.

Cerebral hemorrhage: Cerebral hemorrhage is uncommon in PRES (5 % to 17 % of patients). Reported cases were about evenly distributed in three categories, parenchymal hematoma, subarachnoid hemorrhage, and focal intra parenchymal hemorrhage measuring less than 5mm in diameter . Cerebral hemorrhage may be more common among patients with Allo-genic bone marrow transplantation or anticoagulant treatment[7].

Differential Diagnosis :-
The non-specific clinical manifestations and multiplicity of radiological patterns raise diagnostic challenges. Many conditions may resemble PRES, including ictal or post-ictal state (with or without status epilepticus), progressive multifocal

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leukoencephalopathy (PML), cerebral autosomal dominant. Arteriopathy with subcortical infarcts and leuko-encephalopathy (CADASIL), infectious encephalitis, acute disseminated encephalomyelitis, MELAS, vasculitis , Creutzfeld-Jakob disease, cerebral venous sinus thrombosis, and ischemic stroke[7].

General measures
Patients with PRES require the symptomatic measures usually taken in the ICU.

Although most patients have stable hemodynamics, catecholamines are required occasionally.

The need for upper airway protection should be evaluated continuously in patients with marked consciousness impairment or seizure activity. If endotracheal intubation is performed, rapid-sequence induction with etomidate and succinylcholine can be used, provided there is no evidence of hyperkalemia. Propofol or thiopental are also good choices, since they have anticonvulsant effects.

Neuromuscular blocking agents may transiently mask seizures[8].

Hypoglycemia should be looked for routinely and corrected. If glucose is given, 100 mg of thiamine should be administered concomitantly, most notably when there is evidence of vitamin B1 deficiency. Patients should be routinely evaluated for hyperthermia and metabolic disturbances, in particular Hypomagnesemia , which require prompt correction.

Aspiration pneumonia may complicate the initial consciousness disorders.

Antiepileptic treatment, appropriate for the electrical and clinical pattern in the patient ,should be initiated on an emergency basis and according to current guidelines. Patients with persistent seizure activity at ICU admission should be given intravenous benzodiazepines either before ICU admission or in the ICU. The dose can be repeated up to three times if necessary. Patients with continuing seizure activity despite intravenous benzodiazepines should receive standard complementary intravenous anticonvulsant drugs (phenobarbital 10 to 15 mg/kg, phenytoin 18mg/kg, or equivalent dose of fosphenytoin). Patients with refractory status epilepticus need midazolam, propofol , or thiopental in titrated doses until remission of the clinical seizure activity[8].

When the EEG reveals electrical status epilepticus, these anesthetic drugs are given in titrated doses to induce EEG burst suppression then as a continuous infusion for at least 12 hours . Mechanical ventilation is required in 35 % to 40 % of patients with PRES, for 3 to 7 days and may require ICU admission.

Control of hypertensive emergency, if present, is an important part of the symptomatic management. The aim is not to normalize the blood pressure but rather to decrease the MAP by 20–25 % within the first 2 hours and to bring the blood pressure down to 160/100 mmHg within the first 6 hours . More rapid blood pressure reduction is not recommended since it can aggravate the cerebral perfusion pressure alterations and promote ischemia . Intravenous antihypertensive drugs are necessary. Appropriate choices include labetolol, nicardipine, or fenoldopam[9].

Correction of the underlying cause of PRES .An early etiologic diagnosis allows prompt correction of the cause of PRES.

Patients may require blood pressure control, withdrawal of cancer chemotherapy or immunosuppressive agents, Cesarean section, dialysis, or other interventions.

Prompt correction of the cause is crucial to decrease the risk of ischemia or bleeding and therefore to avoid permanent disability or death [9].

Conclusion
Although the clinical presentation is non-specific, most patients have a suggestive combination of symptoms. MRI is crucial for diagnosing PRES, monitoring the course, and assessing treatment effectiveness. MRA(angiography) performed during MRI can be useful to identify associated cerebral vasoconstriction. Repeated cerebral imaging helps to support the diagnosis and identifies complications potentially responsible for permanent impairments.

The pathophysiology of PRES remains controversial. However, the list of conditions known to be associated with PRES is increasing steadily. Early recognition and resolution of the underlying cause is the keystone of management.

Persistence of the cause carries a risk of ischemia, bleeding, and death. Finally, studies are needed to identify factors of adverse prognostic significance and to develop neuro- protective strategies.

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