A case of Posterior Reversible Encephalopathy Syndrome

* Dr. Pratheesh P.P., Dr. Mohamed Shihab, Dr. Vengojayaprassad, Prof. Dr. Nedumaran, Dr. Balaji, Dr. Sandeep, Dr. Himal Raj M.

Department of Medicine
Government Medical College, Coimbatore
E-mail : drpratheeshpp@gmail.com

Abstract

Posterior reversible encephalopathy syndrome (PRES), also known as reversible posterior leukoencephalopathy syndrome (RPLS), is a clinical and radiological entity characterised by headache, variable mental status, seizures, visual disturbances and typical transient changes in the posterior cerebral perfusion. It may occur due to a number of causes, predominantly in malignant hypertension, eclampsia and some medical treatments. PRES is diagnosed by CT scan and MRI brain. Treatment is correction of high blood pressure or underlying cause1,2. We report a case of posterior reversible encephalopathy syndrome in a female patient who presented with malignant hypertension.

Key-words Posterior reversible encephalopathy syndrome (PRES), malignant hypertension, seizures, papilloedema, white matter edema.

Introduction

The cerebral white matter is composed of myelinated-fiber tracts in a cellular matrix of glial cells, arterioles, and capillaries that makes this region susceptible to the accumulation of fluid in the extracellular spaces (vasogenic edema). Modern neuroimaging techniques are sensitive to changes in the distribution of water in the brain and make it possible to detect white matter edema even in its early phases. Patients with hypertensive encephalopathy, hypertension associated with acute glomerulonephritis, and eclampsia of pregnancy have been known to have edema in the brain, predominantly in the posterior portions of the cerebral white matter. Recently, patients treated with cyclosporine and other immunosuppressants have been reported to have similar findings on neuroimaging. A variety of disorders associated with findings on neuroimaging that suggest white-matter edema, mostly in the posterior parietal–temporal–occipital regions of the brain. The clinical findings in these patients make up a recognizable syndrome characterized by headache, decreased alertness, altered mental functioning, seizures, and visual loss, including cortical blindness. The clinical signs and abnormalities on imaging are always reversible. This syndrome, which we call posterior reversible encephalopathy syndrome, is unfamiliar to many. In this report we describe the clinical and neuroimaging features of the syndrome, which appears to involve capillary leakage and acute disruption of the blood–brain barrier.

Case History

34 year old female presented to our emergency department with history of headache, vomiting, seizures and altered mental status. She was apparently normal two days back, then she developed headache which was severe in nature. The next day she developed vomiting and blurring of vision. Then she developed two episodes of seizures which were generalised tonic clonic in type and became drowsy. No past history of hypertension, diabetes, bronchial asthma or seizures. No history of intake of any immunosuppressive drugs. On examination she was drowsy, blood pressure was 230/136 mm Hg and fundoscopic examination showed bilateral papilloedema. CT scan brain showed bilateral hypodense areas suggestive of extensive white matter edema in parietal lobes, both occipital lobes and right temporal lobe. MRI brain confirmed these findings, showed bilateral hyperintense areas of white matter edema in the above mentioned areas. Serum potassium 4mmol/L, serum sodium 138 mmol/L, serum calcium 9mg/dL,
blood sugar 114mg/dL, screening for HIV was negative. Rheumatoid factor and CRP were negative. The patient was diagnosed as a case of posterior reversible encephalopathy syndrome resulting from malignant hypertension and was treated with intravenous nitroglycerine for blood pressure reduction, mannitol and phenytoin. Next day patient’s blood pressure improved and she regained consciousness and neurological examination was normal without any focal neurological deficits except for papilloedema. After five days the fundoscopic examination revealed the disappearance of papilloedema. We started her on oral anti hypertensive drugs sent the patient home and now she is doing well.

Discussion

The clinical signs and findings on neuroimaging in patients with the posterior reversible encephalopathy syndrome are consistent enough that this entity should be readily recognizable. Its causes are diverse, but common precipitants are acute elevations of blood pressure, eclampsia, treatment with immunosuppressive drugs and renal decompensation. The causes for PRES are given in table-1.

Causes of PRES

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Table -1. *first three causes are most common and most important.

| 1. | Malignant hypertension* |
| 2. | Eclampsia* |
| 3. | Immunosuppressive and cytotoxic medications* |
| 4. | Renal failure and hypertension |
| 5. | Collagen vascular disease |
| 6. | HIV infection |
| 7. | Organ transplanted |
| 8. | Hypercalcemia |
| 9. | Hemolytic uremic syndrome (HUS) |
| 10. | Thrombotic thrombocytopenic purpura (TTP) |

Clinical Findings

The most common clinical symptoms and signs are headache, altered alertness and behaviour ranging from drowsiness to stupor, seizures, vomiting, mental abnormalities including confusion and diminished spontaneity and speech, and abnormalities of visual perception. The onset is usually subacute but may be heralded by a seizure. Seizures are common at the onset of neurologic symptoms but can also develop later. Seizures may begin focally but usually become generalized. Multiple seizures are more common than single events. Most patients have a change in alertness and activity. Lethargy and somnolence are often the first signs noted. Temporary restlessness and agitation may alternate with lethargy. Stupor and frank coma may develop, but usually patients remain responsive to stimuli. The mental functions are slowed, and patients are often confused; spontaneity is decreased, and responses are slowed. Memory and the ability to concentrate are impaired, although severe amnesia is unusual. Abnormalities of visual perception are nearly always detectable. Patients often report blurred vision. Hemianopia, visual neglect, and frank cortical blindness may occur. Some cortical blind patients do not realize that they cannot see (Anton’s syndrome). The tendon reflexes are often brisk, and some patients have weakness and incoordination of the limbs.²,⁶,⁷,⁹

Diagnostic criteria of PRES¹⁰

Table 2

| 1. | The presence of neurological symptoms or findings such as seizures, weakness of an extremity or mental status changes. |
| 2. | Presence of risk factors such as history of hypertension, eclampsia, or immunosuppressive or cytotoxic medications |
| 3. | Absence of other possible causes of encephalopathy. |
| 4. | Reversible course - complete resolution of clinical symptoms and signs following treatment or complete disappearance of signal changes on follow up images. |

The patient met all diagnostic criterias except the second one, that is the presence of risk factors, most probably the patient might have had undiagnosed hypertension in the past.

Abnormalities on Neuroimaging

The most common abnormality on neuroimaging was edema involving the white matter in the posterior portions of the cerebral hemispheres, especially bilaterally in the parieto-occipital regions. The calcarine and paramedian occipital-lobe structures are usually spared, a fact that distinguishes posterior reversible encephalopathy syndrome from bilateral infarction of the posterior-cerebral-artery territory. Involvement of additional areas of the brain in patients with the posterior reversible encephalopathy syndrome, such as the brain stem, cerebellum basal ganglia, and frontal lobes, has also been reported. CT scan shows hypodense areas of white matter edema in affected areas. In MRI brain T1 weighted images show hypointense areas with patchy variable enhancement and T2 weighted images show hyperintense in affected regions. Advantage of MRI is its ability to show small, focal abnormalities beyond the limits of resolution of CT. MRI features are characteristic and has diagnostic and prognostic value.³,⁴ Fluid attenuated inversion recovery (FLAIR) sequences may improve detection of cortical/subcortical areas of injury. With rapid improvement in the patient’s clinical status, a subsequent MRI was deemed unnecessary, as clinical resolution corresponds with radiographic resolution. Diffusion weighted imaging (DWI) can differentiate...
PRES from infarct. In DWI the water mobility is increased in vasogenic edema produced by PRES and water mobility is reduced in infarct.3,4,5

**Pathophysiology and Mechanisms**

Hypertensive encephalopathy is the cause of this syndrome that has been most thoroughly studied both clinically and experimentally. The pathophysiology of PRES is most likely, and most often reported as, vasogenic edema secondary to an acute increase in arterial blood pressure, which overwhelms the autoregulatory capacity of the cerebral vasculature, causing arteriolar vasodilation and endothelial dysfunction, leading to interstitial extravasation of fluid. In some cases acute and significant elevation of arterial blood pressure can cause vasospasm and can lead to cytotoxic edema due to transient ischaemia. Cytotoxic medications produce endothelial dysfunction and damage to blood brain barrier and lead to cytotoxic edema. The posterior circulation is thought to be more susceptible to this type of damage, because there is less sympathetic innervation of the vertebro-basilar vasculature to protect the parenchyma from rapid increases in arterial blood pressure.6,7,8

**Treatment**

Most important aspect in management is to diagnose and treat this condition as early as possible, because of its high potential of reversibility. Here we have to find out the underlying cause and treat accordingly. If it is due to malignant hypertension reduce the blood pressure to normal levels with antihypertensive drugs. Anti cerebral edema measures like mannitol are useful for vasogenic edema of PRES. If it is due to cytotoxic medications discontinue the offending drug. In almost all cases, PRES is reversible with out any complications. Very rarely, if the diagnosis and treatment is delayed it can cause permanent damage and brain injury and can produce complications like frequent seizures.

**Conclusion**

The cause of the posterior reversible encephalopathy syndrome is multifactorial. The mechanism of the syndrome is a brain-capillary leak syndrome related to hypertension, fluid retention, and possibly the cytotoxic effects of immunosuppressive agents on the vascular endothelium. Acute focal neurologic changes should prompt rapid investigations, including imaging of the brain. The characteristic findings on neuroimaging helps to differentiate PRES from other conditions like intracranial bleeding and infarct, which require different line of management. PRES, especially in patient presenting with typical symptoms of headache, seizures, visual deficits and mental changes should be considered and treated without delay to maximize the potential for reversibility.

**References**