ORIGINAL RESEARCH PAPER

General Medicine

POST PARTUM COMPLICATIONS: PRES A CASE SERIES

KEY WORDS: PRES, Hypertension , Eclampsia

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) may present with diverse clinical symptoms including visual disturbance, headache, seizures and impaired consciousness. MRI shows edema, usually involving the posterior subcortical regions. Triggering factors include hypertension, pre-eclampsia/eclampsia, renal failure, cytotoxic agents and autoimmune conditions. The mechanism underlying PRES is not certain, but endothelial dysfunction is implicated. Treatment is supportive and involves correcting the underlying cause and managing associated complications, such as seizures. Although most patients recover, PRES is not always reversible and may be associated with considerable morbidity and even mortality. [1]

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological diagnosis based on a combination of typical clinical features and risk factors, supported by magnetic resonance (MR) brain scan findings. PRES is also known as reversible posterior leukoencephalopathy syndrome. The classic presentation is a combination of visual loss, headache, altered mental function, seizures, and nausea, but there may be other visual impairments, including blurred vision, sensitivity or difficulty speaking. Neurological symptoms may be multiple or appear separately and may develop during the acute phase of the disease. PRES has many causes, and may result from medical treatment (such as antineoplastic therapy) or occur as part of a medical condition associated with PRES (such as autoimmune disease, eclampsia etc). (box 1) (2,3)

box 1 Conditions associated with the development of PRES

General conditions	***Cytotoxic and immunosuppressive medications***
• Hypertension	• Hydroxydaunorubicin/adriamycin
• Sepsis	• Vinblastine/vincristine
• Solid organ transplantation	• Gemcitabine
• Eclampsia and pre-eclampsia	• Platinum-containing drugs: cisplatin, oxaliplatin and carboplatin
• Renal failure	• Bortezomib
• Malignancy (solid organ and haematological)	• Cyclophosphamide
• Bone marrow transplantation	• Daunorubicin
• Stem cell transplantation	• Interferon therapy
• Hypomagnesaemia	• Capecitabine, 5-fluorouracil
• Hypercalcaemia	• Cytarabine
• Hypercholesterolaemia	• Etoposide
• Late radiation-associated encephalopathy, for example, SMART	• Corticosteroids
Autoimmune disorders	• Rituximab
• Rheumatoid arthritis	• Ciclosporin
• Crohn's disease	• Tacrolimus
• Systemic lupus erythematosus	• Sirolimus
• Scleroderma	• Mycophenolate mofetil
• Vasculitis	• Methotrexate
• Neuromyelitis spectrum disorder	• Azathioprine
Toxins	***Other medications***
• Scorpion poison	• Lithium
• LSD intoxication	• Linezolid
• Ephedra overdose	• Intravenous contrast
• Alcohol intoxication	• Intravenous immunoglobulin
• Cocaine	

PRES may develop at any age from infants to the elderly, but most frequently affects young or middle-aged adults, with a mean age of 45 years. [2,4] There appears to be a female predominance, even after excluding patients with eclampsia. [3,5,6] Among adults, PRES is present in up to 98% of patients with eclampsia [7]; in 2.7%–25% of patients following bone marrow transplantation [8,9]; in 0.4%–6% of patients following solid organ transplantation [10]; and less commonly (0.4%–0.8%) in end-stage renal disease or systemic lupus erythematosus. [11-13]

Case 1

Case 1 is of a 19 year old female with 9 months of amenorrhea with no comorbidities who came to Dhiraj General Hospital in a convulsed state with involvement of both upper and lower limbs, up rolling of eyeballs, frothing from the angle of the mouth with post-ictal confusion. She already had 3-4 episodes of seizures at home. No history of fever, cough, cold, abdominal pain, trauma was present. No history of bowel or bladder incontinence. As she came in convulsing state, loading dose of Inj MgSO4 14mg and Inj Levetiracetam 1gm were given. She was then taken for emergency LSCS under GA and shifted to MICU immediately after that.

She has no past history of hypertension, DM, TB, thyroid disorders, asthma, CVA stroke, IHD, any major surgery or blood transfusion. She does not have a significant family history. On presentation she was afebrile , her pulse was 102/min , BP was 160/100 mm Hg , bilateral air entry was present with bilateral generalized fine crepts , S1S2 heart sounds were heard with no murmur, Spo2 was 99% on VAC mode of ventilator with FIO2 of 100%, PEEP 4 and FTrig 2. Bilateral pupils were reactive to light. Plantars were extensors bilaterally. RBS was 169mg/dl. On neurological examination tone was slightly increased and reflexes were exaggerated. Ophthalmology reference was done in view of papilloedema which showed no evidence of the same at present. CT scan report showed finings of hypodense area in bilateral occipital lobes suggestive of edema. Her 2D Echo showed LV global hypokinesia with LVEF 35-40%. Her urine routine micro showed albuminuria (+2), 6-8 pus cells, 4-5 RBCs and 8-10 epithelial cells. ABGA showed normal results. She was treated with Injection Levetiracetam, Injection Clexane 0.6mg, Tab Ramipril (2.5), Tab Ecosprin –AV (75/20).

Investigation	Patient's Value	Reference Values
Haemoglobin	13.1	13-17 gm/dl
Total counts	9900	4000-11000 cells/mm3
Platelets	1.87	1.5-4.5 lacs/mm3
Prothrombin time	17.3	11-14 sec
APTT	35.7	30 sec
Sodium	138	135-145 mEq/L
Potassium	4.1	3.5-5.5 mEq/L
Chloride	104	98-110 mEq/L
S. creatinine	0.9	0.6-1.3 mg/dl
D dimer	2489.7	0-500 ng/ml
CRP	22.14	0-6 mg/l

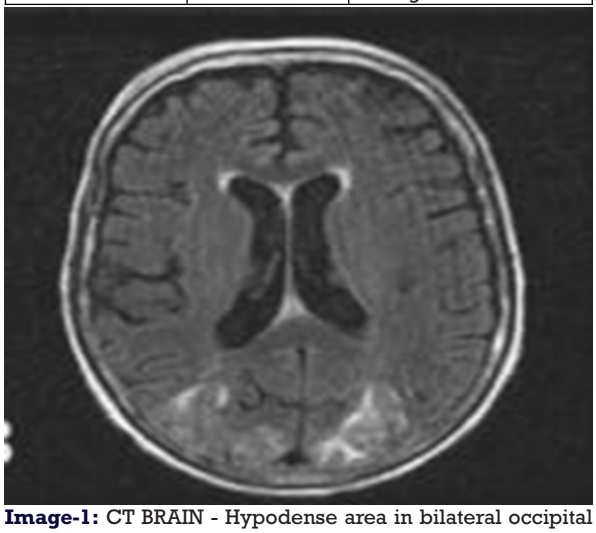

Image-1: CT BRAIN - Hypodense area in bilateral occipital lobes.

Case 2

Case 2 is of a 28 years old female patient having no known comorbidities with complaint of headache since 1 day followed by blurred vision at around 11o clock in the morning followed by generalized tonic clonic seizures associated with up rolling of eyeballs and frothing from the angle of the mouth. Post-ictal confusion was present for around 8-10 minutes. Deviation of angle of mouth or bowel bladder incontinence was not present. She got second episode of GTCS at around 2:30 o'clock in afternoon during MRI brain scan, after which she was admitted in Dhiraj General Hospital where she was treated with Injection Levetiraetam, Inj Mannitol, Inj Nimodipine. Patient was intubated and kept on controlled mode of MV. On admission she was afebrile, pulse rate was 94/min, BP was 130/90 mm Hg, SpO2 was 98% on PRVC mode of ventilation with Fio2 30%, per abdomen was distended, wound of LSCS with dressing was present, was drowsy and arousal, was moving all 4 limbs, eye opening on painful stimuli was present. Bilateral pupils were reactive to light. Bilateral plantars were extensors and no facial asymmetry was present.

MRI with angio was done which was suggestive of acute infarct involving left cerebellum plus diffuse gross subarachnoid hemorrhage and angio was found to be normal. MRI brain with venography showed possibility of reversible leucoencephalopathy involving bilateral cerebellum, parieto-occipital lobes, deep nuclei and splenium of corpus callosum. Also showed possible early SAH in both high fronto-parietal sulci. Major dural sinuses and the deep veins were found to be normal.

CT Brain was done which showed subtle ill-defined hypodense area in bilateral parieto-occipital lobes suggestive of edema. Rest of the areas of edema in cerebellum and deep grey nuclei were not appreciated in CT scan. Subtle subarachnoid hemorrhage was seen in bilateral high fronto-parietal cortical sulci.

2D Echo was done suggestive of normal LV systolic function, LVEF 55%, mild TR/PAH, RVSP 38mm Hg.

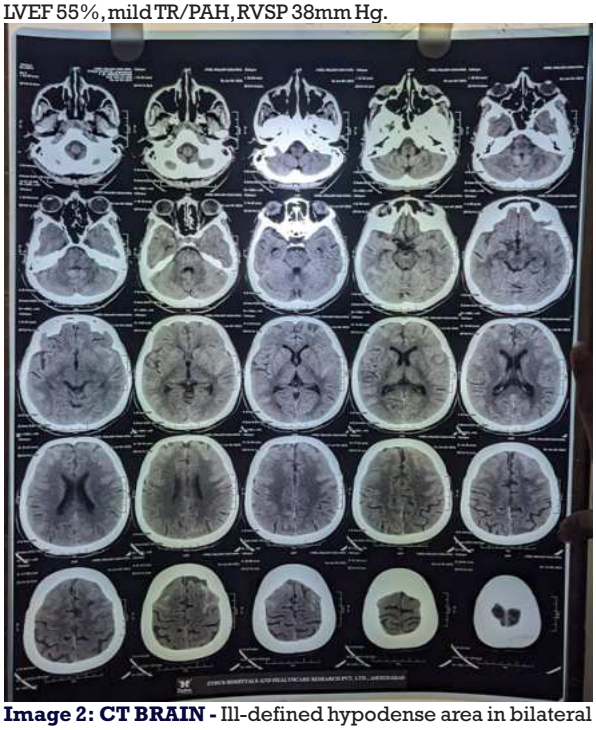

Image 2: CT BRAIN - Ill-defined hypodense area in bilateral parieto-occipital lobes.

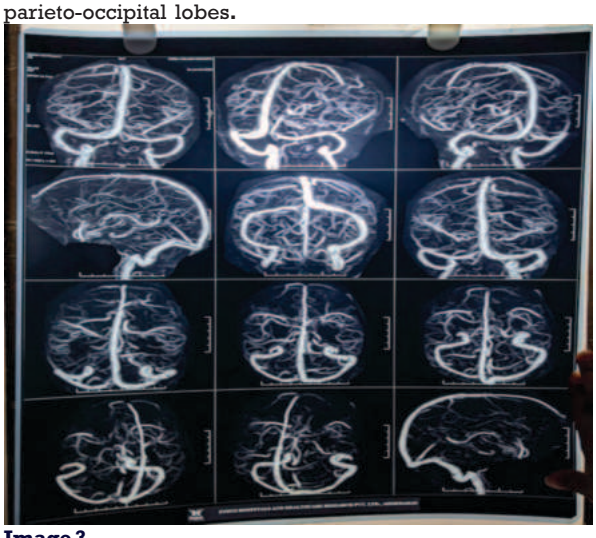

Image 3

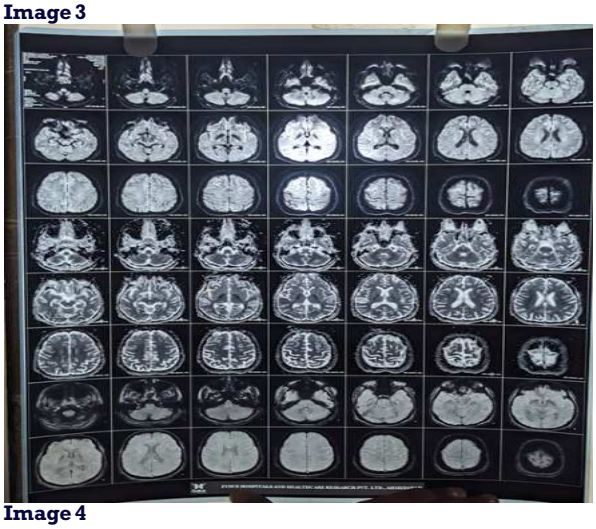

Image 4

Image 3-4: MRI BRAIN - Acute infarct involving left

cerebellum plus diffuse gross subarachnoid hemorrhage with normal angio and venography showed involvement of bilateral cerebellum, parieto-occipital lobes, deep nuclei and splenium of corpus callosum.

Case 3

Case 3 is of a 21 year old female patient named Bhavnaben with no known comorbidities who was completely alright 2 days back had 2 episodes of seizures on 23/2/24 at home which were sudden in onset, each episode lasting for 2-3 minutes, involving all four limbs, frothing from the angle of the mouth with post ictal confusion, not associated with up rolling of eyeballs and bowel or bladder incontinence. Patient came to Dhiraj General Hospital and urgent LSCS was done and another 2 episodes of seizures occured post LSCS for which loading dose of $MgSO_4$ was given along with 2 maintenance dose. Due to raised BP, Inj Labetalol 20 mg was given and patient was shifted to MICU. On examination her pulse rate was 90/min, BP was 170/100mm Hg, bilateral pupils were reactive to light and plantars were extensors bilaterally. Tone was normal in all 4 limbs, power was 4/5 in all limbs, all reflexes were exaggerated. Rest all systemic examination was normal. 2D Echo was normal with LVEF 55%. ECG showed sinus tachycardia. On fundus examination papilledema was absent. Her urine routine micro showed albuminuria (+1), 5-6 pus cells, nil RBCs and 8-10 epithelial cells. CT scan of brain (plain) was done which showed ill -defined hypodense areas noted involving bilateral occipital lobes with loss of grey white matter differentiation. Due to persistent high BP patient was kept on Infusion labetalol, Inj Mannitol and Tablet Nifedipine was given. Patient was also started with Injection Levetiracetam.

Investigation	Patient's Value	Reference Values
Haemoglobin	11.7	13-17 gm/dl
Total counts	8300	4000-11000 cells/mm3
Platelets	2.3	1.5-4.5 lacs/mm3
Prothrombin time	14.1	11-14 sec
APTT	32	30 sec
Sodium	140	135-145 mEq/L
Potassium	3.9	3.5-5.5 mEq/L
Chloride	108	98-110 mEq/L
S. creatinine	0.7	0.6-1.3 mg/dl
LDH	1076	140-280 U/Lt
S. Mg^{2+}	6.1	1.7-2.2 gm/dl
S. Ca^{2+}	8.7	9-11 mg/dl

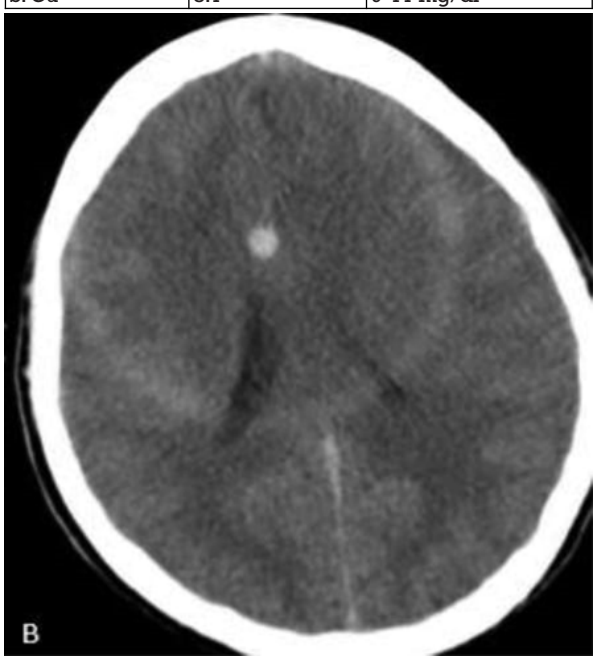

Image 5: CT BRAIN Hypodense areas noted involving bilateral occipital lobe.

Case 4

Case 4 is of a 21year old female patient named Mitvaben primigravida with 9 months of amenorrhea had 3 episodes of seizures involving all limbs with up rolling of eye balls, tongue bite, frothing from mouth with loss of consciousness, at home hence shifted to Gotri medical college, where she was intubated and urgent LSCS was done. CT BRAIN PLAIN was done showing diffuse cerebral edema on fronto-parietal and occipital lobe, focal area of hypodensity on right basal ganglia S/O sub-acute/acute infarct. Diagnosis of Posterior reversible encephalopathy was made from CT SCAN findings and after 2 days patient took DAMA and shifted to Dhiraj General Hospital in intubated state. On examination patient was febrile on touch, pulse was 100bpm, BP was 140/90mmhg. Patients GCS was $E_1V_TM_1$. Right pupil was dilated and left pupil was sluggishly reactive to light. Plantars were extensors. Rest systems were normal. Patient was treated with Inj Mannitol, Inj Levetiracetam along with antibiotic coverage. Patient was kept on ventilator support and treated accordingly. Patient suddenly collapsed and CPR was given but patient could not be revived.

Investigation	Patient's Value	Reference Values
Haemoglobin	7.9	13-17 gm/dl
Total counts	20,000	4000-11000 cells/mm3
Platelets	1.7	1.5-4.5 lacs/mm3
Prothrombin time	16.4	11-14 sec
APTT	30	30 sec
Sodium	142	135-145 mEq/L
Potassium	3.3	3.5-5.5 mEq/L
Chloride	103	98-110 mEq/L
S. creatinine	0.6	0.6-1.3 mg/dl
LDH	898	140-280 U/Lt
CRP	22.6	0-6 ng/dl
PCT	14.4	0-0.05 ng/ml
D-dimer	1369	0-500

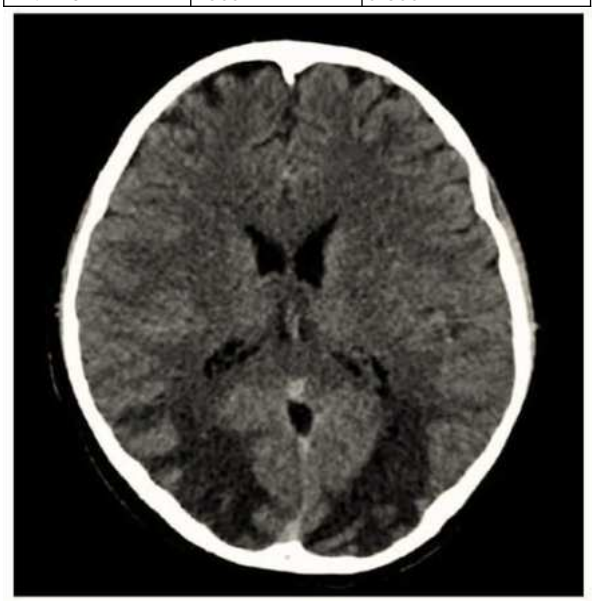

Image 6: CT BRAIN- diffuse cerebral edema on fronto-parietal and occipital lobe.

DISCUSSION

In 1996, Hinchey et al. first described PRES as the Reversible Posterior Leukoencephalopathy Syndrome in a group of 15 people.[14] White matter edema encompassing the occipital and parietal lobes is a characteristic of PRES, a neurological disorder that is reversible. It has been reported in nearly every age range, from young children to the elderly, but it is more common in younger and middle-aged adults, with women accounting for the majority of instances.[15] The pathophysiological mechanism responsible with PRES remains unclear. Hyperperfusion and the extravasation of

macromolecules and plasma result from an insufficient auto-regulating response to rapid and substantial rises in blood pressure. The posterior circulation of the brain has comparatively less innervation from sympathetic nerves, which accounts for the main involvement of the posterior region of the brain by PRES.[17] The characteristic of posterior reversible encephalopathy syndrome (PRES) is a wide range of neurological symptoms, usually concomitant with elevated arterial blood pressure. Patients with hypertension were the first patients to be observed with PRES instances; later, patients with normotension and sepsis were also identified with cases. Acute blood pressure elevation, renal failure, preeclampsia/eclampsia, autoimmune disorders, infection, transplantation, and chemotherapy medications are common risk factors for PRES [18]. Acute or subacute PRES can cause neurological symptoms that vary in intensity over a few hours to weeks.[19] Both quantitative and qualitative disturbances of consciousness, such as stupor, somnolence, coma, or cognitive impairment, can be symptoms of encephalopathy. It has been demonstrated that localized or generalized epileptic episodes occur in about two thirds of PRES patients.[19, 20–21]. Due to the frequent involvement of the occipital lobes in PRES, approximately two-thirds of patients experience visual disturbances such as anomalies in the visual field, including hemianopia and cortical blindness, a loss in visual acuity, or visual hallucinations.[14,19] A few cases of myelopathic symptoms and spinal cord involvement have been reported. Additional rare clinical symptoms include abulia, anxiety, delusions, opisthotonus, optic ataxia, ocular apraxia, and simultagnosia.[18] The following criteria were put forth by Fugate and Schmutzhard for the diagnosis of posterior reversible encephalopathy syndrome (PRES): reversibility of radiological and clinical findings, abnormalities on neuroimaging suggesting (focal) vasogenic edema, and sudden onset of neurological symptoms.[19]

Comorbidities or trigger factors in the clinical setting, together with the presence of acute onset neurological symptoms, concurrently labile blood pressure, and vasogenic edema shown in neuroimaging, all point to PRES. Verifying a PRES diagnosis requires brain imaging. Non-contrast computed tomography (CT) may rarely detect vascular edema; however, brain MRI is far more sensitive, particularly when employing the T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences.[22] The classic imaging patterns often show bilateral, subcortical, symmetrical vasogenic edema affecting the parieto-occipital region. In addition to the parietal occipital pattern, two further patterns are described in the literature: the superior frontal sulcus pattern and the holohemispheric watershed pattern.[18] Post-stroke syndrome (PRES) differential diagnosis includes meningoencephalitis, cerebral demyelinating diseases, cerebral venous thrombosis, and cerebrovascular accidents. The accuracy of the diagnosis hinges on early imaging.[23]

Since there is no established management procedure, PRES is being treated symptomatically. Treating the underlying medical issue that leads to the development of PRES is crucial. The underlying pathology should be addressed or the triggering cause should be eliminated as early in the disease's progression as feasible.[19] Especially for people with altered mental status, supportive care should be provided, such as hydration, correction of electrolyte deficits, airway monitoring, and ventilatory support. For patients with kidney disease, rapid blood transfusion is recommended. In patients suffering from hypertensive problems, it is recommended to lower the blood pressure by 20-25% in the first hours to reduce the risk of brain, coronary and renal ischemia. Because most people with PRES have neurological symptoms that are mostly treatable. Secondary episodes can lead to brain damage and death, although it is reversible. These complications include acute ischemic stroke, hemorrhage, and epileptic seizures. Although symptoms of PRES can recur, they are rare (less than 10%).[23]

CONCLUSION

Our case series presents a wide range of clinical and neuroradiological manifestations of PRES, which were not reversible in all cases. Delaying the diagnosis can lead to poor recovery and poor outcome. Histopathological findings are rare in PRES and may improve understanding of the pathophysiology.

REFERENCES

1. Triplett JD, Kutlubaev MA, Kermode AG, *et al*Posterior reversible encephalopathy syndrome (PRES): diagnosis and managememt, *Practical Neurology* 2022;**22:**183-189.
2. Lee VH , Wijdicks EFM , Manno EM , *et al* Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol 2008;**65**:205–10.
3. Fugate JE , Claassen DO , Cloft HJ , *et al* . Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. Mayo Clin Proc 2010;**85**:427–32.
4. Legriel S , Schraub O ,Azoulay E , *et al* . Determinants of recovery from severe posterior reversible encephalopathy syndrome. PLoS One 2012;**7**:e44534.
5. Bartynski WS , Boardman JF . Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. American Journal of Neuroradiology 2007;**28**:1320–7.
6. Liman TG , Bohner G , Heuschmann PU , *et al* . The clinical and radiological spectrum of posterior reversible encephalopathy syndrome: the retrospective Berlin preS study. J Neurol 2012;**259**:155–64.
7. Brewer J , Owens MY , Wallace K , *et al*. Posterior reversible encephalopathy syndrome in 46 of 47 patients with eclampsia. Am J Obstet Gynecol 2013;**208**:468.e1–468.e6.
8. Reece DE , Frei-Lahr DA , Shepherd JD , *et al* . Neurologic complications in allogeneic bone marrow transplant patients receiving cyclosporin. Bone Marrow Transplant 1991;**8**:393–401.pmid:http://www.ncbi.nlm.nih.gov/pubmed/1768975.
9. Bartynski WS , Zeigler ZR ,Shadduck RK , *et al* . Pretransplantation conditioning influence on the occurrence of cyclosporine or FK-506 neurotoxicity in allogeneic bone marrow transplantation. AJNR Am J Neuroradiol 2004;**25**:261–9.pmid:http://www.ncbi.nlm.nih.gov/pubmed/14970028.
10. Staykov D , Schwab S . Posterior reversible encephalopathy syndrome. J Intensive Care Med 2012;**27**:11–24.doi:10.1177/0885066610393634 pmid:http://www.ncbi.nlm.nih.gov/pubmed/21257628.
11. Bartynski WS , Tan HP , Boardman JF , *et al* . Posterior reversible encephalopathy syndrome after solid organ transplantation. AJNR Am J Neuroradiol 2008a;**29**:924–30.doi:10.3174/ajnr.A0960 pmid:http://www.ncbi.nlm.nih.gov/pubmed/18272559.
12. Canney M , Kelly D , Clarkson M . Posterior reversible encephalopathy syndrome in end-stage kidney disease: not strictly posterior or reversible. Am J Nephrol 2015;**41**:177–82.
13. Lai C-C , Chen W-S , Chang Y-S , *et al* . Clinical features and outcomes of posterior reversible encephalopathy syndrome in patients with systemic lupus erythematosus. Arthritis Care Res 2013;**65**:1766–74.
14. A reversible posterior leukoencephalopathy syndrome. Hinchey J, Chaves C, Appignani B, et al. *N Engl J Med.* 1996;334:494–500.
15. Posterior reversible encephalopathy syndrome. Fischer M, Schmutzhard E. *J Neurol.* 2017;264:1608–1616.
16. Posterior reversible encephalopathy syndrome: a case report. Sodalagunta MB, Sudulagunta SR, Kumbhat M, Sepehrar M, Nataraju AS, Raja SK. *J Neurol Res.* 2016;6:106–110.
17. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. *Mayo Clin Proc.* 2010;85:427–432.
18. Hinduja A: Posterior reversible encephalopathy syndrome: clinical features and outcome. Front Neurol. 2020, 11:71. 10.3389/fneur.2020.00071
19. Posterior reversible encephalopathy syndrome. Fischer M, Schmutzhard E. *J Neurol.* 2017;264:1608–1616.
20. Status epilepticus as initial manifestation of posterior reversible encephalopathy syndrome. Kozak OS, Wijdicks EF, Manno EM, Miley JT, Rabinstein AA. *Neurology.* 2007;69:894–897.
21. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. *Arch Neurol.* 2008;65:205–210.
22. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. Bartynski WS, Boardman JF. *AJNR Am J Neuroradiol.* 2007;28:1320–1327.
23. Posterior reversible encephalopathy syndrome (PRES) in a patient with late postpartum eclampsia. Rijal JP, Giri S, Dawadi S, Dahal KV. *BMJ Case Rep.* 2014;2014.