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(CASE REPORT)

Posterior reversible encephalopathy syndrome with functional and motor sequelae: A case report

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Abstract

Posterior Reversible Encephalopathy Syndrome (PRES) is a rare clinicoradiological neurological disorder, initially elucidated in 1996, Since this first description of PRES numerous case reports and case series, as well as retrospective observational studies describing the syndrome have been published. Importantly, no randomized controlled studies have been performed, We present the case of a young patient with no significant medical history who presented with neurological symptoms consistent with Posterior Reversible Encephalopathy Syndrome (PRES). Brain MRI confirmed the diagnosis of Posterior Reversible Encephalopathy Syndrome (PRES). Additionally, the etiological assessment yielded negative results. A notable aspect in our patient's case is the persistence of sequelae, characterized by dexterity and grip impairment on the right side, hindering various activities of daily living. The diagnosis of PRES is both radiological and clinical, with MRI playing a crucial role. Treatment is primarily symptomatic, sometimes requiring intensive care unit admission. Prognosis is favorable in the majority of cases, but severe complications and even death can occur. The reversibility of initial symptoms is well-documented in the literature. Long-term functional impairment outcomes following PRES have not been adequately characterized in the literature. Therefore, it is necessary to conduct follow-up screenings in more patients presenting both typical and atypical PRES syndromes. This will provide insight into whether the functional and motor sequelae of PRES are less reversible.

Keywords: Posterior Reversible Encephalopathy Syndrome; PRES; MRI; Prognosis; motor sequelae; Functional sequelae.

1. Introduction

Posterior Reversible Encephalopathy Syndrome (PRES) is a rare clinicoradiological neurological disorder, initially elucidated in 1996 through an analysis of a cohort comprising 15 patients [1]. Since this first description of PRES numerous case reports and case series, as well as retrospective observational studies describing the syndrome have been published. Importantly, no randomized controlled studies have been performed, a fact that has to be taken into account when discussing epidemiological data, diagnostic criteria and treatment recommendations [2]. PRES is associated with a wide array of clinical presentations including headaches, focal neurological deficits, seizures, visual disturbances, and encephalopathy. The severity and acuity of clinical symptoms vary, although typically occur with rapid onset [3]. 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 [4]. There appears to be a female predominance, even after excluding patients with eclampsia [5].

We present the case of a young patient with no significant medical history who presented with neurological symptoms consistent with Posterior Reversible Encephalopathy Syndrome (PRES). Brain MRI confirmed the diagnosis of Posterior Reversible Encephalopathy Syndrome (PRES). Additionally, the etiological assessment yielded negative results. A

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notable aspect in our patient's case is the persistence of sequelae, characterized by dexterity and grip impairment on the right side, hindering various activities of daily living.

2. Case report

26-year-old women, right-handed, student, Without any particular pathological history,admitted to emergency for initial symptomatology that was characterized by a sudden onset of consciousness disorders and seizures without headaches or neurological deficits, in a non-traumatic and afebrile context. Three days later, the course was marked by spontaneous improvement in consciousness, resolution of seizures. However, there was the onset of functional impairment not present initially in both upper limbs.

Upon admission to the neurology department, the clinical examination reveals lethargy, episodes of confusion, Glasgow Coma Scale (GCS) score of 15/15, afebrile and stable on cardiovascular and respiratory levels, normal blood pressure, patient catheterized with preserved diuresis. Neurological examination highlights flaccid brachial diplegia and tetrapyramidal irritation, while ophthalmological examination shows no abnormalities. The first cerebral angiography MRI reveals bilateral signal abnormalities in the frontal, posterior, and parieto-occipital lobes, with isosignal on T1-weighted images, hypersignal on T2-weighted, T2 flair, and diffusion with restricted apparent diffusion coefficient (ADC) (figure 1). The diagnosis of posterior reversible encephalopathy syndrome (PRES) was made.

Complete Blood Count : Hemoglobin: 13.4 g/dl, Erythrocyte Sedimentation Rate : 22 mm/hr , Blood Urea Nitrogen and Creatinine: 0.15 g/l-4.6mg/l, 24-hour Urinary Protein: 0.17g/24H, Antinuclear Antibodies , Double-stranded DNA , anti-Smith Antibodies : Normal, Magnesium level: 1,8 mg/dl (Normal), Cortisol level: 178.4 ng/ml(Normal), tests for HIV, HBV, HCV: Negative, Lumbar Puncture with Cerebrospinal Fluid (Analysis: Clear; White Blood Cells less than 3 elements per microliter; Protein: 0.23g/l; Glucose: 0.77g/l (with blood glucose 1.21g/l),

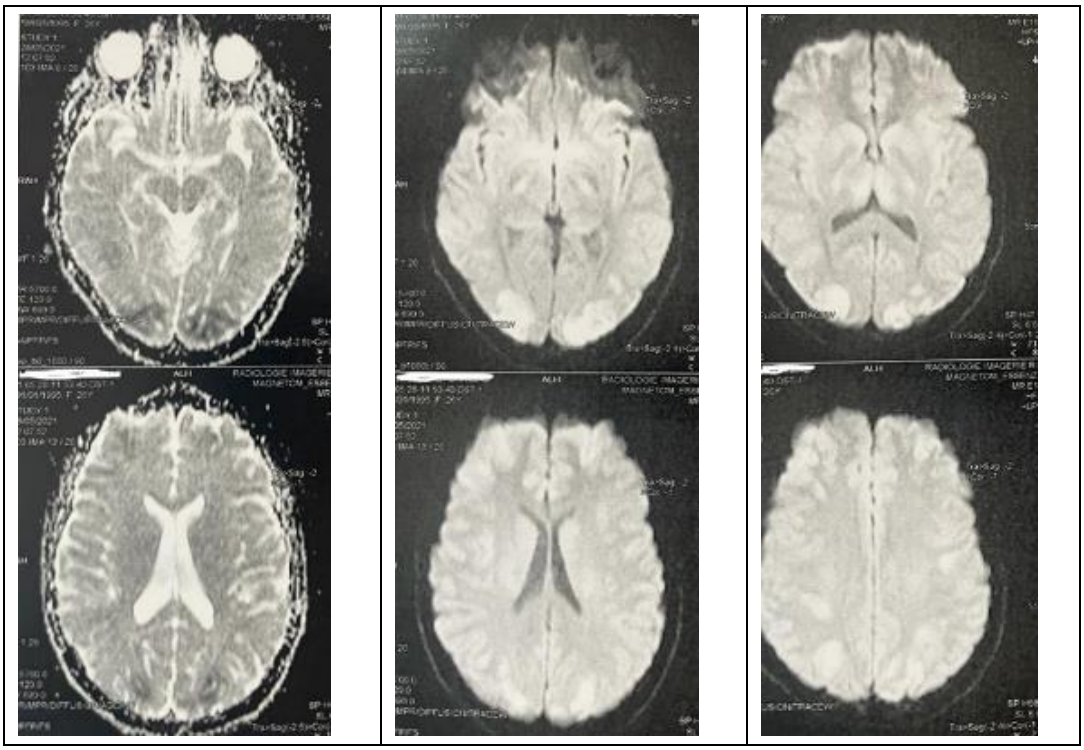

Figure 1 Sequences of MRI brain show the presence of bilateral and symmetric cortico-subcortical occipital and posterior fronto-parietal signal abnormalities. These lesions demonstrate isosignal on T1-weighted images and hypersignal on T2 and T2 FLAIR sequences. They exhibit hypersignal on diffusion-weighted imaging with a restricted apparent diffusion coefficient (ADC), suggesting restricted diffusion. These findings are consistent with bilateral supra-tentorial fronto-temporo-parietal lesions indicative of Posterior Reversible Encephalopathy Syndrome (PRES)

Polymerase Chain Reaction (PCR) and IgG tests for COVID-19: Negative.

Electroencephalogram (EEG): Normal background rhythm interspersed with periods of slowing; no periodic or epileptic abnormalities detected,

The patient's progress in the neurology department was marked by pronounced bradyphrenia. There was improvement in muscle strength, with a muscle testing score of 4 out of 5 proximally and 1 out of 5 distally in both upper limbs. A brain MRI with angiographic sequences for diagnostic evidence of lesion reversibility after 3 months of progression was NORMAL, demonstrating complete reversibility of the lesions (figure 2). Furthermore, after an exhaustive etiological assessment, no cause of PRES was identified in the case of our patient.

In light of the persistent deficit in the upper limbs, the patient was referred to the Department of Physical Medicine and Rehabilitation for further management. The initial evaluation in our department revealed a distal deficit in both limbs, more pronounced on the right side. Muscle strength was graded as 4 out of 5 for wrist extensors and palmar interossei. The rest of the neurological examination did not reveal any other abnormalities, nor did the orthopedic evaluation. The electromyoneurography (EMNG) of the upper limbs did not reveal any abnormalities.the box and block test (BBT) was 70 blocks on the left side , and 45 blocks on the right side. the nine-hole peg test (NHPT) was completed in 1 minute on the left side, while on the right side, the patient was unable to complete the test. Consequently, we recommended motor rehabilitation and occupational therapy focusing on improving grip strength and dexterity.

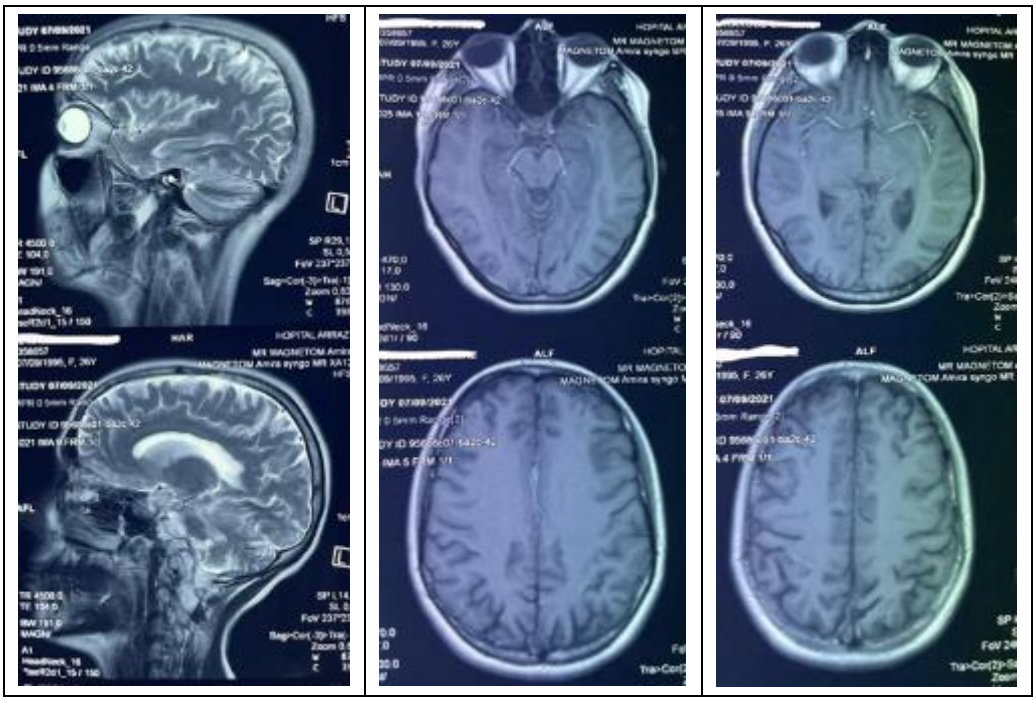

Figure 2 Sequences of MRI brain 03 month after first symptoms for follow up, noted significant improvement with reversibility of the initial lesions

After 3 months of rehabilitation, the boxe and block test (BBT) was 55 blocks on the right side and 70 blocks on the left side. the nine-hole peg test was within normal limits on the left side, completed in 25 seconds. However, on the right side, the patient still experienced significant difficulty in completing the test, with a delay of more than 3 minutes. Additionally, dystonic movements appeared, hindering activities of daily living such as dressing, eating, and writing, despite the absence of muscle deficits. Muscle strength in various muscle groups was restored. For this, we emphasized constraint-induced movement therapy during rehabilitation to aid in the recovery of grip strength and dexterity in the right upper limb.

At the one-year follow-up after the initial hospitalization, the patient continues to experience difficulties with dexterity and grip on the right side, accompanied by dystonic movements of the right hand. We recommended botulinum toxin injection for dystonia management, but the patient declined.

3. Discussion

The clinical picture of PRES includes several typical features: seizures, an acute encephalopathy syndrome, and visual disturbances. Seizures commonly represent the first clinical manifestation of the syndrome and are the most frequently seen symptoms in PRES.Seizures are generalized in the majority of cases but may also have a focal onset with following secondary generalization. Multiple seizures are even more frequent and status epilepticus (SE) may also occur [6]. Our patient presented with the clinical picture typical of PRES, including headaches, visual disturbances, and seizures. These symptoms were most commonly associated with renal insufficiency, hypertension, certain autoimmune diseases, pre-eclampsia, or eclampsia [7]. Our patient did not present any of these symptoms; her renal function was normal, blood pressure was within the normal range at 120/75, and there was no evidence of autoimmune pathology. During her admission, the patient was menstruating. In the absence of intervention, the symptoms worsen progressively over several days to weeks. They can escalate to encephalopathy, confusion, seizures, and even coma [8]. The evolution of our patient's symptoms occurred over a period of three days, marked by the onset of headaches complicated by seizures and confusion.

Two theories explain the mechanism of PRES occurrence: The first theory is that of cerebral hyperperfusion: indeed, arterial hypertension exceeds the brain's autoregulatory capacity, leading to vascular impairment and arteriolar vasodilation. Subsequently, the rupture of the blood-brain barrier causes a leakage of fluid from the vessels into the cerebral parenchyma, resulting in reversible vasogenic edema. The second theory is that of cerebral hypoperfusion, which is secondary to arterial hypertension or a systemic process. It can be observed in conditions such as pre-eclampsia, infections, or chemotherapy. When the immune system is activated, endothelial cells are subsequently damaged, leading to cytotoxic edema [8].

The diagnosis of PRES is typically made with magnetic resonance imaging (MRI) of the brain. Imaging characteristically shows focal regions of symmetric hyperintensities on T2- weighted studies most commonly in the parietal and occipital lobes, followed by the frontal lobes and the cerebellum [3]. this patient had extensive lesions on the initial MRI, abnormalities in the frontal, posterior, and parieto-occipital lobes, with isosignal on T1-weighted images, hypersignal on T2-weighted, T2 flair, and diffusion with restricted apparent diffusion coefficient (ADC); in many clinically convincing cases, the MRI is normal, especially if the duration of syndrome has been brief. Therefore, CT and MRI cannot be used to rule out this diagnosis [9]. Vasculopathy is a common finding in patients with PRES. Angiography, if performed, can show evidence of constriction of the blood vessels, which suggests a possible overlap with reversible cerebral vasoconstriction syndrome (RCVS) [3]. In this patient, angiography was not performed. Fugate et al. suggested the following criteria for the diagnosis of PRES: neurological symptoms of acute onset, neuroimaging abnormalities of (focal) vasogenic edema and the reversibility of clinical and/or radiological findings [5].

The nonspecific clinical manifestations of PRES, along with the multiplicity of radiological presentations, sometimes make its diagnosis difficult [10]. There are numerous differential diagnoses, mainly characterized by white matter abnormalities found on MRI [5]. The differential diagnosis of PRES includes severe neurological conditions such as stroke, encephalitis, reversible cerebral vasoconstriction syndrome, intracranial venous thrombosis, intoxication with anticholinergic drugs and primary CNS vasculitis. Although the clinical picture of PRES may not be specific, an early MRI leads to the correct diagnosis in most cases and may, therefore, forestall further investigations [11]. The most important differentials include viral and autoimmune encephalitis, demyelinating disease, toxic leucoencephalopathies, malignancy such as gliomatosis cerebri, CNS vasculitis, central/ extrapontine myelinolysis and acute stroke, especially due to cerebral venous thrombosis. Differentiating PRES from these other conditions requires a thorough review of risk factors, additional targeted testing and follow-up imaging [7,12]. In this patient, we conducted a comprehensive etiological assessment which allowed us to eliminate all differential diagnoses.

Commonly associated etiologies with PRES include: Toxic agents: Exposure to toxic agents represents the main etiology associated with PRES, found in 11 to 61% of cases [4,13]. However, in our case, no intake of toxic agents was found. Hypertensive crisis/urgency: Acute hypertensive crisis and urgency represent the second etiology of PRES [10]. During her admission to the emergency department, our patient's blood pressure was within normal limits. Infection-sepsis-septic shock: Cases of infection have been described in series. Typically, this involves Gram-positive bacteremia occurring within 15 days before PRES. PRES has also been reported in association with bacteremic infection with Escherichia coli. The infectious workup of the patient was negative, and there were no antecedents in the days preceding the onset of symptoms. Pre-eclampsia and eclampsia is also among the etiologies found in PRES. However, our patient was not pregnant. Autoimmune diseases are encountered in some cases of PRES. However, the search for an autoimmune pathology in this patient was negative.

The treatment of PRES is symptomatic, since no specific therapeutic strategy is currently available. The management of the underlying disease or pathology leading to PRES development is of major importance [2]. The key thing to remember in the management of PRES is early diagnosis and initiation of therapy. Many patients may require intensive care unit (ICU) care for aggressive management of their symptoms such as seizures, encephalopathy and status epilepticus. In cases of PRES caused by factors other than pre-eclampsia and eclampsia, the most effective therapy includes withdrawal of the offending agent, immediate control of blood pressure, anticonvulsive therapy and temporary renal replacement therapy (hemodialysis/peritoneal dialysis) if required [14]. The management of hypertensive episodes and maintenance of normal blood pressure is an essential component of PRES treatment. However, there is no evidence, based on prospective controlled studies, that strict blood pressure control limits neurologic injury, or results in a regression of clinical or imaging findings [2]. Patients with seizures should be treated with antiepileptic drugs, but for how long is controversial. Although there is a case report of a PRES patient who developed epilepsy despite complete resolution of the MRI lesions, seizures do not normally progress to chronic epilepsy [11]. Patients need to be hydrated and to have any electrolyte disturbances corrected. Patients in whom cerebral oedema is causing raised intracranial pressure may require neurosurgical measures [12]. In the case of our patient, the initial management consisted of treating the convulsive seizures with sodium valproate, with a loading dose for the seizures, followed by maintenance with the same medication for one month. Additionally, our patient did not present with any other symptoms, notably blood pressure remained within normal range.

Although PRES was initially described as a benign entity that was reversible with a good outcome, mortality has been observed in 19% of patients and functional impairments of varying degree have been reported in 44% of patients. Certain deficits that require long-term care include epilepsy and motor deficits [15]. This patient retained a deficit in the right upper limb, with impairment in motor skills and handwriting, considering that our patient is right-handed.

Recovery of the imaging abnormalities confirms the diagnosis and might help differentiate PRES from chronic leukoencephalopathies, The ideal timing of repeat MRI is about 7–10 days after onset of symptoms when there should usually be clear improvement of the MRI abnormalities [11]. In our case, the interval between the first MRI and the second one was one month. The second MRI showed a resolution of the lesions present on the first one. Poor prognosis is associated with factors such as severe encephalopathy, chronic hypertension, neoplastic aetiology, delayed diagnosis of causative factor, multiple comorbidities, elevated C-reactive protein (CRP) and coagulopathy. Involvement of the corpus callosum, extensive cerebral oedema or haemorrhage, restrictive diffusion and subarachnoid haemorrhage are the MRI features which predict a worse prognosis [14]. Despite our patient not having any of these factors, she retained functional sequelae that hindered various activities in her daily life. Very few studies have focused on post-hospitalization evolution, particularly on functional sequelae and quantifying them. Only one study has addressed characterizing the progression of patients upon discharge. The authors found a Rankin score of 2.5, indicating mild to moderate impairment of their autonomy [10]. Modified Rankin Scale (mRS) score evaluation for this patient was 2, Slight disability. Able to perform daily activity without assistance, but unable to carry out previous activities. this case further supports existing evidence that the long-term sequelae of PRES are poorly understood.

Recurrence of PRES has been infrequently documented in single-case reports. Relapsing PRES has been reported in patients after solid organ transplantation, chemotherapy, Allogeneic Bone Marrow Transplantation, autoimmune disease, sickle cell disease, and in a patient with a mitochondrial disorder. Multiple episodes of PRES in a single patient have been reported in children with renal disease and in a patient with Systemic Lupus Erythematosus, for a total of 4 recurrent episodes of PRES that have been documented [6].

4. Conclusion

The diagnosis of PRES is both radiological and clinical, with MRI playing a crucial role. Treatment is primarily symptomatic, sometimes requiring intensive care unit admission. Prognosis is favorable in the majority of cases, but severe complications and even death can occur. The reversibility of initial symptoms is well-documented in the literature. Long-term functional impairment outcomes following PRES have not been adequately characterized in the literature. Therefore, it is necessary to conduct follow-up screenings in more patients presenting both typical and atypical PRES syndromes. This will provide insight into whether the functional and motor sequelae of PRES are less reversible.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

All the data has been collected anonymously following patient confidentiality.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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