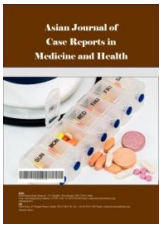

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Hemorrhagic Posterior Reversible Encephalopathy – A Case Report and Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author MFDLD designed the study. Author IDSA wrote the first draft of the manuscript. Authors MFDLD, CDCL, MDGMM and DDSD managed the analyses of the study. Authors IDSA, APFV, CBFL and CTR managed the literature searches. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

We aim to review the etiological investigation and differential diagnosis of PRES, including viral infectious diseases, considering the current Coronavirus disease 2019 (COVID-19) pandemic. Our case report showed a critical patient with hemorrhagic PRES associated with nephropathy. Posterior reversible encephalopathy syndrome (PRES) is an acute neurological syndrome that can be presented as a variety of symptoms and it is usually associated with hypertension status, sepsis, eclampsia, autoimmune diseases, immunosuppressive therapy, or infectious diseases. Recently, an association between that hemorrhagic PRES and COVID-19 was reported. The mechanism of posterior reversible encephalopathy syndrome (PRES) is unknown, but there are two main theories to explain the vasogenic brain edema. The typical imaging pattern includes brain

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vasogenic edema located in the subcortical white matter and the cerebral cortex of the parieto-occipital lobes. There is no specific treatment for PRES and it can be reversible if the predisposing cause is identified and controlled.

Keywords: Hemorrhagic; encephalopathy; PRES; brain.

1. INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is an acute neurological syndrome that can be presented as a variety of symptoms such as headache, altered mental status, visual loss, epileptic seizures or focal neurological deficits. This syndrome is usually associated with hypertension status, sepsis, eclampsia, autoimmune diseases, immunosuppressive therapy or infectious diseases [1]. The mechanism that can precipitate this pathology remains controversial. There are two main theories: one related to hypertension / hyperperfusion status leading to an endothelial damage and vasogenic edema or systemic toxicity with endothelial dysfunction and subsequent vasoconstriction, resulting in brain hypoperfusion/ischemia and vasogenic edema [2]. The reversibility and posterior region predominance of lesions are the main features in its original description but not a rule. It affects preferentially brain areas supplied by the posterior circulation and usually in the watershed zones [3]. The imaging shows a parietooccipital and posterior frontal cortical and subcortical lesions resembling vasogenic edema. The brainstem, basal ganglia, and cerebellum may be involved. The lesions may present contrast enhancement, hemorrhage, and diffusion restriction (DWI) on Magnetic Resonance imaging (MRI) [3–5]. The incidence of hemorrhage in PRES patients is between 9 to 33% [1,4]. In this report, we discuss the importance of the etiological investigation and differential diagnosis of PRES, including viral infectious diseases, considering the current COVID-19 pandemic [6–8]. All authors have made a significant contribution to the manuscript and there has been no financial support for this work.

2. CASE REPORT

An 81-year-old male was admitted to the hospital emergency room with a history of mental confusion for 5 days. The patient was being treated for facial herpes zoster and had multiple comorbidities such as hypertension, diabetes and chronic renal failure. He underwent brain MRI (T1WI, T2WI, FLAIR, T2WI echo gradient and the diffusion technique) at admission without significant findings and laboratory tests being negative for infectious screening (including COVID-19). During hospitalization, the patient evolved with worsening of the mental confusion and decreased level of consciousness, after a hemodynamic instability with acute worsening of chronic renal failure (Creatinine= 4.38 mg/DL) and subfebrile peaks. Therefore, he underwent a second brain MRI, which shows multiple areas of signal abnormality, more evident in bilateral frontoparietoccipital regions, including vascular watershed areas, possibly representing edema of cytotoxic pattern with DWI of water molecules and gray-white matter indistinction. In addition, the MRI showed extensive and predominant cortical hematic components (multiple deposits of gyriform distribution), associated with marked edema of the adjacent white matter. Relatively symmetrical DWI restrictions affecting both globus pallidus were also found. This suggests a diffuse parenchymal insult, with loss of vessel modulation possibly representing PRES, which may be secondary to infection (including COVID-19 or another agent), drugs, or nephropathy. The patient underwent to etiological investigation and research of the predisposing factor for PRES, laboratory tests showed negative infectious screening, including for COVID-19 (PCR and serology). The cerebrospinal fluid was also negative for meningitis and encephalitis agents. The PRES was secondary to acute worsening of chronic renal failure associated with hypertensive peaks and the patient was managed with dialysis and intensive support, considering the multiple comorbidities, however, there was no clinical improvement wit persistence of neurological injuries. It was opted in common agreement for palliative support.

3. DISCUSSIONS

Posterior reversible encephalopathy syndrome (PRES) is an acute or subacute neurological syndrome, also known as acute hypertensive encephalopathy or reversible posterior leukoencephalopathy, first described by Hinchey and colleagues in 1996 [9]. The symptoms and signs are diverse such as headache, altered

mental status, visual loss, epileptic seizures, or focal neurological deficits (hemiparesis, aphasia, and even myelopathic symptoms) [1]. PRES is not an exclusive posterior phenomenon; it is more like a gradient posterior to anterior disease, which is presumably related to sympathetic innervation gradient [1,10].

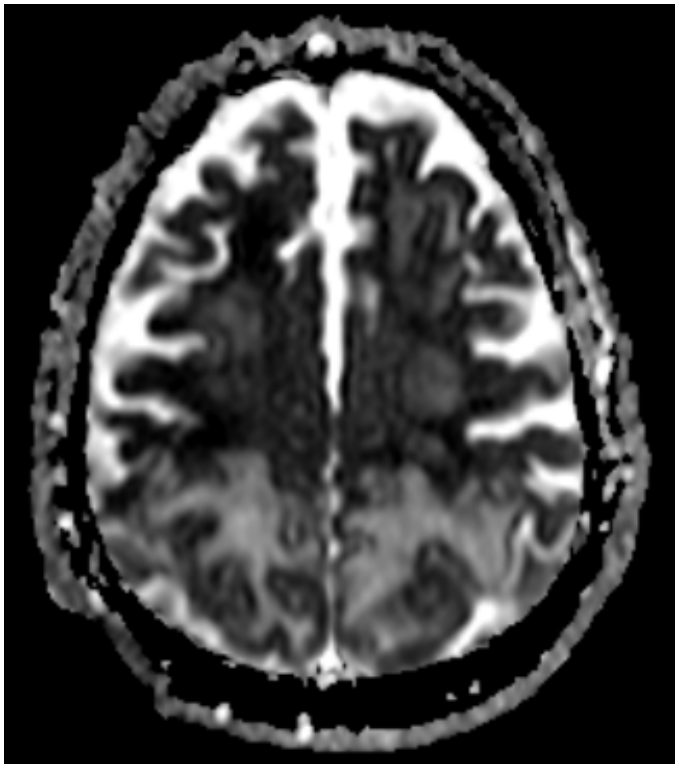
The mechanism of posterior reversible encephalopathy syndrome (PRES) is unknown, but there are two main theories to explain the vasogenic brain edema. The first described and most popular theory, also called hypertension/hyperperfusion theory, suggests that severe hypertension exceeds brain autoregulation limits, leading to breakthrough brain edema. This theory is usually supported by acute hypertension that frequently accompanies PRES and the treatment of this condition, resulting in clinical and radiological resolution [5]. However, 15–20% of patients with PRES are normotensive or hypotensive [1,11] and most of these patients have a complex 'systemic process' with multiple biologic features [2]. The second theory is that inflammatory cytokine response in systemic toxic conditions causes hypoperfusion/vasoconstriction brain status with endothelial dysfunction, resulting in vasculopathy and cerebral hypoperfusion with brain vasogenic edema [1,2]. This theory is also used to explain some cases of hemorrhage, the endothelial dysfunction associated with blood-brain barrier disruption and coagulopathy might be related with hemorrhagic PRES [12,13].

There are several conditions that can precede PRES such as preeclampsia/eclampsia, autoimmune diseases, transplantations, chemotherapy, drugs and infections/sepsis. Among the infectious causes, the most frequently associated organisms with PRES are the gram-positives bacteria [14,15], viruses (especially HIV and influenza), and now Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) associated with hemorrhagic PRES was reported [4]. Although this is a multifactorial pathology, PRES may be a neurologic manifestation of COVID-19 [4,6–8].

Neuroimaging has an important role in PRES diagnosis and MRI is the imaging choice, although CT can be helpful. The typical patterns are brain vasogenic edema located in the subcortical white matter and the cerebral cortex of the parieto-occipital lobes [3]. Therefore, lesions can be found in other sites as the frontal lobe, cerebellum and diencephalon. PRES can be divided according to imaging findings in some types based on lesion location: mainly parieto-occipital, superior frontal sulcus and holohemispheric watershed pattern [3]. There are partial (absence of bilateral typical imaging findings in either parietal lobes or occipital lobes) or asymmetric expression (absence of unilateral typical imaging findings in either parietal or occipital lobes) of these primary patterns, and rarer types such as the "central-variant PRES" with severe edema in the brainstem, thalamus, and deep white matter and lack of parieto-occipital edema [16] or isolated involvement of the posterior fossa structures which can lead to hydrocephalus and tonsillar herniation [3,17]. The other imaging aspects that can be noticed on PRES are areas of DWI restriction on MRI (15–30% of cases), without enhancement [18]. The magnetic resonance angiography (MRA) 3D TOF (time of flight) may be normal or may show signs of vasculopathy with vessel irregularity and focal vasodilatation/vasoconstriction pattern and sometimes if MRA follows up is done, it usually shows a reversible process [2,14]. The presence of intracranial hemorrhage in PRES range from 9 to 33% and there are 3 types of hemorrhage: 1) parenchymal hematoma, 2) subarachnoid hemorrhage, and 3) focal hemorrhages (< 5 mm) in the brain parenchyma [5]. As there is no definitive criterion for diagnosing PRES, the knowledge of its typical imaging patterns, as well as the atypical presentations, help the radiologist to place PRES in differential diagnoses according to imaging findings and the clinical context [1].

There is no specific treatment for PRES and it can be reversible if the predisposing cause is identified and controlled. The consensus between physicians suggests that as the effect of blood pressure plays an important role in the pathophysiology of PRES the hypertension control is crucial and fluctuations of blood pressure should be avoided [1,16].

PRES has a favorable prognosis and follow-up imaging shows radiologic complete or almost-complete resolution in about 70% of cases [5,18]. The clinical outcome in patients with PRES is related to multiple factors, including intracranial hemorrhage, which increases the morbimortality [12]. The recovery time ranges from 2–8 days, but some patients may take several weeks to complete a full recovery [1]. The mortality is about 3-6% and the recurrence ranges from 5-10% and is more common in patients with uncontrolled hypertension [1,19,20].



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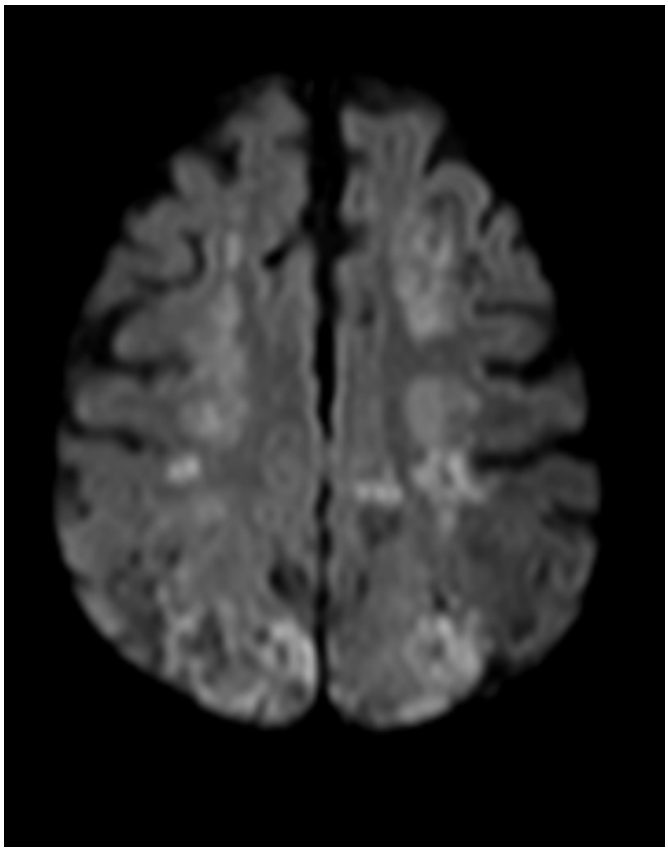

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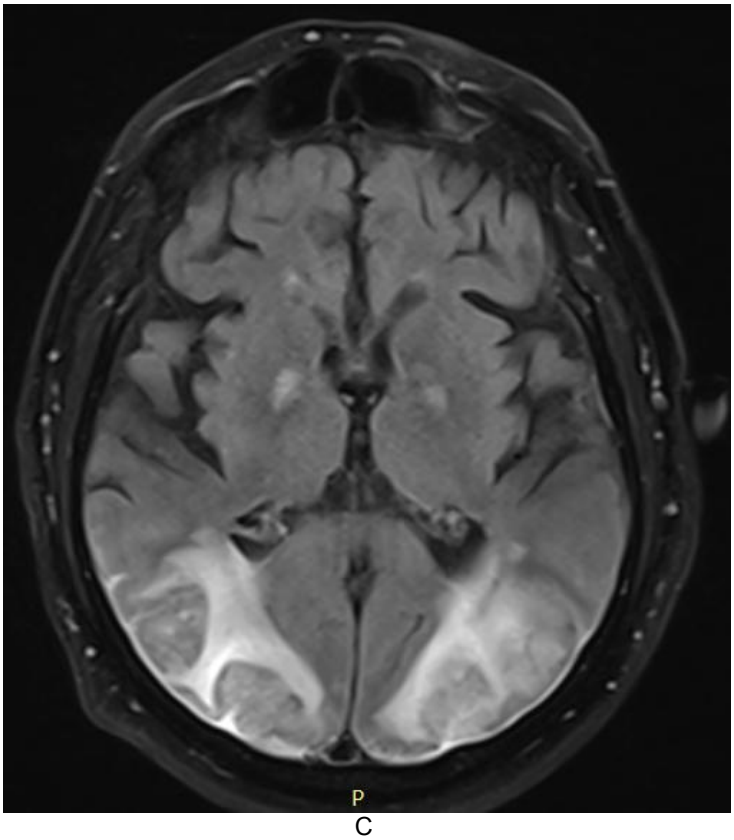

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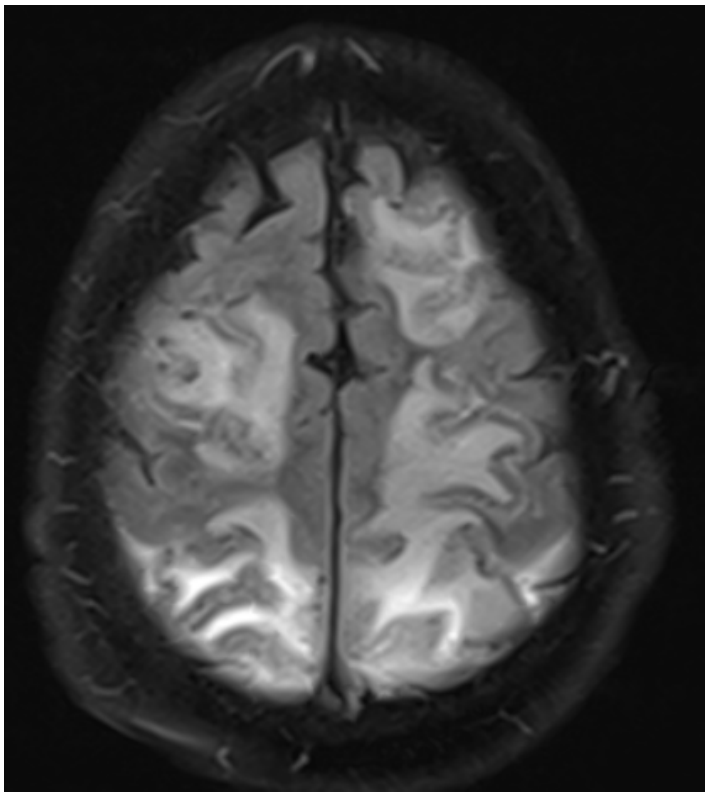

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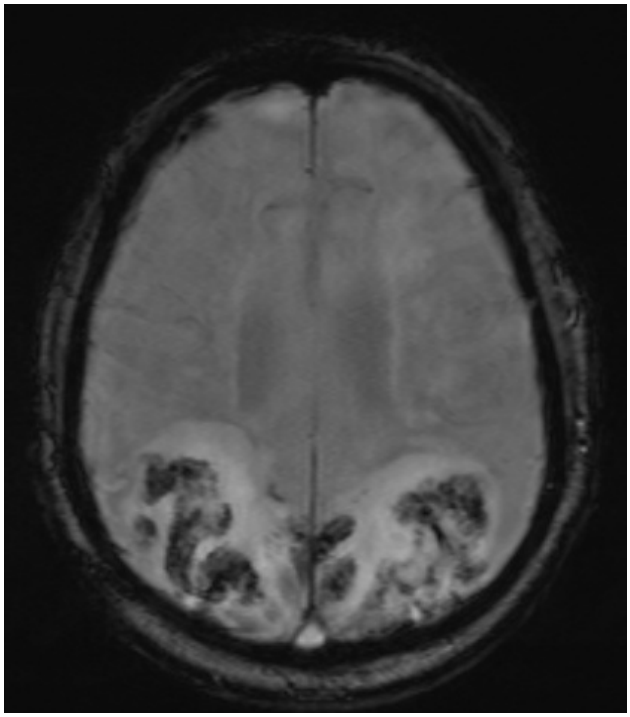

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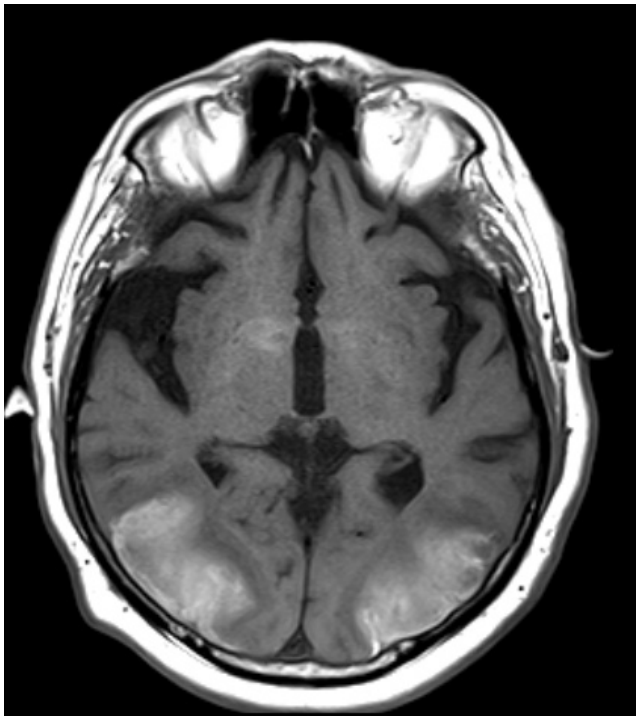

F

Fig. 1. Brain MRI sequences ADC map (A) and DWI (B), FLAIR (C and D), SWI (E) and T1WI (F). Diffuse areas of T2/FLAIR high signal (C and D), more evident in bilateral frontoparietoccipital regions, including vascular watershed areas associated with cytotoxic edema (A and B) and extensive hematic components predominantly cortical (E and F), associated with marked edema of the adjacent white matter (C and D)

4. CONCLUSION

Posterior reversible encephalopathy syndrome (PRES) is an acute neurological syndrome that can be presented as a variety of symptoms and on different clinical scenarios. Our report showed a critical patient with hemorrhagic PRES associated with nephropathy, but in the actual pandemic world phase, it is necessary to exclude COVID-19 as a cause of PRES.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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