



## Case Report

# Asymmetric posterior reversible encephalopathy syndrome secondary to epilepsy occurring in the chronic phase of subarachnoid hemorrhage

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## ABSTRACT

**Background:** Posterior reversible encephalopathy syndrome (PRES) is a rare clinical syndrome that refers to a disorder with reversible subcortical vasogenic brain edema involving the parieto-occipital lobe, temporal lobe, basal ganglia, and its surroundings. Radiologically, it is characterized by symmetrical lesions; however, atypical findings have sometimes been reported.

**Case Description:** A 79-year-old woman experienced subarachnoid hemorrhage (SAH) a year and a half previously before this hospitalization. She presented with sudden-onset coma, dacryorrhea, and moderate right hemiparesis and was taken to our hospital. Computed tomography showed no apparent abnormal acute lesions. Electroencephalography confirmed periodic lateralized epileptiform discharges in the left hemisphere. First, based on the findings, she was diagnosed with nonconvulsive status epilepticus and started antiepileptic therapy. Six days after admission, however, multiple asymmetric lesions were confirmed on magnetic resonance imaging. Considering that findings subsequently improved, we finally diagnosed her with asymmetric PRES secondary to epilepsy occurring in the chronic phase of SAH. Aphasia and right hemispatial neglect persisted as sequelae and she was transferred to a rehabilitation hospital with a modified Rankin scale of 3.

**Conclusion:** Excessive elevation of blood flow in the hemisphere is inferred to lead to blood-brain barrier collapse and subsequent asymmetric PRES.

**Keywords:** Asymmetric posterior reversible encephalopathy syndrome, Blood-brain barrier, Epilepsy, Subarachnoid hemorrhage, Vasogenic brain edema

## INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a rare clinical syndrome that refers to a disorder with reversible subcortical vasogenic brain edema involving the parieto-occipital lobe, temporal lobe, basal ganglia, and its surroundings. Patients diagnosed with PRES may require intensive care monitoring and treatment due to severe complications, such as epilepsy attack, cerebral ischemia, intracranial hemorrhage, or increased intracranial pressure. Few specific affections such as hypertensive encephalopathy, eclampsia, bacterial infections, transplantation,

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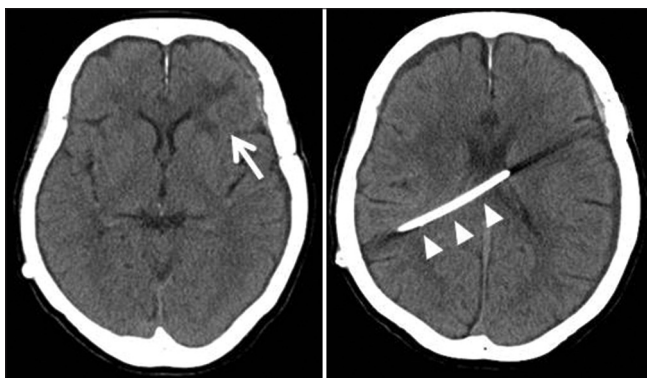
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renal failure, autoimmune disorders, and some kinds of drugs are considered to induce this condition. Radiologically, it is characterized by symmetrical lesions; however, atypical findings have sometimes been reported. We herein report a case of asymmetric PRES secondary to epilepsy occurring in the chronic phase of subarachnoid hemorrhage (SAH). In addition, we summarize and review this subject, as this condition is extremely rare.

## CASE DESCRIPTION

A 79-year-old woman, who had experienced SAH of a Hunt and Kosnik Grade II a year and a half previous, presented with sudden-onset coma, dacryorrhea, and moderate right hemiparesis and was taken to our hospital. She had undergone aneurysmal neck clipping for a ruptured internal carotid artery-posterior communicating artery aneurysm and ventriculoperitoneal (VP) shunt placement during her first hospitalization. She was discharged with 1 of modified Rankin scale (mRS) score and had a good clinical course.

On admission, computed tomography showed no apparent abnormal lesions, except for the left frontal cerebral lobe contusion that occurred in the SAH treatment [Figure 1]. However, on electroencephalography (EEG), periodic lateralized epileptiform discharges (PLEDs) were confirmed in the left hemisphere [Figure 2]. We diagnosed her with nonconvulsive status epilepticus and started antiepileptic therapy (1000 mg/day of levetiracetam). A day after admission, the patient's neurological defect improved. However, her consciousness redeteriorated due to partial convulsions on the right side after another 5 days. General anesthesia was administered because the PLEDs had not disappeared. At that time, the most characteristic radiological findings for this patient, including asymmetrical hyperintensity on fluid-attenuated inversion recovery (FLAIR) imaging of magnetic resonance imaging in the left



**Figure 1:** CT on admission shows no apparent abnormal lesions except for the left frontal cerebral lobe contusion (arrow) and shunt tube (arrowhead) that occurred in the SAH treatment. CT: Computed tomography, SAH: Subarachnoid hemorrhage.

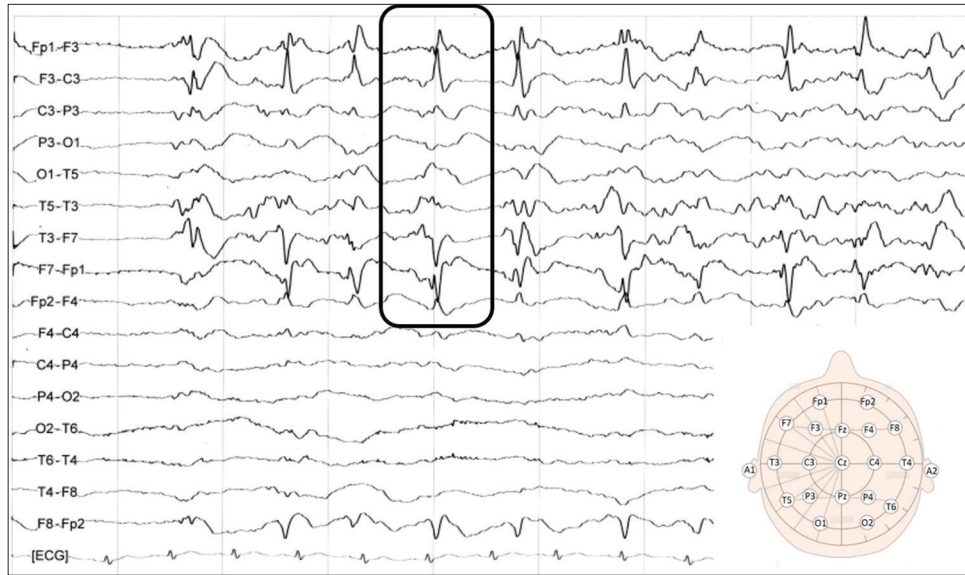
rectal gyrus, temporal lobe, parietal lobe, insular cortex, and thalamus, were revealed [Figure 3a]. Furthermore, lesions were described as mild high-intensity areas on diffusion-weighted imaging (DWI) [Figure 3b] and apparent diffusion coefficient (ADC) maps [Figure 3c]. Time-of-flight MR angiography showed increased visualization of the left middle cerebral artery [Figure 3d]. After the EEG normalized with an increasing dose of anticonvulsant drugs, she was extubated. Hemiparesis improved; however, motor and sensory aphasia and right hemispatial neglect persisted as sequelae. Finally, using 3000 mg/day of levetiracetam, 1200 mg/day of sodium valproate, and 4 mg/day of perampanel could control her epilepsy attack. Abnormal radiological findings disappeared 132 days after admission [Figure 4a and b]. Based on the findings, a series of progress was thought to be caused by asymmetric PRES secondary to epilepsy. She was transferred to a rehabilitation hospital with a mRS score of 3.

## DISCUSSION

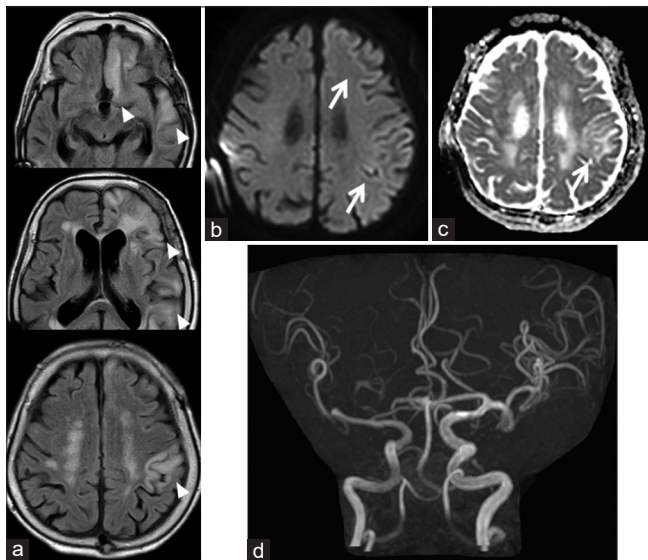
PRES was first reported by Hinchey *et al.* in 1996.<sup>[5]</sup> It was initially reported as reversible posterior leukoencephalopathy syndrome, although PRES named by Casey *et al.* has become common.<sup>[2]</sup> PRES is a rare clinical syndrome that involves the acute onset of headache, confusion, optical impairments, and epilepsy, which is accompanied by reversible subcortical vasogenic brain edema on radiological neuroimaging. These findings are characterized by symmetrical lesions in the parieto-occipital lobe, temporal lobe, and basal ganglia. Established diagnostic criteria are lacking and clinical and radiological findings are often not specific. Therefore, the diagnosis of PRES may often only be made only after excluding other important diagnoses.

PRES is thought to be associated with various systemic conditions such as severe hypertension, eclampsia, bacterial infections, transplantation, renal failure, and patients with autoimmune diseases receiving immunosuppressive therapy or high-dose chemotherapy.<sup>[14]</sup> At present, COVID-19-associated PRES has also attracted the attention of scholars.<sup>[1,12,18]</sup> In the field of neurosurgery, PRES has been reported to occur in cases associated with the treatment for SAH,<sup>[11]</sup> subsequent shunt placement for normal pressure hydrocephalus (NPH),<sup>[13]</sup> or hyperperfusion syndrome associated with surgical treatment for internal carotid artery stenosis.<sup>[4,8]</sup>

On average, approximately 40% of all patients diagnosed with PRES require intensive care monitoring and treatment due to severe complications such as epilepsy attack, cerebral ischemia, intracranial hemorrhage, or increased intracranial pressure.<sup>[10]</sup> However, there have been no randomized controlled trials focusing on the treatment, which should be considered when discussing epidemiological data, diagnostic criteria, and treatment recommendations.

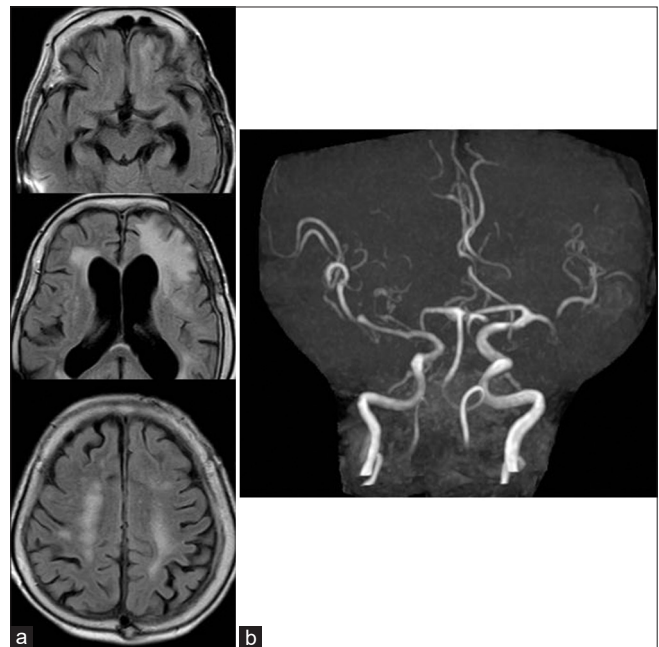


**Figure 2:** Electroencephalography on admitting showed periodic lateralized epileptiform discharges in the left hemisphere (square).



**Figure 3:** MRI findings 6 days after admission are shown as follows. (a) There are asymmetrical hyperintensity areas such as the left rectal gyrus, temporal lobe, parietal lobe, insular cortex (not shown), and thalamus (not shown) on FLAIR imaging (arrowhead). (b and c) DWI and ADC map show hyperintensity in the left cortical areas (arrow). (d) Increased signal intensity of the left MCA on MRA is revealed. DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient, FLAIR: Fluid-attenuated inversion recovery, MCA: Middle cerebral artery, MRA: Magnetic resonance angiography.

Recognizing the exact mechanism of PRES, there are two leading theories regarding the pathophysiology. One is the breakthrough theory that the blood-brain barrier (BBB) collapses due to impaired cerebrovascular autoregulation, which leads to subsequent cerebral edema. The other is the



**Figure 4:** The following MRI shows that all radiological abnormal findings on admission had almost disappeared. (a) FLAIR and (b) MRA.

vasospasm theory that neurological deficits appear because of cerebral ischemia associated with cerebral vasospasm. Both theories have been confrontationally argued, but now breakthrough theory seems to be somewhat more espoused.<sup>[7,15,17]</sup>

In the patients of PRES, lesions are mostly symmetric, affecting the temporal, parietal, and occipital lobes, and exhibit characteristics such as the hyperintensity area on

**Table 1:** Asymmetric PRES in association with SAH.

	Age/sex	Location of aneurysm	Surgical procedure	Phase	Side	Related factors	Vasospasm	Shunt placement
Voetsch <i>et al.</i> <sup>[15]</sup>	35/F	R.MCA	Clipping	Acute	Affected	Epilepsy attack	(+)	
Dhar <i>et al.</i> <sup>[3]</sup>	47/F	R.IC-PcoA	Clipping	Acute	Healthy	Triple-H therapy	(+)	
Wartenberg <i>et al.</i> <sup>[16]</sup>	73/F	L.ICA	Clipping	Acute	Healthy	Triple-H therapy	(+)	
Sato <i>et al.</i> <sup>[13]</sup>	79/M	R.MCA	Clipping	Chronic	Affected	Shunt placement	(-)	(+)
Huijgen <i>et al.</i> <sup>[6]</sup>	36/F	L.ACA	Coil	Chronic	Affected	Cessation of nimodipine	(+)	(-)
Our case	79/F	L.IC-PcoA	Coil	Chronic	Affected	Epilepsy attack	(-)	(+)

F: Female, M: Male, MCA: Middle cerebral artery, IC-PcoA: Internal carotid-posterior communicating artery, ICA: Internal carotid artery, ACA: Anterior cerebral artery

FLAIR images and increasing ADC value without abnormal signal on DWI images. In our case, however, the lesions were asymmetric and involved the anterior lobes. Few papers have summarized cases of PRES that developed during SAH treatment, most of which lesions were bilateral.<sup>[3,11]</sup> To the best of our knowledge, asymmetric PRES in association with SAH is very rare, with six cases including ours [Table 1]. Of these cases, there were three cases of acute onset and chronic onset each. Two patients of acute onset except for a case of convulsions developed PRES on the healthy side. In addition, cerebral vasospasm occurred in all the cases. Conversely, all the cases of chronic onset including our case developed on the affected side. Furthermore, two patients underwent VP shunt placement.<sup>[3,6,13,15,16]</sup>

The differences in the affected side depending on the time of onset are interesting. In the acute phase of SAH, the combination of induced hypertension, hypervolemia, and hemodilution (triple-H therapy) is often utilized to maintain blood flow and prevent cerebral vasospasm. Consequently, cerebral blood flow is presumed to paradoxically increasing in healthy hemisphere, and it induces the breakdown of BBB. Therefore, in patients with SAH accompanied cerebral vasospasm, unilateral PRES may be more likely to occur on the healthy side. Conversely, in the chronic phase, blood flow and metabolism in the affected hemisphere that strongly suffers initial damage of SAH are easily increased by triggers such as epilepsy attack, hypertension, and hydrocephalus.

As stated above, vasogenic edema following the breakdown of BBB has been postulated as a central mechanism of PRES.<sup>[9]</sup> Although it is already recognized that the acute phase of SAH causes BBB damage, whether it is sustained in the chronic phase which has not been investigated. However, as BBB damage in patients with idiopathic NPH is confirmed, we speculated that similar changes occur in patients who are required shunt placement in the chronic phase of SAH.

This is how excessive elevation of blood flow in the hemisphere is inferred to lead to BBB damage and subsequent asymmetric PRES.

## CONCLUSION

We report a case of asymmetric PRES secondary to epilepsy occurring in the chronic phase of SAH. If asymmetrical radiological changes were observed after SAH, even in the acute or chronic phase, we should consider this clinical condition.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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