Posterior Reversible Encephalopathy Syndrome

INTRODUCTION
Posterior reversible encephalopathy syndrome (PRES) refers to a potentially reversible neurotoxic state occurring in association with vasogenic cerebral edema. Although the reported age range varies between 4 and 90 years, most affected patients are in their fourth or fifth decade of life. There is a female predominance, often attributable to the underlying etiology. Clinically, PRES usually present with a constellation of symptoms, with altered mental status (50%–80%) and seizures (60%–75%) being the most common, followed by headaches and visual disturbances. Occasionally, patients present with focal neurologic deficits, sensorimotor symptoms, or status epilepticus. These symptoms usually develop over several hours to a few days and are gradually progressive.

PRES occurs more commonly in patients with eclampsia, organ transplantation, or hypertension. The association is perhaps strongest with eclampsia, with some authors reporting neuroimaging findings of PRES in up to 98% of these patients. Within the organ transplantation subgroup, the incidence is higher with myeloablative regimens and allogeneic bone marrow transplants (7%–9%) when compared with patients receiving solid organ transplants (0.4%–6%). PRES can also accompany organ rejection or infection. Another common association is hypertension, which is seen in approximately 75% of patients and is usually moderate to severe (hypertensive encephalopathy). Other reported associations include sepsis, other infections, connective tissue disorders, autoimmune disorders, and chemotherapeutic agents such as cyclosporine, tacrolimus, and cisplatin.

EVALUATION: OVERVIEW
The pathogenesis of PRES remains controversial. The more widely accepted theory postulates failure of cerebral autoregulation in the setting of rapidly increasing blood pressure. Subsequent hyperperfusion and breakdown of the blood-brain barrier result in extravascular displacement of macromolecules and plasma and the appearance of vasogenic edema on neuroimaging. Because the posteriorly located regions within the brain have poor sympathetic innervation, they are more severely affected. The theory is supported by the frequent coexistence of hypertension in PRES. In addition, lowering of blood pressure results in both clinical and radiologic improvement.

However, the theory fails to explain both the absence of underlying hypertension in up to 20% to 30% of patients and lack of positive correlation between cerebral edema and severity of hypertension. In fact, patients with more severe hypertension often have less vasogenic edema and arterial spasm. In addition, perfusion studies in patients with PRES demonstrate reduced cerebral blood volumes implying hyperperfusion, contrary to the theory that suggests hyperperfusion.

Some authors therefore believe that PRES results from cerebral autoregulatory vasodilatation precipitated by endothelial dysfunction from systemic conditions (Fig. 3.1). Subsequent hyperperfusion occurs and results in involvement of watershed territories on neuroimaging. The hypertension is felt to represent a compensatory reaction to reduced brain perfusion. This theory postulates upregulation of cytokines (tumor necrosis factor-α, interleukin-1, and interferon-γ), resulting in endothelial dysfunction, vasculopathy, and increased vascular permeability. These cytokines may provide a common pathway in various systemic conditions such as eclampsia, sepsis, other infections, autoimmune disorders, and organ transplant patients while also explaining the frequent association of these entities with PRES.

IMAGING APPEARANCE
PRES most frequently appears as symmetric areas of parenchymal vasogenic edema that evolve over a period of days to weeks, becoming more prominent before eventually resolving in most cases (Fig. 3.2). Cortical and subcortical white matter involvement most frequently affects the occipital and parietal regions, followed by the frontal lobe (68%), inferior temporal region (40%), and cerebellum (32%) (Fig. 3.3). Involvement of the deep white matter, basal ganglia, thalamus, brainstem, and splenium is less common but occurs in approximately 10% to 20% of cases. Atypical patterns of involvement, with lesions predominantly localized to the brainstem (Fig. 3.4), posterior fossa (Fig. 3.5), or basal ganglia (Fig. 3.6), occasionally occur. In addition, involvement can be asymmetric and rarely even unilateral (Fig. 3.7).

The varying distribution of parenchymal involvement can be broadly divided into four patterns, each seen in approximately 20% to 30% of cases. Patients with a holohemispheric border zone pattern typically show bilateral symmetric edema in the anterior cerebral artery–middle cerebral artery (ACA-MCA) and posterior cerebral artery–middle cerebral artery (PCA-MCA) territory border zones (Fig. 3.8). In the superior frontal sulcus border zone pattern, there is distinct frontal lobe involvement predominantly along the mid to posterior aspect of the superior frontal sulcus. In contrast to the holohemispheric pattern, the frontal pole is usually spared (Fig. 3.9).

The parietal-occipital pattern manifests on imaging with predominant involvement of the parietal and occipital lobes along with variable temporal lobe involvement (Fig. 3.10). The partial or asymmetric expression pattern refers to cases that show incomplete or variable expression of the three primary patterns (Fig. 3.11). However, interestingly, the various patterns do not correlate with the presentations, clinical associations, or the course of the disease.

Computed tomography (CT) may be normal (22%) or show nonspecific hypodensities suggesting vasogenic edema secondary to PRES may be seen in up to 45% of cases (Fig. 3.12). On magnetic resonance imaging (MRI), involved regions manifest as areas of T2 and T2 prolongation. PRES lesions are most commonly characterized by facilitated diffusion due to vasogenic edema, with elevated signal on apparent diffusion coefficient (ADC) maps and variable signal on diffusion-weighted imaging (DWI) images because they have both diffusion and T2 weighting. PRES lesions can also have foci of restricted diffusion due to cytotoxic edema with low signal on ADC maps and increased signal on DWI images. In addition, because PRES can often present with seizures, patients may show coexisting postictal changes (Fig. 3.13).

Gyriform contrast enhancement, implying breakdown of the blood-brain barrier, occurs in approximately 20% to 40% of cases (Fig. 3.14). The presence or absence of enhancement does
Figure 3.1. Posterior reversible encephalopathy syndrome pathophysiology illustration.
Figure 3.2. (A–C) Axial FLAIR images at the level of midbrain on days 1, 7, and 14 (A, B, and C, respectively) demonstrate patchy hyperintense regions in the bilateral posterior temporal and occipital subcortical white matter and overlying cortex (A) that are less prominent on follow-up imaging at 1 week (B) and show complete resolution at 2 weeks (C).
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Figure 3.3. Axial illustrations of the brain depict differential parenchymal involvement, which is most frequent in the occipital and parietal regions, followed by the frontal lobe, inferior temporal region, cerebellum, deep gray nuclei, and brainstem.

Figure 3.4. (A and B) Atypical posterior reversible encephalopathy syndrome. Axial T2-weighted image (A) and coronal FLAIR (B) images demonstrate confluent edema predominantly involving the brainstem with only minimal involvement of the periventricular white matter and left mesial temporal lobe.
**Figure 3.5.** (A–C) Atypical posterior reversible encephalopathy syndrome (PRES). An axial FLAIR (A) image demonstrates edema in the left greater than right cerebellar hemispheres. A fat-saturated, gadolinium-enhanced T1-weighted (B) image at the same level reveals scattered punctate-enhancing foci. More cranially, an axial FLAIR image (C) demonstrates edema in the bilateral posterior temporal and occipital lobes commonly seen in PRES.

**Figure 3.6.** (A and B) Atypical posterior reversible encephalopathy syndrome. Axial FLAIR images demonstrate foci of edema involving the bilateral basal ganglia and deep white matter (A) as well as the bilateral paramedian frontal and parietal lobes (B). (Images courtesy Dr. Achint K. Singh, University of Texas Health Science Center, San Antonio, TX.)
Figure 3.7. (A and B) Unilateral posterior reversible encephalopathy syndrome (PRES). Axial FLAIR images at the level of centrum semiovale (A) and midbrain (B) demonstrate patchy edema in the left frontal, parietal, posterior temporal, and occipital lobes in a patient with unilateral PRES.

Figure 3.8. (A–C) Holohemispheric posterior reversible encephalopathy syndrome. Coronal FLAIR images reveal presence of relatively symmetric edema in the anterior cerebral artery–middle cerebral artery (A and B) and posterior cerebral artery–middle cerebral artery (C) border zones. There is also edema in the cerebellar white matter and the bilateral mesial temporal lobes.
Figure 3.9. (A and B) Superior frontal sulcus posterior reversible encephalopathy syndrome pattern. Axial FLAIR images reveal extensive relatively symmetric edema centered in the anterior cerebral artery–middle cerebral artery (A) and posterior cerebral artery–middle cerebral artery (B) border zones, with edema adjacent to the superior frontal sulci (A). More inferiorly, the involvement is predominantly posterior with sparing of the frontal poles (B). (Images courtesy Dr. Achint K. Singh, University of Texas Health Science Center, San Antonio, TX.)

Figure 3.10. (A and B) Dominant parieto-occipital posterior reversible encephalopathy syndrome pattern. Axial FLAIR images demonstrate extensive symmetric edema involving the bilateral parietal and occipital lobes. There is minimal involvement of the bilateral frontal lobes.
Figure 3.11. (A and B) Partial expression posterior reversible encephalopathy syndrome. Axial FLAIR images reveal relatively symmetric edema involving the bilateral occipital lobes with sparing of the parietal lobes.

Figure 3.12. (A and B) Axial computed tomography images reveal relatively symmetric hypodensity in the bilateral parietal lobes in a patient with posterior reversible encephalopathy syndrome.
Figure 3.13. (A–D) Axial FLAIR (A and B) and DW (C and D) images in a patient with posterior reversible encephalopathy syndrome (PRES) who presented with seizures. Images A and C were obtained on day 1 and images B and D on day 4 of hospital admission. Images from the day of admission reveal symmetric regions of T2 prolongation in the bilateral occipital lobes, consistent with PRES. There is associated FLAIR hyperintensity (A) and restricted diffusion (C) involving the right thalamic pulvinar, consistent with coexisting postictal changes. Images from day 4 reveal partial resolution of the signal abnormalities involving the right thalamic pulvinar. Signal abnormalities involving the bilateral occipital lobes are slightly less prominent.

Figure 3.14. (A and B) Axial post contrast images reveal patchy gyriform enhancement and white matter hypodensity in the bilateral parietal lobes, corresponding to regions of T2 signal abnormality (not shown).
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Figure 3.15. (A and B) Conventional angiogram images following injection of the right internal carotid (A) and vertebral (B) arteries in a patient with posterior reversible encephalopathy syndrome. There is multifocal narrowing and irregularity of the distal anterior cerebral artery and middle cerebral artery branches (A), as well as of the basilar artery and distal posterior cerebral artery (PCA) branches. In addition, there is reduced parenchymal blush in the PCA territories compared with the posterior inferior cerebral artery territory.

Figure 3.16. Hemorrhagic PRES. (A and B) Axial noncontrast computed tomography image (A) in a patient with posterior reversible encephalopathy syndrome reveals focal intraparenchymal hemorrhage in the right posterior temporal occipital region, surrounded by vasogenic edema. Axial T2-weighted image at the same level (B) more clearly demonstrates edema in the bilateral posterior temporal occipital regions and basal ganglia. (Images courtesy Dr. Amit Agarwal, Penn State University College of Medicine, Hershey, PA.)

Correlate with the overall extent of fluid-attenuated inversion recovery (FLAIR) abnormality, and it is unclear if enhancement portends poor outcome.

Catheter, CT, or MR angiography may reveal vessel irregularity with focal areas of vasoconstriction and vasodilatation, resulting in a "string of pearls" appearance. Other reported findings include diffuse vasoconstriction, reduced capillary blush, and vessel pruning (Fig. 3.15). When present, the vasoconstriction most commonly involves second and third order branches and usually resolves on follow-up imaging as the clinical status of the patient improves. Interestingly, the vasospasm is often less prominent in severely hypertensive patients who also demonstrate significantly less vasogenic edema.

On perfusion studies with CT, MR, and Tc-99m hexamethylpropyleneamine oxime (HMPAO) SPECT, regions affected by PRES are hypoperfused with respect to the normal brain, a finding that argues against the more popular hyperperfusion theory. The relative cerebral blood volume (rCBV) in affected regions is reduced in up to 86% of patients with PRES.

COMPLICATIONS

1. Intracranial hemorrhage (ICH) can occur in 10% to 25% of cases and is often intraparenchymal and less commonly subarachnoid, although both may coexist (Fig. 3.16). ICH is more common in patients receiving anticoagulation and
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Figure 3.17. PRES complicated by cerebral infarction. (A–D) The axial computed tomography (CT) image (A, same patient as Fig. 3.14) reveals symmetric hypodensity in the bilateral parietal lobes in a patient with posterior reversible encephalopathy syndrome. There is corresponding hyperintensity on the axial T2-weighted image (B) and restricted diffusion on the DW image (C), more prominent on the left side. The follow-up CT image (D) obtained after 6 months reveals bilateral parietal encephalomalacia.

Figure 3.18. Border-zone infarcts. (A and B) Axial FLAIR (A) and DWI (B) at the level of centrum semiovale show abnormal hyperintense FLAIR signal involving the anterior cerebral artery–middle cerebral artery and middle cerebral artery–posterior cerebral artery border zones, with corresponding areas of restricted diffusion, consistent with infarctions.

in patients who have undergone allogeneic bone marrow transplantation.

1. Cerebral infarction, characterized by restricted diffusion, occurs in 10% to 30% of cases. When present, it is often associated with incomplete clinical recovery (Fig. 3.17).

2. Cerebral herniation can occur, especially in cases with severe posterior fossa involvement.

MIMICS AND DIFFERENTIAL DIAGNOSIS

PRES may be mimicked both clinically and radiologically by a myriad of conditions that present with encephalopathic features and demonstrate vasogenic or even cytotoxic edema on neuroimaging.

Cerebral ischemia secondary to hypoperfusion may present with involvement of the border zone vascular territories, mimicking PRES (Fig. 3.18). Lesions typically show more extensive areas of restricted diffusion, a clinical state predisposing to hypoperfusion is present, and the patients rarely present with seizures.

Occasionally, acute disseminated encephalomyelitis (ADEM) can mimic PRES (Fig. 3.19). Lesions usually have elevated diffusion but can also have restricted diffusion. Patchy contrast enhancement can also occur. In contradistinction to PRES, ADEM is typically not symmetric, is frequently preceded by a viral illness, and can
The presence of reversible cerebral angiographic abnormalities and reversible brain edema brain associated with both PRES and reversible cerebral vasoconstriction syndrome (RCVS) suggests an overlapping pathophysiology. In addition to multifocal vascular narrowing and transient edema, patients with RCVS may present with border zone cerebral infarctions, subarachnoid hemorrhage, and/or parenchymal hemorrhage (Fig. 3.20). RCVS often affects young and middle-aged females and typically follows exposure to sympathomimetic or recreational drugs. Other known triggers include eclampsia, binge drinking, and strenuous physical activity.

Postictal changes may be mistaken for PRES. There is often extensive cortical involvement, and the lesions are typically unilateral. The pulvinar of the thalamus and the hippocampus are often affected. In addition, involved regions show hyperperfusion, unlike PRES, which shows hypoperfusion.

Other conditions producing vasogenic edema such as venous sinus thrombosis, inflammatory or infectious vasculitides, autoimmune disorders, and metabolic conditions such as uremic encephalopathy may mimic PRES. These entities are rare, and the clinical history often leads to the correct diagnosis.