Sudden Blindness in a 50-Year-Old Woman

Sheikh Mujeeb, MD
Steven R. Bruhl, MD, MS
Prashanth Reddy, MD
Haitham Elsamaloty, MD
Basil E. Akpunonu, MD

CASE PRESENTATION

A 50-year-old African-American woman presented to the emergency department complaining of sudden-onset complete bilateral blindness. Past medical history was significant for hypertension and stage 4 chronic kidney disease managed with hemodialysis 3 times per week. At presentation, she also complained of mild global headache but denied fever, vomiting, arm or leg weakness, visual hallucinations, or seizure-like activity. Vital signs included a blood pressure of 150/85 mm Hg and a heart rate of 78 bpm. Although the physical examination was essentially normal, ophthalmologic examination revealed a fundus with grade 2 hypertensive changes, a normal anterior segment, and normal pupillary reflexes. Visual acuity was limited to the perception of light. No other deficits were noted on neurologic examination. Routine laboratory testing was unremarkable except for an elevated blood urea nitrogen level of 56 mg/dL (normal, 24–49 mg/dL) and a serum creatinine level of 6.9 mg/dL (normal, 0.6–1.2 mg/dL).

The patient underwent noncontrast computed tomography (CT) scan of the brain, which revealed large lesions of decreased attenuation in both parietal lobes extending into the occipital lobes (Figure 1). Follow-up magnetic resonance imaging (MRI) of the brain revealed an area of high signal intensity in the cortex and subcortex on T2-weighted (Figure 2) and fluid-attenuated inversion recovery (FLAIR) sequences. No evidence of acute ischemia was seen on diffusion-weighted MRI. Magnetic resonance arteriography and venography showed no abnormalities.

WHAT IS YOUR DIAGNOSIS?

(A) Bilateral posterior cerebral artery infarction
(B) Intracranial hemorrhage
(C) Multiple sclerosis
(D) Posterior reversible encephalopathy syndrome

Drs. Mujeeb, Bruhl, and Reddy are residents in internal medicine; Dr. Elsamaloty is an associate professor of radiology; Dr. Akpunonu is a professor of internal medicine; all are at the University of Toledo Medical Center, Toledo, OH.
ANSWER
The correct answer is (D), posterior reversible encephalopathy syndrome (PRES).

DISCUSSION
PRES is characterized by sudden onset of neurologic symptoms and characteristic findings of posterior cerebral white matter edema on neuroimaging. The lesions of PRES are classically distributed within the occipital and paroccipital regions, are almost always bilateral, and are readily seen as increased signal intensity on T2-weighted and FLAIR MRI, as in the case patient. Although lesions of multiple sclerosis can produce a hyperintense signal on T2-weighted and FLAIR MRI sequences, these lesions are found in an asymmetric distribution periventricularly and are virtually never found within the cortex. In addition, the calcarine and parmedian occipital lobes are not affected in PRES, and this is an important distinguishing factor in differentiating PRES from bilateral infarction of the posterior cerebral arteries. Intracranial hemorrhage produces a high-attenuation pattern on CT, whereas PRES produces a low-attenuation pattern. Also, intracranial hemorrhage is almost never bilateral and symmetrical. Features on neuroimaging that distinguish PRES from other causes of acute encephalopathy are shown in the Table.

CLINICAL COURSE OF CASE PATIENT
The patient was treated with intravenous labetalol and admitted to the hospital for further management of her hypertension and hemodialysis. By hospital day 2, the patient’s blood pressure normalized and her vision returned. She was discharged home after 72 hours of hospitalization. Repeat MRI 40 days later showed almost complete resolution of the patient’s cerebral edema.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME
PRES is also known as reversible posterior leukoencephalopathy syndrome, reversible posterior cerebral edema syndrome, posterior leukoencephalopathy syndrome, hyperperfusion encephalopathy, and brain capillary leak syndrome. Although a review of the literature reveals several case reports describing multiple symptoms and findings consistent with PRES, it was not recognized as a syndrome until 1996. Since then, there have been several publications describing the syndrome with varying presentations and severity.

Clinical Manifestations
Classic neurologic signs and symptoms of PRES include headache, mental status changes, seizures, and visual disturbances. Although not typical, cases of complete blindness have been reported. The most common abnormality seen on neuroimaging is edema involving the white matter in the posterior portions of the cerebral hemispheres. Involvement of the frontal lobes, pons, and cerebellum has also been reported. In the setting of acute mental status changes, the most common differential diagnoses for these neuroradiologic changes include bilateral cerebral infarction in the posterior cerebral artery distribution and demyelinating lesions.

The ability to distinguish PRES from the other diagnoses depends on a basic understanding of CT and MRI. Increased extravascular blood as seen in acute hemorrhage leads to an increased density on CT scan. Alternatively, echoplanar diffusion-weighted imaging can determine the diffusion of hydrogen molecules in tissue. This has proven useful in the evaluation of ischemic strokes, as extracellular fluid movement around the damaged tissue is decreased or halted due to cellular edema. In these situations, ischemic tissue appears hyperintense on diffusion-weighted imaging. FLAIR MRI is another imaging technique that suppresses the brain’s ventricular signal while at the same time accentuating the appearance of edema and brain pathology. This has proven especially useful in the diagnosis of multiple sclerotic lesions and more recently PRES (Table).

Table. Acute Changes in White Matter on Neuroimaging in Common Neurologic Syndromes

<table>
<thead>
<tr>
<th>Modality</th>
<th>PRES</th>
<th>Hemorrhagic CVA</th>
<th>Ischemic CVA</th>
<th>Acute Hypertensive Encephalopathy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT without contrast</td>
<td>Low attenuation</td>
<td>High attenuation</td>
<td>Normal*</td>
<td>Normal</td>
</tr>
<tr>
<td>Diffusion-weighted MRI</td>
<td>Normal</td>
<td>Variable</td>
<td>Hyperintense</td>
<td>Normal</td>
</tr>
<tr>
<td>FLAIR</td>
<td>Hyperintense</td>
<td>Variable</td>
<td>Normal*</td>
<td>Normal</td>
</tr>
</tbody>
</table>

CT = computed tomography; CVA = cerebrovascular accident; FLAIR = fluid-attenuated inversion recovery; MRI = magnetic resonance imaging; PRES = posterior reversible encephalopathy syndrome.

*Within the first 12 hours of presentation.
Pathogenesis

The most common risk factors implicated in the development of PRES include accelerated hypertension, eclampsia, renal decompensation, and use of immunosuppressive medications. Less common associations include autoimmune diseases, such as systemic lupus erythematosus, and receipt of bone marrow and solid organ transplants or high-dose chemotherapy. To date, there are 3 theories that attempt to explain the characteristic imaging patterns seen in PRES. The first theory is that systemic hypertension overwhelms the autoregulatory ability of the brain, causing cerebral vasodilatation, reduced cerebral perfusion pressure, relative ischemia, and brain edema. The second and more recent theory is that hypertension leads to a defect in sympathetic cerebral pressure regulation, which causes inappropriate brain vasoconstriction, hypoperfusion, hypoxemia/ischemia, and resultant vasogenic edema. Both theories are supported by the fact that prompt treatment of hypertension in patients with PRES has been associated with resolution of symptoms in both clinical and experimental studies. However, these theories do not address the 25% of patients with PRES who are normotensive. The third theory suggests that immunosuppressive drugs, systemic disease, and/or neurotoxins can lead to endothelial dysfunction and subsequent failure of the blood-brain barrier, resulting in local hyperperfusion and brain edema. This theory appears to be supported by the fact that elevations in markers of endothelial dysfunction (e.g., lactate dehydrogenase) and abnormal red blood cell morphology have been seen in cases of PRES. This theory further explains PRES in normotensive patients, those with liver or kidney disease, and patients taking immunosuppressants, such as cyclosporine and tacrolimus. Cyclosporine-induced PRES has been reported in patients with both therapeutic and supratherapeutic blood levels in the setting of bone marrow and liver transplantation.

Treatment

Current treatment recommendations for PRES remain mostly anecdotal but involve blood pressure-lowering even when blood pressure is only mildly elevated. When blood pressure is significantly elevated, current recommendations include lowering of the mean arterial blood pressure to 105 to 125 mm Hg with intravenous antihypertensive agents such as nicardipine or labetalol. Because uremia and hypomagnesemia appear to be risk factors for development of PRES, prompt correction of metabolic derangements is essential to the treatment of PRES. Similarly, administration of cytotoxic and immunosuppressive drugs such as cyclosporine and tacrolimus appear to increase the risk of PRES, and withdrawal of these drugs is also important. Delayed treatment appears to be associated with prolonged or even irreversible symptoms.

CONCLUSION

PRES is a neuroradiologic diagnosis often characterized by neurologic abnormalities such as headache, mental status changes, seizures, or vision changes. The diagnosis of PRES is confirmed by decreased attenuation signals bilaterally in the occipital and paroccipital regions on CT as well as increased signal intensity on T2-weighted and FLAIR MRI with sparing of the calcarine and paramedian occipital lobes. Prompt treatment is required to prevent permanent sequelae and includes aggressive hypertension control, correction of electrolyte disturbances, withdrawal of cytotoxic agents, and hemodialysis as needed.