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Practical Pearl

Asymmetric Reversible Posterior Leukoencephalopathy Syndrome

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Abstract

Reversible posterior leukoencephalopathy syndrome (RPLS) is characterized radiographically by magnetic resonance imaging as white matter hyperintensities, which reflect cerebral edema. These changes are typically restricted to the parietal and occipital lobes, and are usually quite symmetric. We report a case of asymmetric RPLS involving only one frontal lobe in a patient with severe hypertension, chronic internal carotid artery stenosis, and ipsilateral vasogenic edema.

Key Words: Reversible posterior leukoencephalopathy; hyperperfusion syndrome; carotid stenosis; vasogenic edema; cerebrovascular autoregulation.

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Introduction

Reversible posterior leukoencephalopathy syndrome (RPLS) presents with the clinical constellation of headache, encephalopathy, visual disturbance, and seizures. It is most commonly reversible with treatment of the underlying cause, but it can sometimes cause focal intracerebral hemorrhage and permanent injury *(1)*. The most common causes include acute hypertension, eclampsia *(2)*, and toxicity of immunomodulatory therapies *(3)*. RPLS arises from mechanical disruption of the blood–brain barrier (BBB), either by overwhelming hydrostatic factors (as with hypertension) or by endothelial cell dysfunction (as with toxin-associated etiologies). The characteristic MRI changes are best appreciated on fluid-attenuated inversion recovery (FLAIR) sequences, and show a predominant white matter pattern of hyperintensity consistent with vasogenic edema. Diffusion-weighted imaging (DWI) is most often normal, but apparent diffusion coefficient (ADC) values are increased, helping to distinguish vasogenic from cytotoxic edema *(4)*. The changes are typically confined to areas supplied by the posterior circulation. This vascular bed has lower pressures and less sympathetic innervation compared to the anterior circulation, and is thus more easily overwhelmed by relative systemic hypertension *(5)*. Recently, there have been reports of atypical manifestations of RPLS, with symmetric changes also including the basal ganglia and frontal lobes *(6)*. We report the first case of RPLS presenting asymmetrically, extending into only one frontal lobe, in a patient with severe acute hypertension and a chronic internal carotid artery (ICA) stenosis ipsilateral to the affected hemisphere.

Case

A 51-year-old right-handed woman with a history of hypertension, hypercholesterolemia, migraine, and smoking had been followed for several years in the stroke clinic for left ICA stenosis. She initially presented with a subarachnoid hemorrhage in 1980, which went untreated at that time. She subsequently was found to have an asymptomatic bruit in 1999. A computed tomography angiogram (CTA) revealed left ICA stenosis, as well as a right anterior cerebral artery (ACA)

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aneurysm. She underwent elective carotid endarterectomy (CEA), followed by uneventful clipping of the right ACA aneurysm.

The following year, she developed blurring of vision in the left eye with certain head positions, and was found to have left ICA re-stenosis. She underwent successful angioplasty and stent placement, but her symptoms returned 6 months later, and she underwent repeat angioplasty within the stent. When her visual blurring returned after the second angioplasty procedure, we elected to follow her conservatively. At no time did she develop additional neurological symptoms or signs, such as language disturbance or weakness. She was maintained on aspirin, clopidogrel, and a statin. Her blood pressure was well controlled on an ACE-inhibitor, with average systolic blood pressures ranging 130–140 mmHg.

In 2004, she was electively admitted for iliac angioplasty for symptomatic peripheral arterial disease. The intervention was complicated by ischemia to the right foot, and she subsequently underwent aorto-bifemoral bypass grafting and distal thrombectomy. She was treated with aspirin and warfarin, and underwent a series of hyperbaric oxygen (HBO) treatments. During one HBO treatment, she developed a severe bifrontal headache and right arm and leg twitching, at which time the treatment was aborted. The headache persisted for several hours, and later became accompanied by bilateral decreased vision and expressive speech difficulties. She then had a generalized tonic–clonic seizure, and subsequently had profound right-side weakness affecting the face, arm, and leg. Her systolic blood pressures over the 3 days preceding this event were significantly higher than her baseline, ranging 160–190 mmHg.

She underwent an emergent head CT scan, which showed hypodensities predominantly in left subcortical white matter (Figure 1, head CT). At the time, these findings were felt to be consistent with infarction in the left middle cerebral artery (MCA)–ACA watershed territory, given her known severe left ICA stenosis. CTA, however, showed a severely stenotic but still patent left ICA, with good distal filling of the cerebral circulation. She then underwent MRI, which showed no areas of restricted diffusion on DWI. It did, however, show FLAIR hyperintensities in the bilateral occipital and parietal white matter, as well as the left frontal white matter (Figure 2, FLAIR, DWI, ADC).

Her blood pressure was then strictly controlled to systolic pressures of less than 140 mmHg. Over the next 3 days, her symptoms improved to a normal neurological baseline. A brain MRI was repeated 2 months later, showing complete resolution of the previously seen changes.

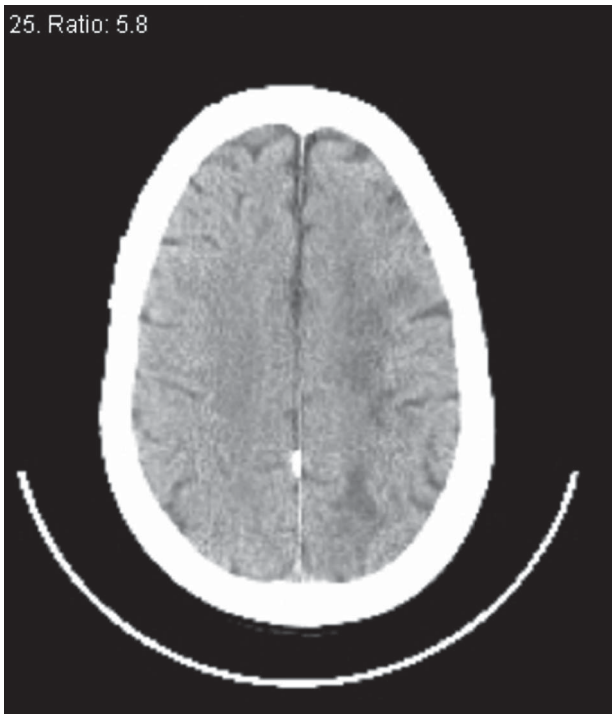

Fig. 1. Non-contrast head computed tomography, demonstrating hypodensity in the subcortical white matter of the left cerebral hemisphere.

Discussion

RPLS represents a state in which inadequacy of the BBB leads to vasogenic edema. The syndrome most commonly occurs in the setting of acute hypertension. The posterior circulation, which has a relative paucity of sympathetic innervation compared with the anterior circulation, is classically affected first, as a result of inadequate autoregulatory capacity. A similar phenomenon, known as reperfusion injury, can arise from cerebral revascularization (e.g., CEA). In this phenomenon, the post-intervention increase in perfusion pressure exceeds arteriolar autoregulatory capacity *(7)*. With carotid stenosis, chronic hypoperfusion is thought to lead to distal vasodilation as a compensatory mechanism. When "normal" flow is established through the parent vessel, the distal circulation may be unable to vasoconstrict normally in response to this relative hyperperfusion, resulting in a breach of the BBB *(8)*.

An interestingly similar reperfusion phenomenon likely occurred in this case. In the setting of relative and prolonged hypertension, this patient developed a clinical syndrome reminiscent of RPLS, with vision changes, headache, confusion, and seizure. However, there were also symptoms referable to the left anterior hemisphere, with expressive speech difficulties and right-sided weakness. Initially, we were concerned that she had occluded her chronically stenotic left ICA, as the CT suggested watershed injury in the MCA–ACA territory. Fortunately, the MRI DWI did not show evidence of infarction, and rather showed FLAIR and ADC changes consistent with vasogenic edema in characteristic RPLS locations. We were surprised to also find involvement of the left frontal lobe. We posit that the vascular bed distal to the left ICA stenosis was chronically vasodilated as a compensatory mechanism. In the setting of elevated systolic blood pressures, the vascular bed was unable to autoregulate, resulting in BBB breach and vasogenic edema. Although the patient also underwent treatment with hyperbaric oxygen, it is unlikely to have contributed to the clinical picture, as there are no reports of MRI changes induced by HBO. With control of the patient's blood pressure, both the clinical and radiographic changes reversed entirely.

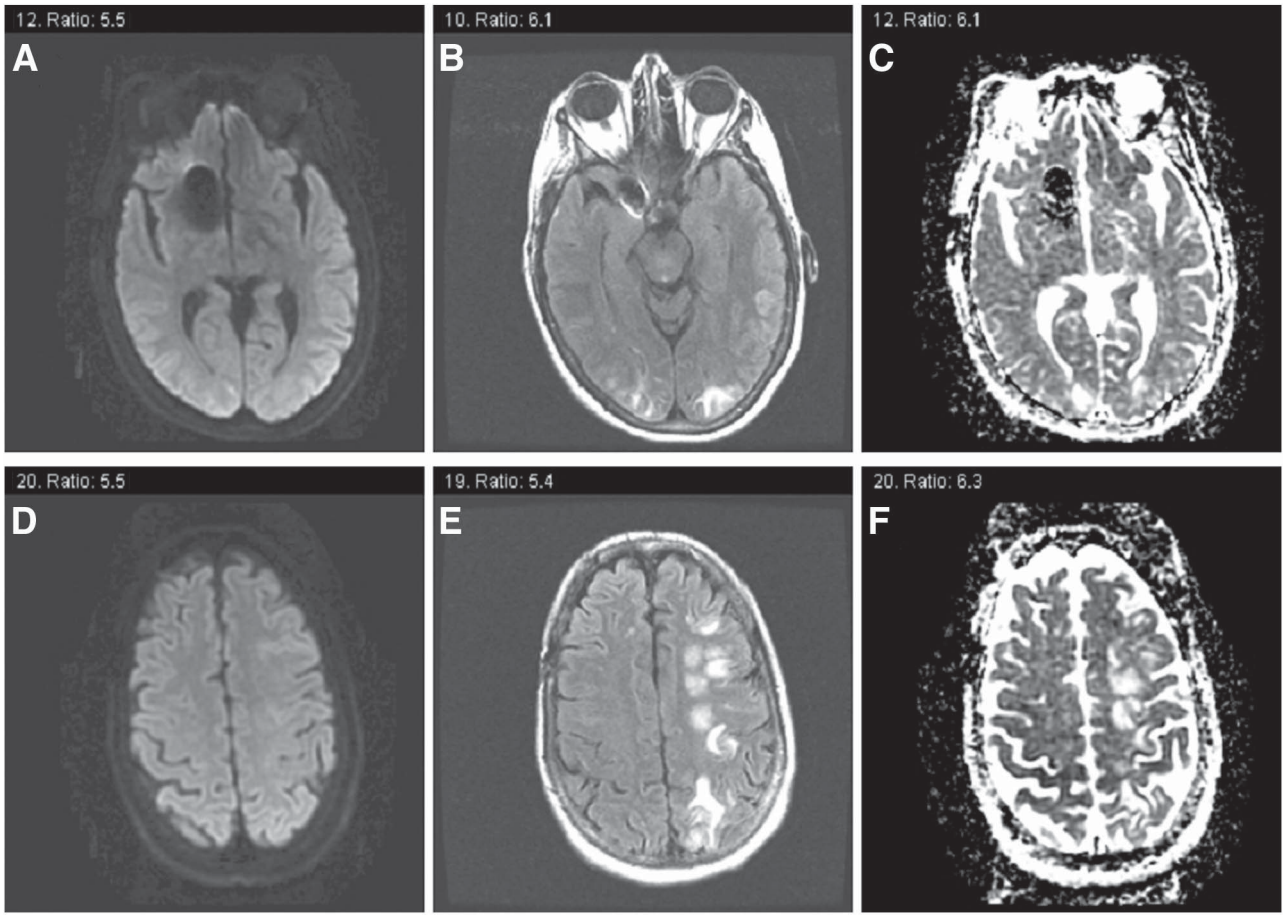

Fig. 2. Non-contrast brain magnetic resonance imaging, demonstrating changes consistent with asymmetric reversible posterior leukoencephalopathy. **(A)** A diffusion-weighted image (DWI), essentially normal (with the exception of artifact created by her aneurysm clip). **(B)** A fluid-attenuated inversion recovery (FLAIR) image with changes affecting the subcortical white matter of the classic locations in the parieto-occipital regions. **(C)** The apparent diffusion coefficient (ADC) map showing increased signal consistent with increased diffusion of water (and not restricted diffusion, which would be characteristic of ischemia/infarction). **(D)** DWI, **(E)** FLAIR, and **(F)** ADC show similar changes affecting the anterior hemisphere white matter, but only on the left.

This case represents an unusual presentation of asymmetric RPLS, with unilateral extension to the anterior circulation in a vascular bed with likely compensatory vasodilatation and impaired autoregulation.

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