

Permanent Bilateral Cortical Blindness Due to Reversible Posterior Leukoencephalopathy Syndrome

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Abstract

Reversible posterior leukoencephalopathy syndrome (RPLS) is induced by acute cerebral edema. Its symptoms include seizures, headache, altered mental status, and visual disturbances. The clinical and radiological findings are usually transient. This report describes a case of RPLS resulting in bilateral total blindness. A 40-year-old man presented with lethargy and bilateral visual loss. He had a 20-year history of hypertension, but had never been treated. On presentation, the left eye was able to perceive light, but the right eye was not. Radiological examination showed diffuse edema in the brain, and ocular fundus examination revealed severe bilateral hypertensive retinopathy. Antihypertensive therapy improved the patient's general condition, including blood pressure. Radiological findings 5 months later showed resolution of most of the abnormal signal areas. However, total blindness had developed in both eyes by day 15, and two courses of pulsed corticosteroid therapy failed to restore the visual loss.

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Key words: posterior leukoencephalopathy syndrome, hypertension retinopathy, blindness

Introduction

Reversible posterior leukoencephalopathy syndrome (RPLS) is a clinical and radiological concept proposed by Hinchey et al¹. Its symptoms include headache, decreased alertness, mental abnormalities, seizures, and visual loss. The visual impairment is sudden and severe. These symptoms are associated with cerebral edema. The predominant lesion is in the white matter of the posterior lobe, especially in the parieto-occipital area². Occasionally, the cerebral stem, cerebellum,

basal ganglia, frontal, and parietal lobes are affected. The major cause of RPLS is hypertension; other possible causes include eclampsia, renal dysfunction, and immunosuppressive therapy^{1,3–9}. The clinical course of RPLS is transient and reversible. Treatment involves antihypertensive therapy or discontinuation of immunosuppressive drugs; occasionally, systemic corticosteroid therapy is given when the response to the initial treatment is poor^{10–12}. Once the patient's general condition, including blood pressure, has improved, the clinical symptoms generally resolve and the radiological findings return to normal.

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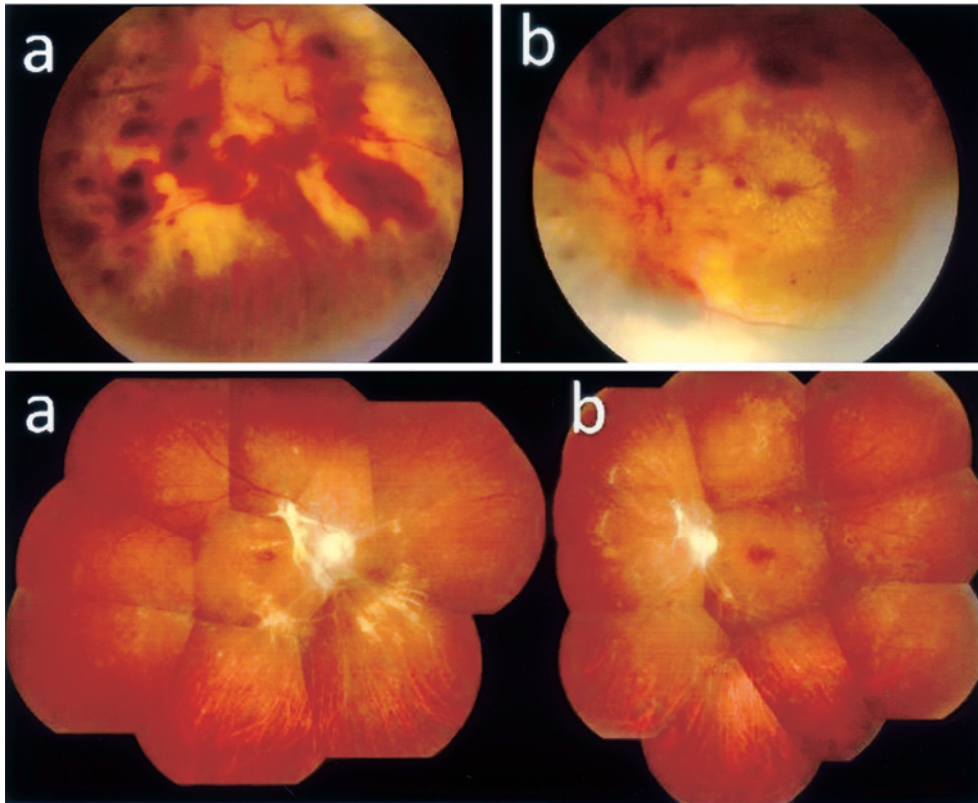


Fig. 1 I. Ocular fundus photographs of day 1. They showed severe hypertensive retinopathy with multiple retinal hemorrhages and hard exudates and optic disc swelling.
 II. Ocular fundus photographs after 5 months. They showed optic disc atrophy, multiple pigmented spots in the peripheral area, venous sheathing, and proliferative membrane formation. a) Right eye, b) Left eye.

In this report, we describe a patient who developed RPLS following uncontrolled hypertension. Even though the systemic condition was stabilized, visual loss progressed to bilateral total blindness. Furthermore, the ocular symptoms did not respond to systemic pulsed corticosteroid therapy.

Case Report

A 40-year-old man was admitted with vertigo, lethargy, and visual disturbance. He had been informed 20 years earlier that he had hypertension, but had declined treatment. He had noticed bilateral visual problems 5 months prior, but had been able to continue working as a truck driver.

On admission, the patient's blood pressure was 240/120 mm Hg. He was somnolent and disoriented. The pupillary reflex to light was absent in both eyes. He was able to perceive light with the left eye but not with the right eye, which was totally blind. A peripheral blood test showed an elevated white

blood cell count, anemia, and a low platelet count. Serum biological testing showed renal dysfunction with a blood urea nitrogen level of 62 mg/dL and a serum creatinine level of 9.07 mg/dL. Ocular fundus examination revealed severe hypertensive retinopathy with multiple retinal hemorrhages and hard exudates and optic disc swelling corresponding to grade 4 in the Keith-Wagener classification (**Fig. 1**). Fluorescein angiography could not be performed because of renal failure. Intraocular pressure and anterior chamber findings were normal in both eyes. Non-enhanced computed tomography (CT) on admission showed hypodensity in the bilateral subcortical white matter, thalamus, left internal capsule, pons, and right cerebellar hemisphere.

Antihypertensive therapy with nicardipine hydrochloride was started immediately, resulting the following day in clear consciousness without somnolence or disorientation. The patient's blood pressure gradually decreased. T₂-weighted magnetic resonance imaging (MRI) on day 5 showed abnormal high-intensity areas, and a diffusion-weighted image

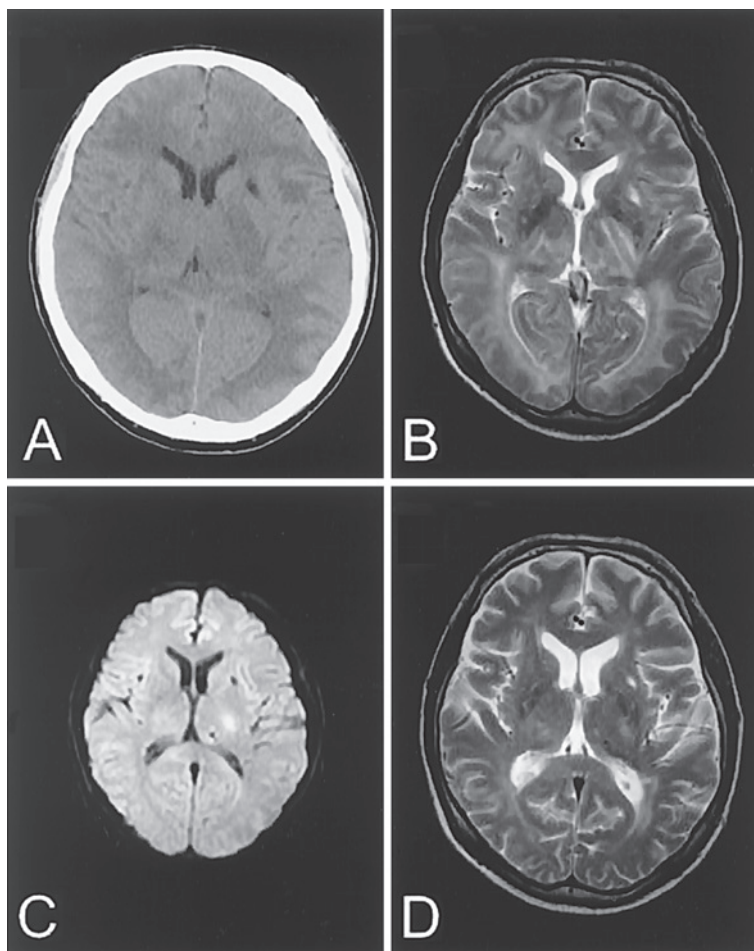


Fig. 2 Non-enhanced CT (A) demonstrates bilateral subcortical hypodensity in the frontal and parietal regions in the acute stage. On day 5 MRI study, a T₂-weighted image (B) also shows bilateral subcortical hyperintensity; however, a diffusion-weighted image (C) demonstrates normal signal intensity in the subcortical region and a small area of hyperintensity in the region of the left internal capsule. On a follow-up MRI study in the 5th month, a T₂-weighted image (D) demonstrates resolution of the abnormal signals in the bilateral subcortical regions, except in the posterior white matter and the left internal capsule.

showed a small high-intensity area in the left internal capsule and parietal subcortical region (**Fig. 2**).

In spite of the improvement in the patient's general condition, visual acuity was unchanged. On day 18, systemic steroid pulse therapy (methylprednisolone sodium succinate [1 g/day for 3 days]) was administered. On day 19, light perception was lost in the left eye. Steroid pulse therapy was repeated on day 26, but the patient remained totally blind.

Five months later, the patient's general condition had stabilized. Ocular fundus examination revealed a reduction in hard exudates and no retinal

hemorrhaging or optic disc swelling. However, optic disc atrophy, multiple pigmented spots in the peripheral area, venous sheathing, and proliferative membrane formation were observed (**Fig. 1**). Retinal photocoagulation was not performed. T₂-weighted MRI showed that the hyperintense areas had mostly been resolved, except in the white matter of the posterior portions, including the parieto-occipital regions (**Fig. 2**). Ten months later, there were no changes in the patient's vision or fundus appearance.

Discussion

The patient described here had symptoms and radiological findings consistent with RPLS, but the bilateral visual loss was severe and permanent. Generally, both hypertensive retinopathy and RPLS are reversible, with most patients showing full recovery within 2 weeks, even when visual impairment at onset is severe¹⁶. Our patient had an unusual clinical course of cortical blindness due to encephalopathy and proliferative hypertensive retinopathy leading to permanent total visual loss.

Among the few reports describing visual sequelae of RPLS, the report of Autunes et al. describes an infant boy with hypertension; immunosuppressive therapy initially improved the patient's vision, but the symptoms subsequently recurred¹³. Other reports describe cases of improved vision following treatment but subsequent residual damage. However, full ophthalmologic data are not given in these reports¹⁴.

RPLS is a clinical and radiographic syndrome associated with cerebral edema; most patients with RPLS have hypertension. Although the clinical features and radiological findings are clearly recognizable, the mechanism of RPLS is not fully understood. It is thought that acute hypertension or other causes of RPLS induce a breakdown of cerebral autoregulation and passive vasodilation of the cerebral vasculature, resulting in capillary leakage and acute disruption of the blood-brain barrier (vasogenic edema)¹⁵⁻¹⁷. Hypertension and renal failure most likely contribute to the development of vasogenic edema. However, reports of RPLS in patients without hypertension raise the possibility of direct endothelial dysfunction due to circulating toxins, which may damage the blood-brain barrier and lead to extravasation. In RPLS, edematous change is common in the posterior cerebral region, especially in the parieto-occipital white matter. The posterior circulation may be predisposed to RPLS when perivascular sympathetic activity is reduced in the posterior cerebral region relative to the anterior cerebral region, leading to a loss of protective vasoconstriction and, consequently, breakthrough vasodilation in the face of hemodynamic challenge. Therefore, vasogenic edema develops preferentially in the posterior

cerebral territories and manifests as areas of hypointensity on CT and hyperintensity on T₂-weighted MRI. In our patient, MRI during the acute stage showed a massive elongation of the cerebral white matter, cerebellar hemisphere, basal ganglia, thalamus, brain stem, pons, and cerebellum. Antihypertensive treatment normalized most of the abnormal high-intensity areas, including the parieto-occipital area. However, hyperintensity was still present in both cerebellar hemispheres after 5 months. We speculate that this was the result of irreversible cytotoxic edema, even though no sequelae were observed in the motor nervous system. On the other hand, the patient's persistent cortical blindness may have been induced by cellular damage in the posterior cerebral region which was not visible on radiological images.

Hypertensive retinopathy occurs as a result of retinal vascular changes related to microvascular damage caused by elevated blood pressure. Because hypertension is the major cause of RPLS, it is not unusual for hypertensive retinopathy and RPLS to occur concurrently; 1 report states, for example, that of 18 infant patients with RPLS, 14 also had hypertensive retinopathy⁷. The initial fundus examination in our case showed multiple hemorrhages and extensive subretinal exudates and optic disc swelling. It is understandable that retinopathy of this severity would lead to some degree of visual impairment, but not as far as blindness without light perception.

Ocular findings in malignant hypertensive retinopathy are divided into 3 distinct categories: hypertensive retinopathy, hypertensive choroidopathy, and hypertensive optic neuropathy. The causes of these findings include constriction of vascular beds by circulating catecholamines, obstruction of arterioles, and breakdown of the blood-retina barrier. In retinopathy, focal arteriolar narrowing, cotton-wool spots, intraretinal transudates, macular edema, and retinal hemorrhages are typical changes. Our patient showed all of these changes on initial examination, but they responded gradually to treatment. The clinical changes in hypertensive choroidopathy are related to the delay of choroidal filling followed by late leakage from choroidal vessels into the subretinal space. Focal occlusion of the choriocapillaris leads to necrosis and atrophy of the

retinal pigment epithelium and the formation of Elschnig's spots, which were seen in the later stages in our patient. Proliferative membrane formation was also found in our patient. We assumed that multifocal retinal ischemia caused by capillary nonperfusion induced proliferative membrane formation at first, but that later the blood circulation supply and perfusion demand in the retina decreased so that the proliferative changes did not become advanced. However, its pathogenesis is not clear because of the lack of fundus angiography due to the patient's renal dysfunction. Hypertensive optic neuropathy causes optic disc edema, which can usually be reversed with blood pressure control. In our patient, however, the optic disc atrophied. It is difficult to determine whether cerebral damage or optic neuropathy was responsible for our patient's blindness.

The treatment of RPLS requires amelioration of hypertension or discontinuation of the causative immunosuppressive agent, but it is important to differentiate between ischemic stroke and RPLS before deciding on the appropriate treatment: guidelines for patients with acute stroke recommend mild to moderate treatment of hypertension, whereas hypertension in RPLS should be treated aggressively to prevent progression to irreversible brain damage. Some reports indicate that by relieving edema and suppressing vascular permeability, adrenocorticosteroid agents are effective when patients do not respond to initial treatment for RPLS¹⁰⁻¹². However, prudent administration is required, because the side effects of corticosteroids include elevation of blood pressure and renal dysfunction. Furthermore, in some cases corticosteroid administration is considered to be the cause of RPLS¹⁸. In our case, corticosteroid therapy did not affect the patient's blood pressure or renal function, but it did not restore the vision loss, either.

In the present case of RPLS with irreversible visual disturbance, we suggest that the patient's long history of uncontrolled hypertension and renal dysfunction led to massive cerebral edema, resulting in permanent neurologic damage.

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