Two Similar Cases of Encephalopathy, Possibly a Reversible Posterior Leukoencephalopathy Syndrome: Serial Findings of Magnetic Resonance Imaging, SPECT and Angiography

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Two young women who had encephalopathy that resembled reversible posterior leukoencephalopathy syndrome are presented. The brain magnetic resonance imaging (MRI) of these patients exhibited similar T2-high signal lesions, mostly in the white matter of the posterior hemispheres. Xe-SPECT during the patients’ symptomatic period showed hypoperfusion in the corresponding areas, and angiography demonstrated irregular narrowing of the posterior cerebral artery. Clinical manifestations subsided soon after treatment, and the abnormal radiological findings also were almost completely resolved. Thus, we concluded that transient hypoperfusion followed by ischemia and cytotoxic edema might have had a pivotal role in these cases.

(key words: cytotoxic edema, vasogenic edema, encephalopathy, posterior cerebral artery)

Introduction

Recently, Hinchey et al (1) proposed a new clinical entity of reversible posterior leukoencephalopathy syndrome. This syndrome might include several different diseases: eclampsia (2, 3), hypertensive encephalopathy (4, 5), and cyclosporine-induced encephalopathy (6, 7) have been known to provoke similar conditions, while their pathologic mechanisms remain the subject of debate. Based on the similar magnetic resonance imaging (MRI) findings of such cases, substantial edema mainly in the white matter is regarded as a major pathogenic event. The current thinking holds that the cause of focal brain edema is vasogenic and results from the breakdown of the autoregulation of the cerebral vessels (8); there is less supportive evidence for a cytotoxic edema theory associated with vasospasm (9). Here, we present two quite similar Japanese cases of encephalopathy and discuss their possible diagnosis as reversible posterior leukoencephalopathy syndrome (RPLS). Intriguingly, and contrary to the current hypothesis on the etiology of RPLS, in our cases insufficient posterior perfusion, followed by ischemia and cytotoxic edema, was thought to play a key role in the onset of RPLS.

Case Report

Case 1

A 34-year-old woman was admitted to our hospital because of left homonymous hemianopsia. She was a non-smoker and had never suffered from migraine attacks. The patient had been receiving oral estrogen and progesterone therapy for several years after a diagnosis of dysmenorrhea. She experienced a complete loss of vision in a very short period of time. She soon regained her eyesight, though slight visual impairment persisted. General physical examination disclosed no abnormalities, and neurologically, only left homonymous hemianopsia was noticed. Her blood pressure was normal and laboratory data, including those from cerebro-spinal fluid examination and auto-antibodies, were all within normal limits. Anti-phospholipid antibodies were negative. Radiologically, her MRI revealed T1-low signal and T2-high signal lesions in the bilateral parieto-occipital regions involving the subcortical white matter and cortex (Fig. 1). These lesions did not show any Gd-DTPA
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enhancement (Fig. 1). Xe-SPECT exhibited low uptake in the corresponding area (Fig. 2), and a cerebral angiogram revealed irregularly narrowed posterior cerebral arteries (PCAs) (Fig. 2). The carotid artery system was normal and sinus thrombosis was excluded (Fig. 2). Cerebral infarction was suspected and the patient was started on thrombolytic therapy. Her clinical manifestations disappeared after one month, and a follow-up MRI did not reveal any abnormal signals (Fig. 3, 32 days after admission).

A magnetic resonance angiography (MRA) examination was normal and IMP-SPECT also confirmed that intracranial perfusion had returned to the normal level (36 days after admission, data not shown).

Case 2

A 19-year-old healthy woman suddenly experienced bifrontal headache and blurred vision. She was a non-smoker and did not have a past history of migraine. An ophthalmologist discovered left homonymous hemianopsia, after which the patient was transferred to our hospital. On examination, the patient was alert and seemingly well, except for the left homonymous hemianopsia. Laboratory data, including that from cerebrospinal fluid (CSF) examination, were all within normal limits. No

Figure 1. An axial T2-image exhibited bilateral subcortical and cortical high signal intensities in the parieto-occipital regions. These lesions were depicted as T1-low intensity areas, and no Gd-DTPA enhancement was seen.

Figure 2. Xe-SPECT showed low-uptake in the posterior part of the brain (arrowheads). Carotid artery system was normal and a vestibobasilar angiography demonstrated the irregularly narrowed PCAs (arrowheads).
A follow-up MRI (32 days after admission) revealed that the previously recognized T2-high signal lesions resolved completely (proton and T2 axial images are shown).

Radiologically, MRI demonstrated T2- and proton-high signal foci in the cortex and subcortical white matter in the occipital lobes (Fig. 4). Xe-SPECT also indicated broader low uptake in the bilateral-occipital regions (Fig. 5). A cerebral angiogram also revealed an irregularly narrowed PCA (Fig. 5). The carotid artery system was normal and there was no evidence of sinus thrombosis or isolated angitis of the central nervous system. The patient was suspected of cerebral infarction and treated with thrombolytic agents. Her headache soon subsided, and her visual defect improved but was not fully resolved. Previously recognized occipital T2-high signal intensities were demonstrated to be smaller (Fig. 6, 27 days after admission). MRA did not reveal any significant abnormalities. IMP-SPECT revealed hyperperfusion in the very restricted foci (Fig. 6, 30 days after admission).

**Discussion**

These two similar cases were in accordance with the concept of the reversible posterior leukoencephalopathy syndrome postulated by Hinchey et al (1). Briefly, both exhibited MRI T2-high signal lesions in the posterior part of the brain, and their radiological abnormalities returned to nearly normal in a short period of time. Clinical manifestations disappeared concurrent with the resolution of MRI abnormalities.
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Figure 5. Xe-SPECT showed low uptake in the areas indicated by arrowheads and the irregularly narrowed PCA was identified by the vestibobasilar angiography (arrowhead). Carotid artery system was normal.

Figure 6. Twenty-seven days after admission, the smaller T2-high signal lesion remained visible on MRI, and hyperperfusion was recognized in that area on IMP-SPECT (arrowhead).

with radiological improvement.

Although detailed characteristics of SPECT and angiography have rarely been described in the previous cases (4), frequent observation of posterior involvement indicated the existence of mechanisms associated with intracranial blood systems and their circulation. Susceptibility of posterior circulation to the development of encephalopathy is unclear, but several researchers have identified ultrastructural differences
among intracranial vessels (4, 10). In the present study, we detected serial alterations in SPECT findings accompanied by angiographic observations. In the symptomatic phases, hypoperfusion in the foci responsible for clinical manifestations was clearly identified. It was intriguing that only irregular PCA narrowing was observed by angiography. Neither the carotid artery system nor the venous system was affected, and there was no evidence of central nervous system angitis. Cerebral blood flow returned from conditions of insufficiency to normal, and we therefore supposed that the focal PCA spasm and transient hypoperfusion induced ischemia, which was followed by cytotoxic edema. The case report, recently published by Ito et al supports our speculation (9).

Contrary to our hypothesis, vasogenic edema caused by loss of autoregulation following a breakdown of the brain vessels is the predominant theory for the pathogenesis of RPLS (4, 7, 8). Schwartz et al (4) published a report on hypertensive encephalopathy, in which they revealed that hyperperfusion in the affected areas and some Gd-enhancement, suggesting that vasogenic edema leads to encephalopathy. However, neither of our cases showed significant blood pressure elevation or renal failure. This pathogenic difference might be in part due to the patients' respective background.

In case 2 a follow-up IMP-SPECT detected the hot spot in the affected area, implying refractory hyperperfusion after hypoperfusion, and this result also supported the vasospasm theory. Additionally, negative findings of the Gd-DTPA enhancement in case 1 indicated that the blood-brain barrier remained intact.

Despite this, major critical questions concerning migraine attack and cerebrovascular disease could be raised. We now know that migraine attacks, especially basilar artery migraine, may cause similar clinical pictures, and sometimes leave permanent deficits like those following an ischemic stroke. Although we could not completely exclude first migraine attack of either patient, clinical observation in both cases did not reveal the typical throbbing headache accompanied by nausea and vomiting, and neuroimaging studies exhibited intracranial lesions of symmetrical distribution, which are unlikely to be migraine related.

On the other hand, cerebrovascular disease, especially that associated with oral contraceptive use still remains a possibility in the first case. Four-vessel angiography did not detect any atherosclerotic areas or embolic sources to account for the radiologically-proven lesions distributed symmetrically. Moreover, relevant laboratory data did not indicate any autoimmune disorders, or hematologic disturbances such as anti-cardiolipin syndrome which induces juvenile cerebral infarction. Subsequently, we suspected that our cases could be included in the clinical entity of reversible posterior leukoencephalopathy syndrome.

In this study, we presented the possibility of transient insufficiency posterior circulation in this type of encephalopathy syndrome and its simultaneous recovery in conjunction with the patients' clinical condition. Moreover, we showed that the posterior insufficiency originated from an irregular narrowed PCA. On the basis of our findings, we consider that this syndrome was not a homogenous entity, but rather several diseases having different pathological mechanisms which might be included under RPLS. Detailed examination of numerous similar cases will be necessary for the further evaluation of RPLS.

References