Hypertensive brainstem encephalopathy involving deep supratentorial regions: does only blood pressure matter?

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Abstract

We report on a 42-year-old female patient who presented with high arterial blood pressure of 245/150 mmHg and hypertensive brainstem encephalopathy that involved the brainstem and extensive supratentorial deep gray and white matter. The lesions were nearly completely resolved several days after stabilization of the arterial blood pressure. Normal diffusion-weighted imaging findings and high apparent diffusion coefficient values suggested that the main pathomechanism was vasogenic edema owing to severe hypertension. On the basis of a literature review, the absolute value of blood pressure or whether the patient can control his/her blood pressure seems not to be associated with the degree of the lesions evident on magnetic resonance imaging. It remains to be determined if the acceleration rate and the duration of elevated arterial blood pressure might play a key role in the development of the hypertensive encephalopathy pattern.

Introduction

Hypertensive encephalopathy (HE) is a life-threatening condition characterized by severe hypertension, altered mental status, headache, dizziness, visual changes, and seizure. The condition is reversible if promptly diagnosed and treated, but if treatment is delayed it may progress to coma or death. Because the lesions improve after the stabilization of paroxysmally accelerated hypertension, HE is classified as a reversible posterior leukoencephalopathy syndrome. The most common abnormality detected by magnetic resonance imaging (MRI) is hypointensity of T2-weighted and fluid-attenuated inversion recovery (FLAIR) images of the white matter bilaterally, especially in the parieto-occipital areas. This is consistent with cerebral edema.

Predominant hypertensive brainstem encephalopathy (HBE) with supratentorial involvement is another form of HE. Cases of HBE involving supratentorial deep gray and white matter extensively are rare. We describe here a patient with HBE involving deep supratentorial gray and white matter. In addition, we have tried to elucidate the possible pathophysiological mechanism involved, on the basis of a literature review.

Case Report

A 42-year-old woman (high-school graduate) had been diagnosed with hypertension two years earlier. Following diagnosis, she was prescribed antihypertensive medication for one month only. Her mother and her elder and younger sisters also had hypertension.

One day before her admission, she developed dizziness. When she was first examined on admission day, she showed drowsiness and mental confusion. She also complained of an inability to stand or to walk owing to dizziness. Her vital signs included a blood pressure of 245/150 mm Hg, a pulse rate of 94/min, a respiratory rate of 18/min, and a body temperature of 36.5°C. There was no abnormal finding on physical examination. On neurological examination, her mental status was drowsy. She had marked truncal and limb ataxia. She did not present with dysarthria, facial or limb weakness, or sensory loss. Cranial nerve examination, including extraocular movement and bulbar function, was normal. Her deep tendon reflexes were normal and without pathological reflex.

On the second day after admission (46 hours after symptom onset), a brain MRI examination was conducted. Extensive hypertensive changes in the periventricular and subcortical deep white matter, the internal capsule, the thalamus, the midbrain, the pons, and the cerebellum were revealed bilaterally on fluid-attenuated inversion recovery (FLAIR) images (repetition time/echo time TR/TE 11000/140 ms), on T2-weighted images (TR/TE 4230/100 ms), as well as on apparent diffusion coefficient (ADC) mapping (Figure 1). The same lesions showed near isointensity on diffusion-weighted (DWI, b-values = 1000 s/mm²) and T1-weighted (TR/TE 474/12 ms) images. These findings were suggestive of widespread vasogenic edema. A lacunar infarction (asymptomatic old lesion) was noted incidentally in the right anterior thalamus. No evidence of abnormal enhancement was found in the brain parenchyma. MR angiography revealed no abnormalities in the major intra- or extracranial arteries. Both posterior cerebral arteries were raised from the vertebrobasilar circulation with no fetal supply.

Serum laboratory findings including glucose, electrolyte, arterial blood gas analysis, hepatic enzyme, and thyroid hormone (T3, T4, thyroid-stimulating hormone) levels were within normal limits except for mildly elevated urea nitrogen (31.1 mg/dL, normal: 5.0-25.0 mg/dL) and creatinine (1.5 mg/dL, normal: 0.5-1.4 mg/dL). An enzyme study for differentiation from Fabry’s disease revealed that the alpha-galactosidase A activity was 92% (normal: >85%). A cerebrospinal fluid study showed unremarkable findings: normal opening pressure (130 mm H2O); white blood cell count, 2/mm³; a glucose level, 86 mg/dL (normal: 40-80 mg/dL); and protein concentration, 49 mg/dL (normal: 12-60 mg/dL). An electroencephalogram showed diffuse theta to delta slowing. An electrocardiogram revealed left ventricular hypertrophy, and thoracic echocardiography showed severe concentric left ventricular hypertrophy with diastolic dysfunction. Abdominal and pelvic computed tomography (CT) scans showed no evidence of pheochromocytoma, but right renal artery stenosis was detected (40%).

We immediately started intravenous infusion of a calcium-channel blocker (nicardipine hydrochloride, 50 mg), which lowered her systolic pressure to 140-170 mm Hg and her diastolic pressure to 70-90 mm Hg. This was followed by an oral calcium-channel blocker (amlodipine, 10 mg), an angiotensin-converting enzyme inhibitor (perindopril, 8 mg), an angiotensin II receptor blocker (valsartan, 160 mg), a beta blocker (bisoprolol, 2.5 mg) and diuretics (lasix, 5 mg and spironolactone, 25 mg). After the elevated blood pressure was consistently lowered for a week, she regained consciousness gradually over a period of three days. On the fourth day following admission, she scored 10/30 on the Korean
mini-mental status examination (K-MMSE),

furthermore, her clinical dementia rating
(CDR) and global deterioration scale (GDS)
score were 3 and 6, respectively. On the sev-
enth day, she could move independently with-
out ataxia and her score on the follow-up K-
MMSE was 23/30. She was discharged on the
23rd day post-admission and subsequently was
followed up and prescribed antihypertensive
medication. During follow-up and eight
months after admission, her score on the K-
MMSE, CDR, and GDS were 20/30, 0.5, and 4,
respectively. Her follow-up MRI revealed that
the abnormal hyperintense signals had dimin-
ished markedly on the FLAIR images, except
for some leukoaraiosis (Figure 2).

Discussion

We present a female patient with untreated
hypertension who developed HBE involving the
total cerebellum and the deep supratentorial
regions. On admission, she presented with
drowsiness, vertigo, and ataxia without accom-
panying motor weakness or visual distur-
ances. Most cases with brainstem or cerebellar
involvement show clinicoradiologic associa-
tion. However, our patient demonstrated
lesions so extensive as to show dizziness as
well as limb and truncal ataxia. These symp-
toms might result from cerebellar lesions, and
the drowsiness probably was secondary to
involvement of the ascending reticular activat-
ing system in the brainstem. The patient was
diagnosed with HE based on the following
three criteria: i) severe hypertension, ii) dif-
fuse symmetrical MRI lesions with no compat-
ible stroke lesions in DWI, iii) subsequent
improvement of clinical symptoms and radi-
ological findings after the normalization
of blood pressure.

The differential diagnosis included cerebral
thromboembolism, encephalitis, hypoxia,
osmotic demyelination syndromes, or metabol-
ic encephalopathy. The affected territory and
symmetrical lesions described here were not
correlated with simple thromboembolic stroke
because of the lack of major brainstem signs,
the absence of acute ischemic findings on ini-
tial DWI, and the reversible radiological find-
ings with a clinical recovery. In consideration
of the clinicoradiologic aspects of the case and
the normal CSF findings, the possibility of an
inflammatory disease (e.g. acute disseminated
encephalomyelitis) was very unlikely because
of the absence of a preceding infection or of
vaccination. Symmetrical signal changes in
the brain MRI are observed in patients with
hypoxia, osmotic demyelination syndromes
(central pontine and extrapontine myelin-
olysis), or metabolic disorders such as hyper-
glycemia, liver cirrhosis, and Fabry’s disease.

However, there was no history of hypoxic brain
damage, hyperglycemia, liver disease, or elec-
trolyte abnormality in our patient. The resolu-
tion of the MRI findings helped to eliminate
the possibility of the above diseases. Furthemore, the possibility of Fabry’s disease
was excluded because the serum enzyme assay
(galactosidase A) was normal.

Our patient had extensive high-intensity
signals in the brainstem and cerebellum, as
well as in the subcortical deep white and gray
matter in T2-weighted and FLAIR images. Howev-
er, they were isointense on DWI where-
as hyperintensity was seen in the initial ADC
mapping. The follow-up FLAIR imaging showed
a near-reversible change following control
of blood pressure. These findings revealed
that the lesions were predominantly a result
of vasogenic edema, which is a hallmark of HE.
The accepted mechanism of HE is vasogenic
edema that results from blood-brain barrier
disruption and extravasation of fluid and pro-
tein. This is caused by a rapidly elevated blood
pressure that exceeds the autoregulatory limit
of the brain vasculature. The hypothesis
that the essential mechanism of HE is severe
hypertension-induced vasogenic edema is sup-
ported by a brain SPECT (single-photon emis-
tion-computed tomography) study. This study
showed increased perfusion in the vicinity of
the brain, and the abnormal MRI signal
showed almost complete resolution after the
normalization of blood pressure.

Although the typical MRI abnormality
observed in cases of HE is hypointensity in
the white matter in the parieto-occipital areas
bilaterally, many cases of HBE have also been
reported. Table 1 shows the reported cases of
HE to date and the variable patterns of HBE
according to the severity of the lesion: i) pos-
terior dominant supratentorial lesion (HE),
ii) HBE only, iii) predominant HBE with rel-
ative sparing of the supratentorial regions, and
iv) HBE extending into the whole deep supratentorial regions. The latter two
cases are similar to our case.

It is unclear how the different pathophysio-
logical mechanisms could be explained
between patients who have HBE with supra-
tentorial lesions, including the posterior corti-
cal region, and those who do not. Mild acceleration of hypertension-produced edema occurred mainly in the supratentorial white matter. Severe acceleration of hypertension ended in more extensive supratentorial edema and extension into the infratentorial regions. Table 1 illustrates that the initial blood pressure in patients with HBE usually was higher than in those with typical HE. In three patients with HBE, however, the absolute value of blood pressure or whether or not the patient controls his/her blood pressure seems not to be associated with the degree of the MRI lesions.

The upper limit of the autoregulatory plateau of cerebral blood flow in the deep regions (e.g. thalamus, basal ganglia, or brainstem) is higher than that in the cerebral cortex in normotensive and spontaneously hypertensive rat models. The deep regions of the brain are supplied directly from branches of the parent artery (e.g. the middle or posterior cerebral artery or basilar arteries), while the cortex and subcortex are fed by the terminal pial arteries. Therefore, it is likely that more intense arterial blood pressure caused vasogenic edema in the deep regions. Regarding the hyperperfusion surges caused by hypertension, although the anterior circulation is known to have more significant sympathetic innervation than does the posterior circulation, we can also suggest that the HE pattern might depend on anatomical characteristics and the severity of hypertension (acceleration rate and duration). The major arteries from the carotid artery comprise at least two paired systems (e.g. the anterior and middle cerebral arteries) and have a larger diameter than does the basilar artery; the latter is involved in a single circulation and the diameter of each vertebral artery is smaller than that of the internal carotid arteries. Mild acceleration of hypertension might affect small-caliber arteries (distal pial branches), such as in the parieto-occipital area as in a report of the influence of mild acceleration of hypertension on the supratentorial white matter. Paroxysmal and lasting acceleration of hypertension, on the other hand, would have its first effect on the brainstem.

Apart from the extensive deep white and gray matter involvement, supratentorial cortices and subcortices were relatively uninvolved in our patient. It is plausible that early extensive fluid leakage from the proximal arteries might spare the supratentorial superficial regions (end portions), including the parieto-occipital regions. It remains to be determined whether the acceleration rate and the duration of elevated arterial blood pressure might have a key role in the development of the HE pattern.

### Table 1. Clinical features of patients with hypertensive encephalopathy and those with variable patterns of hypertensive brainstem encephalopathy who underwent brain computerized tomography scanning, magnetic resonance imaging, or both.

| Author | Sex/Age | Past medical Hx | SBP/DBP, mm Hg |
|--------|---------|-----------------|----------------|
| **Posterior dominant supratentorial lesion (HE)** | | | |
| Hauser<sup>a</sup> | M/45 | None | 236/172 |
| F/54 | None | 200/140 |
| F/53 | uHT, CRF | 220/140 |
| **Only HBE** | | | |
| Karasawa<sup>a</sup> | M/63 | cHT, DM | 240/90 |
| Oho<sup>c</sup> | F/67 | DM | 204/106 |
| Kanazawa<sup>b</sup> | M/75 | None | 200/120 |
| M/76 | cHT | 230/100 |
| Gamanagatti<sup>e</sup> | M/60 | None | 220/150 |
| Uchino<sup>e</sup> | M/29 | None | 240/160 |
| F/45 | uHT | 240/160 |
| Kang<sup>e</sup> | M/53 | uHT | 170/100 |
| F/45 | uHT, CRF | 190/130 |
| Shintani<sup>e</sup> | M/85 | None | 221/112 |
| M/46 | uHT, CRF | 244/150 |
| Bhagavati<sup>e</sup> | M/42 | cHT | 238/147 |
| **Predominant HBE with relative sparing of supratentorial regions** | | | |
| Chang<sup>c</sup> | F/54 | uHT | 210/144 |
| M/49 | cHT | 211/156 |
| de Seze<sup>c</sup> | M/41 | cHT | 220/120 |
| F/52 | uHT | 220/150 |
| Yasuda<sup>c</sup> | M/45 | uHT | 250/160 |
| Nagata<sup>c</sup> | M/67 | uHT, DM, CRF | 230/122 |
| Fujiwara<sup>c</sup> | M/38 | uHT | 240/180 |
| Doi<sup>c</sup> | M/35 | CRF | 180/118 |
| F/52 | uHT | 200/130 |
| **HBE plus extensive supratentorial deep lesions** | | | |
| Yoshida<sup>c</sup> | M/58 | uHT, CRF | 210/90 |
| Kumai<sup>c</sup> | M/73 | uHT | 300/160 |

HE, hypertensive encephalopathy; HBE, hypertensive brainstem encephalopathy; SBP, systolic blood pressure; DBP, diastolic blood pressure; M, male; F, female; uHT, uncontrolled or poorly controlled hypertension; cHT, controlled or chronic hypertension; DM, diabetes mellitus; CRF, chronic renal failure.

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