Severe Hyperthermia Caused by Four-Vessel Occlusion of Main Cerebral Arteries

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Abstract

We present the case of a comatose patient with acute large infarction of posterior cerebral and cerebellar areas and severe hyperthermia (max. 40.4°C). Angiography demonstrated four-vessel occlusion of the main cerebral arteries, suggesting the possibility that both internal carotid and left vertebral arteries were already occluded and he became unconscious following additional occlusion of the right vertebral artery. Autopsy findings revealed bilateral ischemic damage of the hypothalamus in addition to the above infarct areas. Sudden ischemic involvement of both hypothalamic regions may have caused the extremely high fever in this case.

Key words: hyperthermia, four-vessel occlusion, hypothalamus, cerebral infarction

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Introduction

Many reports have described bilateral internal carotid artery (ICA) occlusion or stenosis (1, 2). However, few have reported patients with occlusion of four major cerebral arteries, such as the left and right ICA and vertebral arteries (VAs) (3-5). This paucity may be attributable in part to the difficulty of establishing the diagnosis of four-vessel occlusion. We report the case of a patient with occlusion of bilateral ICAs and VAs who showed high fever in the early stage of ischemia that later reached 40.4°C. Severe ischemic stroke reportedly accompanies moderate central hyperthermia of 37.0-38.0°C. Damage to the hypothalamus, even unilateral, is well known to be related to moderate post-stroke hyperthermia (6, 7). In this case, ischemic insult to the hypothalamus was apparent bilaterally on autopsy.

Case Report

A 72-year-old man was admitted to our institute due to disturbance of consciousness. Medical history included diabetes mellitus, hypertension and an old cerebral infarction for which the details were unknown. High fever was evident

on admission, with an axillary temperature of 39.6°C. Blood pressure was 112/60 mmHg, and heart rate was 133 beats/min. He was comatose (Glasgow coma scale 4) and showed rigidity of the neck and all extremities. Pupils were round and isocoric, 2.5 mm in diameter on both sides. Light and oculocephalic reflexes were absent bilaterally. Plantar responses were extensor bilaterally. Chest radiography showed normal results, and electrocardiography showed regular sinus rhythm and tachycardia. White blood cell count was increased to 10,900/ μ L. C-reactive protein level was 0.1 mg/dL. Creatine phosphate kinase level was normal on admission, but later showed a marked increase to 10,333 IU/mL by 12 hours. Laboratory data on admission are shown in Table 1. Testing for antinuclear antibody and levels of complement (C3 and C4) yielded normal results. Cultures of blood, urine and sputum were negative. Brain computed tomography (CT) on admission failed to demonstrate abnormalities other than old cerebral infarction in the left frontal lobe. Cervical Doppler ultrasonography showed a basilar artery stenosis pattern. Conventional cerebral angiography demonstrated occlusion of the ICA on both sides and the left VA at their origins. The right intracranial ICA was supplied from the right ophthalmic artery. Both sides of the anterior and middle cerebral arteries were faintly apparent, indicating

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Table 1. Laboratory Data on Admission

WBC	10900/ μ L	Na	134mEq/L	Ammon	62 μ g/dL
RBC	501x104/ μ L	K	4.9mEq/L	APTT	25sec
Hb	13.4g/dL	Cl	98mEq/L	PT	107%
PLT	22.6x104/ μ L	BUN	16mg/dL	PT-INR	0.9
TP	7.7g/dL	Cre	1.05U/L	FDP	5 μ g/mL
ALB	4.5g/dL	CRP	0.1mg/dL	D-dimer	2.7 μ g/mL
Tbil	0.5mg/dL	FBS	274mg/dL	PaO ₂	83.9mmHg
AST	25U/L	HbA1c	8.20%	PaCO ₂	32.2mmHg
ALT	29U/L	Tcho	198mg/dL	pH	7.37
ALP	358U/L	TG	50mg/dL	SaO ₂	96.10%
γ GTP	32U/L	H-CHO	43mg/dL	BE	-6.0mmol/L
LDH	218U/L	LDL-C	146mg/dL	HCO ₃	17.9mmol/L
CK	234U/L	UA	5.0mg/dL	(O ₂ 2l/min)	

that these arterial areas were barely supplied by the right IC artery. The origin of the right vertebral artery was severely narrowed, and the posterior inferior cerebellar artery was scarcely detected (Fig. 1). The left vertebral artery was occluded at the origin, and the left anterior and posterior inferior cerebellar arteries were faintly detected by supply from the muscle branches. Diffusion-weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) sequences on brain magnetic resonance imaging (MRI) revealed high-intensity areas in the cerebellar hemispheres and occipital and parietal lobes bilaterally (Fig. 2a, b). No high-intensity changes were apparent in the brainstem except for the mid-brain with slight hyperintensity on DWI. Irregular involuntary movement similar to fasciculation was observed in the lower abdomen and extensor muscles of the proximal lower extremities. Body temperature (BT) increased gradually to 40.4°C. Respiratory function deteriorated as brain edema progressed, and the patient died 18 hours after admission.

The brain weighed 1,100 g at postmortem examination. Macroscopically, fresh infarcted lesions were observed in occipital, parietal and posterior temporal areas bilaterally, predominantly involving the left side and cerebellar area. The midbrain and pons were damaged, mainly due to central and transtentorial herniation. Ischemic damage extended to both hypothalamic regions (Fig. 3). Atherosclerosis of the aorta and associated branches was obvious. Coronary arteries showed triple-vessel disease. The heart showed an old subendocardial myocardial infarct of the posterolateral and anterolateral walls and hypertrophy, although no thrombus was evident in the left atrium and ventricle. The abdominal artery showed no occlusion. Complete chronic occlusion of the left vertebral artery at the orifice and both proximal internal carotid arteries was recognized. Fresh thrombotic occlusion was observed at the orifice of the right vertebral artery, caused by rupture of an atheromatous plaque. Embolic thrombi were observed at the tops of the basilar, both posterior cerebral, and supracerebellar arteries. These thrombi were assumed to have originated from abrupt occlusion of the right vertebral artery. Ischemic changes to the hypothala-

Figure 1. Angiograms showing AP view of the right subclavian artery with severe stenosis of the origin of the right vertebral artery.

mus were observed in the preoptic and paraventricular nuclei bilaterally, and in the right lateral hypothalamus and right supraoptic nucleus as detected by Hematoxylin and Eosin staining (Fig. 4). While mild ischemic insult was observed on the ventral side of the midbrain, most of the brainstem including the pons and medulla oblongata were spared. Evidence of old infarction was found at both anterior parts of the centrum semiovale with lacunar state and cribriform atrophy in the basal ganglia.

Figure 2. a, b) DWI showing high-intensity areas in bilateral cerebellar hemispheres and bilateral occipital and parietal lobes.

Discussion

We present a case showing bilateral obstruction of the ICAs and VAs. This case was characterized by widely infarcted posterior areas resulting from sudden occlusion of the right VA due to plaque rupture in association with specific signs that included stiff limbs with fasciculation-like movements and high fever. On admission, the diagnosis was not readily established because of the peculiar clinical signs and the diffuse abnormal intensities of both cerebral hemispheres on brain MRI. However, cerebrovascular disease was finally diagnosed by conventional angiography.

BT may increase moderately after cerebral injury or infarction, due to enhanced release of neurotransmitters, exaggerated oxygen radical production or breakdown of the blood-brain barrier (8). From a physiological perspective, BT is controlled by the anterior locus of the hypothalamus. Actually, BT has been reported to increase by 1°C following unilateral hypothalamic infarction in rats (6) and humans (7). Bilateral ischemic insult to the hypothalamus may thus result in extreme hyperthermia, as shown in the present case. Muscular rigidity and fasciculation-like movements of the abdomen and limbs, which were of unknown etiology,

Figure 3. Photomicrograph of the hypothalamus in axial view with severe bilateral necrosis (*). Arrow shows old lacunar infarct of the right internal capsule.

Figure 4. Eosinophilic change to neurons in the right nucleus supraopticus of the hypothalamus. Hematoxylin and Eosin staining. Original magnification $\times 400$. Bar, 50 μm .

might also have some relationship to the development of high fever in this patient. Hyperthermia has been clinically noticed in some cases of pontine stroke. We speculated that the brainstem lesion may have had a minor relationship with hyperthermia in this case, since the ischemic damage to the brainstem as seen on MRI and autopsy seemed rather small to induce high BT. Hyperthermia is known to worsen outcomes of cerebral infarction (9, 10). The poor prognosis in the present case may thus have been partly attributable to severe hyperthermia.

Relatively few reports have discussed occlusion of four major vessels in stroke patients (3-5). In those reports, patients with four-vessel occlusion showed small ischemic changes in the brain and rather moderate symptoms, such as headache, dizziness, limb numbness, hemiparesis or visual disturbance. High fever has not been previously described in human cases of four-vessel occlusion. Conversely, experimental four-vessel occlusion in animals always brings about fever in association with far-reaching cerebral ischemia (5). The dissociation between human and animal cases of four-vessel occlusion may be attributable to differences in the manner of ischemic onset, which is gradual in human cases and abrupt in animals. The present case may thus be closer to the animal model of four-vessel occlusion, given the abrupt onset of massive cerebral ischemia. While the anterior part of the cerebral area was barely supplied by collateral arteries from the right ICA via the ophthalmic artery, the rest of the brain area was fairly well supplied by the right

VA alone in this patient with occlusion of bilateral ICAs and the left VA. Abrupt obstruction of the right VA thus resulted in sudden ischemia to the whole brain, particularly the posterior part of the cerebral area and the cerebellar area. In summary, we have reported the case of a patient

with autopsy-confirmed four-vessel occlusion and wide posterior dominant cerebral infarction. He showed exaggerated hyperthermia, probably caused by ischemic involvement of both hypothalamic areas.

References

1. North RR, Fields WS, DeBakey ME, Crawford ES. Brachial-basilar insufficiency syndrome. *Neurology* **12**: 810-820, 1962.
2. Waltimo O, Fogelholm R. Bilateral internal carotid thrombosis. Prognosis and risk factors. *Acta Neurol Scand* **51**: 240-244, 1975.
3. Vitek JJ, Halsey JM, McDowell HA. Occlusion of all four extracranial vessels with minimal clinical symptomatology. *Stroke* **3**: 462-466, 1972.
4. Bogousslavsky J, Gates PC, Fox AJ, Barnett JM. Bilateral occlusion of vertebral artery: Clinical patterns and long-term prognosis. *Neurology* **36**: 1309-1315, 1986.
5. Okada Y, Shima T, Nishida M, Kagawa R. Magnetic resonance angiography visualization of four vessel occlusion—two case reports. *Neurol Med Chir (Tokyo)* **38**: 28-33, 1998.
6. He Z, Yamawaki T, Yang S, Day AL, Simpkins JW, Naritomi H. Experimental model of small deep infarcts involving the hypothalamus in rats. *Stroke* **30**: 2743-2751, 1999.
7. Naritomi H, Uno H, Oe H, Yamawaki T, Yutani C. Post-stroke fever in patients without infectious diseases: The involvement of hypothalamus confirmed by autopsy. *Stroke* **32**: 371b, 2001.
8. Ginsberg MD, Busto R. Combating hyperthermia in acute stroke. *Stroke* **29**: 529-534, 1998.
9. Hajat C, Hajat S, Sharma P. Effects of poststroke pyrexia on stroke outcome. *Stroke* **31**: 410-414, 2000.
10. Kuroiwa T, Bonnekoh P, Hossmann KA. Prevention of postischemic hyperthermia prevents ischemic injury of CA1 neurons in gerbils. *J Cereb Blood Flow Metab* **10**: 550-556, 1990.