Delayed post-anoxic encephalopathy without Relation to Carbon Monoxide Poisoning

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Delayed post-anoxic encephalopathy (DPE) not related to carbon monoxide has rarely been reported and usually carries a poor prognosis. We describe two surviving patients with such DPE and its neuro-otological characteristics. The DPE was caused by shock due to hemorrhage in a 21-year-old student, and by severe hypoxia and hypotension in a 60-year-old man. Our findings suggest that this type of DPE might not be rare, if the patients who suffered from severe anoxia, marked hypotension or both are carefully observed. Recognition of this DPE is important for appropriate management of such patients.

Introduction

Delayed post-anoxic encephalopathy (DPE) is a neurologic deterioration which occurs in patients some time after they recovered from initial hypoxia, generalized ischemia which was caused by severe hypotension, or both (1, 2). DPE is usually caused by carbon monoxide (CO) poisoning (1, 2). DPE induced by other types of anoxia and ischemia has rarely been reported, including complications of surgery and anesthesia, respiratory depression, cyanosis, shock (1, 2) and strangulation (3). Such DPE generally carries a poor prognosis (2). We report here two surviving patients with this type of DPE, who exhibited an excellent recovery and moderate residual neurologic sequelae, respectively. Apparent rarity of such DPE might be due to the unawareness of this condition. We also describe the neuro-otological characteristics of DPE which have not previously been reported.

Case Reports

Case 1

A 21-year-old male student hit with a tree while driving his motorcycle. He returned home by himself. However, he was admitted to a local hospital on the same night because of shock. He underwent surgery twice because of contusions and laceration of the liver, followed by acute renal failure. On the 6th day after the accident, he acutely became blind, being able to recognize lights only, although he apparently remained mentally alert and coherent. Four days later, he underwent hemodialysis. He was transferred to our care on the 33rd hospital day because of uncontrollable gastrointestinal bleeding with a hemoglobin value of 7.6 g/dl and serum total protein of 4.8 g/dl.

The pertinent neurologic abnormalities on admission consisted of a markedly reduced visual acuity with an ability to count fingers with the left eye but only to recognize lights with the right eye, generalized mild to moderate weakness of both proximal and distal muscles of the four extremities, and asymmetrically increased deep tendon reflexes in the legs with a Babinski's sign on the right side. The patient's peripheral visual field could not be examined reliably because of poor vision. His mental status, optic fundi, light reflex of his pupils and cutaneous sensation were within normal limits. An electroencephalogram (EEG) showed basic activity of 10–11 Hz mixed with frequent 4 to 7 Hz on both sides. Three weeks later, neuro-otological examinations (Fig. 1) revealed ataxic eye tracking, with marked impairment of both optokinetic nystagmus and visual suppression. Gaze, positional and positioning nystagmus were not present. An audiogram and cold caloric test yielded normal results. His neurological deficits and EEG abnormalities were almost resolved by the time of his discharge three months later. At that time, he did not remember any events of more than one month's duration from immediately prior to his first abdominal operation to shortly
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after he was transferred to our care, including the neurological examinations performed on him at admission.

Case 2

A 60-year-old man was admitted to our hospital because of cholecystectomy. Induction of his general anesthesia was performed by intravenous administration of thiopental sodium and succinylcholine. Tracheal intubation initially proved difficult. During the intubation procedure, the patient developed cyanosis and his blood pressure temporarily increased to 230/130 mmHg and then declined to a point where it could not be measured for 2 to 3 minutes, without cardiac arrest. Six hours after he was resuscitated, he became awake and exhibited markedly slow responses with prominent perseveration as well as marked flexion posturing of both arms. Four days later, the patient was found to be neurologically normal except for mild loss of recent
Six days after resuscitation, the patient complained of blurring of his vision. The next day, he became blind. Neurological examinations at that time showed that he was mentally alert and well oriented with moderate dysarthria. He perceived light only, although his optic fundi and light reflex of the pupils were normal. He exhibited moderate weakness of his grasp strengths and proximal muscles of the four extremities, hyperactive deep tendon reflexes in both legs with flexor plantar responses, and normal sensation. A cranial computerized tomographic (CT) scan with and without contrast enhancement revealed a normal brain. The next day, his EEG demonstrated basic activity consisting of 50 μV and 11 Hz waves mixed with occasional 5 to 6 Hz waves on both sides. Later the same day, he was transferred to another hospital for hyperbaric oxygen therapy which he underwent at 3 atmospheric pressures for 2 hours once a day for 13 successive days. He was then transferred back to our care.

Examinations performed on the day following completion of the hyperbaric therapy revealed that the patient's dysarthria was improved moderately and his vision minimally. The pertinent findings were as follows: a markedly reduced vision with an ability to recognize hand motion only, moderate pronation contracture of both arms, mild extension contracture of both legs, asymmetrically increased muscle stretch reflexes, in the four extremities with a Babinski's sign on the right side, moderate quadriplegia, mild asymmetric spasticity in the arms, and moderate impairment of graphesthesia in both palms. His mental status, optic fundi, light reflex of the pupils, and superficial and deep sensations were normal. The finger to nose test was almost normal. The heel to shin test and gait could not be tested because of the patient's muscle weakness.

Neuro-otological examinations at four months after the anoxic episode revealed mild abnormalities which were qualitatively identical to those observed in the patient 1. A follow-up study 11 months later demonstrated moderate improvement of the neuro-otological abnormalities. His vision also improved to (0.8) in the right eye and to (0.4) in the left over 5 months following the patient's anoxic episode, and to (1.2) in the right and to (0.9) over the subsequent 2 years and 8 months. However, this patient's other neurological abnormalities improved only mildly. He remained unable to walk by himself because of marked gait ataxia and some spasticity, and exhibited prominent impairment of both fine motor movements of the hands and stereoscopic vision during the subsequent 8-year follow-up. During that time, magnetic resonance imaging of the brain revealed mild atrophy of the cerebral cortex and superior vermis of the cerebellum, and dilatation of the lateral ventricles, consistent with the age of this patient. Single photon emission tomography using Tc-99m hexamethyl-propyleneamineoxime demonstrated a normal blood flow in the cerebrum. Transient pattern electroretinograms (P-ERG) and visual evoked responses to pattern stimuli (VEPs), both recorded simultaneously with pattern reversal stimuli of 0.5 Hz to the full visual field using the check size of 30’, elicited normal P50 and delayed latencies in P100 on both sides, respectively: the latency and amplitude of P50 were 54.0 msec and 3.80 μV in the left eye (Fig. 2), and 59.5 msec and 2.64 μV in the right; those of P100 were 143.5 msec and 7.73 μV in the left (Fig. 2), and 159.5 msec and 5.11 μV in the right, respectively (a normal value±SD of P50 amplitude in our laboratory, 3.01±1.2 μV, and that of P100, 8.1±3.6 μV) (4).

**Discussion**

The present patients displayed similar neurological signs...
and symptoms, which consisted of cerebral blindness (5), pyramidal tract signs and quadriplegia, whereas mental status was preserved. This pattern of abnormalities suggested that the cerebral white matter was primarily involved than the cerebral cortex. This speculation was supported by findings in P-ERG and VEPs recorded simultaneously in the patient 2. Since the normal P-ERG indicated preserved retinal ganglion cells, delayed P100 latency suggested the involvement of the optic pathway after the retina (4, 6, 7), which includes optic nerves and tracts, and optic radiations. Further, the normal light reflex of the pupils as observed in our blind patients suggested that the optic nerves and tracts were unlikely the sites of lesions. We therefore considered that the cerebral blindness in both the patients might be due to subcortical lesions in the optic radiations, although some contribution of the cortical lesions to the blindness cannot be excluded. The gait ataxia in patient 2 indicated involvement of the cerebellum as well. The bilateral and fairly symmetric abnormalities detected by the optokinetic nystagmus pattern and visual suppression tests were also consistent with diffuse involvement of the cerebrum and cerebellum (8, 9).

Further, the neurologic symptoms and signs, and the neuro-otologic abnormalities in our patients were compatible with previous neuropathological studies on patients with fatal DPE (1, 2, 10), which showed that the cerebral white matter was involved predominantly and the cerebellum occasionally.

The DPE was caused by hemorrhagic shock in patient 1, and by hypoxia and hypotension in patient 2. The prognosis of DPE due to this type of anoxia and ischemia is usually poor (2). Such DPE has been rarely reported; Ginsberg et al (2) found only six patients with DPE due to hypoxic-ischemic leukoencephalopathy unrelated to CO reported in the literature, including his own one personal patient. However, we encountered, over a four-year period, two surviving patients with such DPE at our hospital. This indicates that DPE might not be all that rare, if its neurologic signs and symptoms are carefully monitored in patients during the acute stage of anoxia and severe hypotension. Without careful attention, DPE might be overlooked, since some patients lose their memory of the critical period after the anoxia, hypotension or both, as exemplified by the present patient 1. Our comments are consistent with those of Plum et al (10), in that many people do not appear to be aware of this complication.

Plum et al (10) empirically recommended initial prolonged bed rest for 10 days after anoxia to prevent DPE. The present patient 2 was ambulatory two days prior to the onset of DPE, and this early ambulation could possibly have precipitated his DPE. However, patient 1 had been confined to bed until he developed DPE. This indicated that not only bed rest but also rapid restoration of both oxygenation and circulation is critical for preventing DPE. The importance of the latter was suggested by clinico-pathological studies of anoxic white matter lesions (1, 2) as well as by experimental studies on CO poisoning in rabbits (11). Neurologically, patient 2 became slightly better during hyperbaric oxygen therapy. Although such therapy has markedly improved DPE due to CO poisoning in one patient (12) and proved to be effective in the treatment of acute CO poisoning (13), it is unclear to what extent this therapy improved DPE in patient 2 and prevented further progression. The kind of anoxia and ischemia as seen in the present patients is not infrequent in clinical practice, and yet there are no specific therapies for the treatment of DPE at present (2, 13), nor known predictors about the risk of DPE and its final outcome in anoxic patients, hypotensive ones, or both (2). We would like to reemphasize therefore that it is safer to maintain patients with acute anoxia, acute severe hypotension or both on initial prolonged bed rest, in addition to ensuring rapid restoration of their oxygenation and circulation (2).

Acknowledgements: We thank doctors of the Emergency Medical Center at Nihoem Medical College School of Medicine, Tokyo, for hyperbaric oxygen therapy to patient 2, and Yoji Ishiyama, Ph.D., Division of Medical Physiology, Toranomon Hospital, Tokyo, for his comments on the P-ERG and VEPs of patient 2.

References