LATE NEUROPATHOLOGICAL CONSEQUENCES OF STRANGULATION

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SUMMARY

A case of a young man who was a victim of strangulation is presented. He arrived at the hospital in refractory status epilepticus, controlled only with intravenous pentobarbital. The initial CT scan showed mild cortical edema. Two days later, a CT scan showed diffuse cortical swelling and bilateral basal ganglia infarcts. Upon discontinuation of pentobarbital therapy, his neurological examination revealed spontaneous ventilation and a gag reflex. A CT scan 4 weeks after the insult demonstrated hypodensities in both cerebral hemispheres and hydrocephalus. EEG was isoelectric throughout his hospitalization. He survived nearly 5 months and succumbed to pneumonia. Neuropathological examination demonstrated severe encephalomalacia, multiple cystic infarcts and generalized compensatory ventriculomegaly. Microscopic examination was particularly remarkable for a pronounced gemistocytic astrocyte proliferation in the white matter. This case illustrates the long-term neuropathological consequences of severe, global hypoxia/ ischemia and the paucity of intact brain required to maintain a persistent vegetative state.

Key words: Persistent vegetative state - Neuropathology - Brain death

INTRODUCTION

Over 3500 people each year are victims of fatal hanging and strangulation [1]. Survival from such insults or global ischemia/hypoxia from a variety of other causes is becoming more frequent due to modern

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Fig. 1. Computed tomograms (CT) of the head. CT done emergently (a) reveals fattened gyri and no visible sulci (straight arrow) or Sylvian fissures (curved arrow). CT done 2 days after admission (b) reveals no visible parapineal cistens, small ventricles (straight arrow) and lucencies within the basal ganglia (curved arrow). CT done 1 month after admission (c) reveals diffuse cerebral lucencies (outlined arrow) and grossly enlarged ventricles (curved arrow).

resuscitative measures and critical care techniques [2-5]. Neurological recovery in survivors is variable with many patients being rendered persistently comatose. Most succumb within days to weeks although some may survive in this vegetative state for months to years [4,6]. Neuropathological studies are uncommon in these long-term survivors; the present case illustrates the tissue changes in such a patient.

CASE REPORT

A 21-year-old white man developed generalized seizure activity following an altercation 4 h earlier in which he was the victim of a vigorous 'choke hold'. When this strangling maneuver was applied he lost consciousness, but the assailant, believing the patient to be intoxicated and dangerous, continued the strangulation for several minutes. When released, the patient was initially flaccid and unresponsive, but then had a generalized tonicclonic seizure. While in transit to the hospital, he had brief periods of generalized seizure activity interrupted by variable periods of quiescence. There was no history of head trauma. His past medical history was unremarkable except for reports of alcohol and drug abuse.

Examination revealed a blood pressure of 150/70, pulse 100/min and respirations 12/min. Initial neurological examination showed his pupils to be 3 mm in diameter, equal, and reactive to light. He had weak corneal and gag reflexes. Sensory testing revealed withdrawal of all extremities to noxious stimulation. Examination of motor function showed diffusely increased tone. He localized bilaterally to deep pain. Tendon reflexes were normal in the upper extremities but were hyperactive in both lower extremities. No Babinski's responses were seen and ankle clonus was present bilaterally. The patient's general physical examination was unremarkable. Routine laboratory tests were normal. A computed tomogram (CT) scan showed mild cerebral edema (Fig. 1a).

Soon after admission, he developed sustained generalized seizure activity which did not respond to maximal doses of intravenous diazepam, phenytoin, phenobarbital or paraldehyde. He was intubated, ventilated, and treated with intravenous pentobarbital. Continuous EEG monitoring initially showed intermittent bursts of generalized spike activity for 2-3 s each minute. Over the next 24 h, the EEG showed no electrical activity at maximum sensitivity and the pentobarbital therapy was discontinued. A second CT scan two days after admission showed diffuse cortical swelling and bilateral basal ganglia lucencies (Fig. 1b).

Approximately 1 week later the patient's blood barbiturate level was zero, however, his EEG continued to show no activity. Neurological examination revealed weak respiratory efforts and a gag reflex. Nearly 1 month after admission a third CT scan revealed evidence of diffuse cerebral infarction and compensatory hydrocephalus (Fig. 1c). EEGs, recorded approximately weekly, were unchanged. No further intervention or resuscitative efforts were desired by the family. His neurological examination remained unchanged. The patient was slowly weaned from the ventilator, however, he suffered from recurrent pneumonia caused by antibiotic resistant organisms. He expired approximately five months after admission.

Postmortem examination revealed a grossly shrunken brain (weight 1060 g) with palpable subcortical cystic areas (Fig. 2a). Considerable cortical atrophy and necrosis of the cerebellar tonsils was evident. All major vessels were intact and normal. Coronal sections revealed diffuse laminar necrosis (Fig. 2b). Multiple cystic infarcts in the watershed distribution of the anterior, middle and posterior cerebral arteries were present bilaterally (Figs. 2c-2g). The basal ganglia including claustrum, as well as the thalamus and hippocampus revealed extensive cavitation with loss of cellular elements (Figs. 2d-2e). Ventriculomegaly was present with the temporal horns of the lateral ventricles being particularly dilated (Fig. 2f). Multiple large infarcts were seen in the cerebellar white matter with degeneration of the deep nuclei (Fig. 2g). The cerebellar cortex was soft and necrotic. Extensive necrosis was evident throughout the entire brainstem,

most notably in the substantia nigra, pontine tegmentum and medullary pyramids. Large fluid filled cysts were seen in the tegmentum of the pons. Tan discoloration and cavitation was present in areas containing cranial nerve nuclei and fiber pathways in the medulla and spinal cord (Fig. 2h).

Microscopic examination revealed extensive laminar necrosis of the cerebral cortex with extreme rarefaction of gray matter, with only blood vessels and macrophages remaining (Fig. 3a). Rarefied cortex was bordered by intense gemistocytic astrocytosis (Fig. 3b). Basal ganglia, midbrain, and medulla showed a similar pattern (Fig. 3c). Examination of the cerebellar cortex showed an absence of Purkinje cells and depletion of the granular cell layer (Fig. 3d). The spinal cord and medulla had extreme loss in both ascending and descending pathways, particularly involving the spinocerebellar and corticospinal tracts (Fig. 3e).

DISCUSSION

Few reports of the neuropathological alterations following resuscitation from global hypoxia/ischemia with protracted survival are available [2,3,7-9]. Neuropathological studies of survivors from strangulation or hanging either from attempted suicide or criminal assault are rare [1-3]. In general, these reports describe patients surviving an acute global hypoxic or ischemic episode from a variety of causes and expiring in less than one day to a week. The constellation of neuropathological findings that occur in such patients are those of 'respirator brain' classically described by Walker [10]. These brains are soft or semiliquid, often stain poorly, possess edematous white matter and swollen neurons and glial elements. The cortex may show laminar necrosis of varying degree, particularly within the hippocampus, and lytic lesions in the white matter. The thalamus is generally spared, though perhaps swollen, but the basal ganglia often have neuronal loss. The cerebellum shows loss of Purkinje cells with granular cells and molecular layers being relatively intact. The brainstem and spinal cord are frequently normal but can show edema, hemorrhage or infarction secondary to cerebellar tonsil herniation [10].

Selective vulnerability of particular neuronal structures to ischemia/ hypoxia was evident in the present case. The areas exhibiting the greatest degree of tissue necrosis parallel areas possessing relatively high levels of regional blood flow and relatively high rates of glucose metabolism, as determined experimentally by Reivich et al. [11] and Sokoloff et al. [12]. The macroscopic changes in this patient were quite different from respirator brain, and more closely resembled a combination of changes described in vegetative or brain dead patients with prolonged survival [3,6,7,10].

Necropsy findings in 43 patients existing in a persistent vegetative state, reported by Higashi et al. [6,13], revealed extensive gray and white matter destruction but relative sparing of the brainstem. In a series of 25 brain dead patients, Mohandas and Chou [7] described extensive pathology









Fig. 2. Post-mortem specimens obtained by coronal brain sectioning. Brain atrophy (narrow gyri and widened sulci) and necrosis (loss of cerebellar tonsils) are seen on gross inspection (A). Sections through the frontal cortex (B), the temporal lobe tips (C), the hippocampus (D), the thalamus (E), the mesencephalon (F), the pons and cerebellum (G) and the medulla and spinal cord (H) reveal extreme cellular loss and cavitation.







Fig. 3. Microscopic evaluation of the brain and spinal cord (H & E stain 9 μ m sections). Specimens include, (A) a cortical gyrus (×100) and (B) cortical white matter (×400) revealing laminar necrosis and gemistocytic astocytosis, respectively. Cerebellar folia (C) reveal Purkinje cell loss (×100). The brain stem (medullary olive) (D) and spinal cord (corticospinal tract) (E) reveal gemistocytic astrocytosis and axonal loss, respectively (×400).

including severe brainstem autolysis. Dooling and Richardson [2], in reporting a peculiar movement disorder in an 11-year-old child surviving 13 weeks after strangulation, described extensive basal ganglia cavitation, with sparing of the thalamus, brainstem and cerebellum. Watershed abnormalities and neuronal loss in the hippocampus was described but no ventriculomegaly was seen. No abnormalities in glial elements nor myelin loss was described. Parisi et al. [8], in a brief report, described reabsorbative processes, macrophage infiltration, active necrotic decomposition, recanilization of cerebral vessels and revascularization of outer cortical layers in a patient brain dead for 74 days. Because of softening of the intracranial contents, the brainstem could not be adequately examined. Ginsberg et al. [3], in three patients sustaining prolonged somatic survival following global ischemia/hypoxia, reported that the external appearance of the cerebrum and the cut surface of the thalamus and brainstem were normal. The basal ganglia were necrotic in one case and laminar necrosis of the cortex and hippocampus was present in another case.

A striking microscopic feature seen in the present case was the pronounced gemistocytic astrocytosis present throughout the cerebrum and brainstem. Although gliosis is a regular feature of focal cerebral infarction [14], glial reactivity is said not to occur as a chronic process in brains subjected to global hypoxia/ischemia. In a classic review by Kjeldsberg [15], the lack of a true glial reaction in severely hypoxic/ischemic brains is emphasized. Parisi et al. [8], noted only focal accumulations of lipid laden macrophages, plasma cells and lymphocytes in subpial tissue. White matter exhibited only a few polymorphonuclear leukocytes, rare macrophages and karyorrhectic debris. Similar findings were observed by Ginsberg et al. [3] where no gemistocytic astrocyte reaction could be ascertained in three cases. Garcia [16], however, noted that reactive astrocytosis can occur. The degree of astrocytosis, is suggested by a recent series [9], to be directly dependent upon the interval between insult and brain death ranging from 1 h to 13 days in 190 autopsies.

CT examination of this patient's brain showed a radiologic progression of hypoxic/ischemic changes. The initial study performed 4 h after the insult revealed only a mild degree of cortical swelling whereas the study 48 h later showed bilateral basal ganglia lucencies and considerable cortical swelling. The correlation of these early CT findings in such injuries to pathological specimens has only recently been verified by Tippin et al. [17]. Low densities in the basal ganglia and watershed cortex and white matter as well as diffuse swelling of the hemispheres with loss of gray-white matter differentiation has been discussed [18]. Based on these results, the early diagnosis, by radiographic methods, of diffuse hypoxia/ischemia was proposed. The third CT study of the present case illustrated severe, diffuse encephalomalacia and ventriculomegaly which correlated well with the final autopsy results. Although CT abnormalities have been demonstrated in patients in a vegetative state, radiographic studies are often normal even 3 weeks following an injury [18]. In fact, lack of late CT manifestations of diffuse hypoxic/ischemic damage, despite angiographic evidence of arrested cerebral circulation, has been reported in six patients by Radberg and Soderlundh [19]. The results of the present case, however, indicate that early CT abnormalities may not only be useful in the rapid diagnosis of global ischemia/hypoxia, but also for predicting final clinical outcome [17].

Although debated, several investigations indicate that EEG activity does not always correlate with outcome, nor does it differentiate between brain dead patients or those persisting in a vegetative state [20,21]. Several cases of patients declared clinically brain dead have demonstrated low voltage EEG activity [7]. Conversely, Higashi et al. [16] described isoelectric EEGs in three patients persisting in a vegetative state. Our patient demonstrated isoelectric EEGs for nearly 5 months yet by current criteria was not brain dead.

There have been several attempts to correlate brain death or vegetative existence to both neuropathological changes and the neurological exam [4,7]. These studies have met with limited success because the evidence from such reports describe a continuum of changes and not a rigid classification system. This patient certainly met the neuropathological criteria for brain death, as described by Black [22] and met the CT and EEG based criteria as well. However, he did not meet clinical conditions for brain death because he had persistent brainstem reflexes and respiratory efforts [23]. He existed in a persistent vegetative state for nearly 5 months with the resultant emotional and economical consequences. Long-term mortality rates for patients in this condition range 73-98% in recent surveys [4,13]. As illustrated in the present case, little functioning nervous tissue is required to sustain this type of existence. Although considerable clinical variability in neurological function is evident, the present case clearly demonstrates the artificial nature of rigid boundaries between brain death and vegetative patients. The ethical and moral issues regarding the care of such patients are numerous and complex [24,25].

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