Symmetric Brainstem Necrosis in an Adult Following Hypotension: An Arterial End-Zone Infarct?

J. Craig Jurgensen, M.D.,* Javad Towfighi, M.D.,† Robert W. Brennan, M.D.,* and William H. Jeffreys, M.D.

SUMMARY A 44-year-old woman with prolonged coma and hypotension following drug overdosage developed bilateral hemorrhagic infarcts in the dorsolateral brainstem. The regional distribution of these paired lesions corresponds to the area of confluence of penetrating arteries in the brainstem. It is suggested that under exceptional circumstances brainstem arterial end-zones may be vulnerable to anoxic-ischemic insult.

Stroke Vol 14, No 6, 1983

THE STRUCTURAL ALTERATIONS of cerebrum and cerebellum following anoxia-ischemia have been studied extensively in man and in experimental animals. Selective vulnerability of particular regions within the cerebrum and cerebellum has been attributed in part to vascular anatomic factors such as arterial boundary or end-zone distributions. In contrast, studies of the topography of anoxic-ischemic involvement in the brainstem suggest that lesions are topistic; i.e., selective for specific neuronal structures. This pattern of selective vulnerability in brainstem has been attributed to metabolic factors such as the higher blood flow and metabolic requirements of these nuclei and their high level of lactic acid content during anoxia. The influence of vascular anatomic factors in the distribution of anoxic-ischemic lesions in brainstem has been given little attention.

A patient with bilateral symmetric columnar necrosis of the brainstem associated with prolonged hypotension is reported. Evidence implicating vascular anatomic factors in the pathogenesis of these brainstem lesions is reviewed.

Case Report

A 44-year-old woman was found unresponsive at her home. Her blood pressure was unobtainable and respirations were irregular and shallow. She had a past history of epilepsy and had been under treatment with phenytoin 300 mg and phenobarbital 45 mg daily for many years through her family physician. She had also taken chlorpromazine 75 mg daily for a chronic schizophreniform illness. From the circumstances of her discovery, and the clinical observation of early gangrene in one upper extremity it was deduced that she had lain unresponsive for many hours, possibly several days in all. On arrival to a local Emergency Room, treatment for presumed drug overdose was instituted including endotracheal intubation and assisted ventilation. Physical examination revealed a brachial blood pressure of 60/40 mm Hg, pulse rate 32 per minute, rectal temperature 29°C. She was unresponsive to sound, or painful stimulation. There was a superficial pressure sore on the left hip, and gangrene of the left hand. She had spontaneous, nonrhythmic eyelid blinking, random and conjugate roving eye movements lateral, and pupils which were equal, mid-position, round and unreactive bilaterally. Corneal stimulation elicited reflex blinking. The neck was supple. Extremities were flaccid to passive movements and all deep tendon reflexes were absent. Plantar responses were unelicitable. Toxicology studies demonstrated the presence of chlorpromazine and phenytoin in therapeutic levels, and phenobarbital at a toxic level (72 µg/ml). Other laboratory abnormalities on admission included a glucose of 560 mg/dl, BUN 42 units, Creatinine 3.4 mg/dl, Creatine phosphokinase 2288 units. The platelet count was reduced to 86000/mm³. The PT was 77 sec., and PT 19.7 sec., consistent with a consumption coagulopathy. A cerebral CT scan was within normal limits. Despite aggressive treatment with intravenous fluids and Dopamine, and correction of hypothermia, she remained hypotensive for the first three days of hospitalization. With institution of hemodialysis, the barbiturate level fell to 22 µg/ml, with no significant improvement in her condition. She re-
remained unresponsive to pain, with flaccid extremities. Corneal reflexes persisted, and pupillary light reflexes returned. An EEG demonstrated generalized low voltage activity. On the 11th hospital day she developed intermittent generalized seizures, a temperature of 38.5°C, and clinical and radiographic evidence of pneumonia. She expired on the 11th hospital day, in the setting of sudden bradycardia and irreversible shock.

Post-Mortem Examination

General pathology findings included a severe necrotizing tracheitis, bilateral bronchopneumonia, and ischemic enterocolitis. The most significant neuropathologic findings were large, well-defined, bilateral, symmetric areas of hemorrhagic necrosis in the dorso-lateral aspects of the brainstem (figs. 1 and 2) and claustrum (fig. 3). In the brainstem, the lesions appeared as two axial columns or cylinders, extending continuously from the lower segment of the pons to the caudal part of the medulla. Their largest diameter (0.6 cm) was in the medulla and they appeared to join caudally (fig. 2). Three other hemorrhagic but asymmetrically located lesions of about 0.5 cm were found in the right inferior parietal gyrus, left middle frontal gyrus, and just lateral to the left lateral geniculate body. In addition to the above, a well-defined round nodule of about 1 cm was present in the left middle temporal gyrus. Intracranial cerebral arteries including the vertebrobasilar system had a minimal atherosclerosis and were patent. The circle of Willis was complete and roughly symmetric. The spinal cord was not examined.

Microscopic examination of the hemorrhagic lesions disclosed necrosis, containing eosinophilic neurons, axonal spherules, macrophages and reactive astrocytes. This was consistent with a one- to two-week old infarct. A more recent hemorrhage was noted in the periphery of the necrotic areas (figs. 4 and 5). The necrotic columns in pons included the region of the sensory nuclei and tracts of trigeminal nerves as well as their motor nuclei. In medulla the region of cuneate nuclei and fasciculi, nuclei and spinal tracts of the trigeminal, solitary nuclei and tracts, and a portion of the internal arcuate fibers were involved. The cerebellum revealed a modest, diffuse loss of Purkinje cells and Bergmann gliosis. The left temporal lobe nodule proved to be a ganglioglioma. No evidence of conventional boundary zone infarction or of diffuse hypoxic changes were found in cerebral cortex or hippocampi. Basal ganglia and thalami were normal. Brainstem nuclei not included in the infarcts were unaffected except for the inferior colliculi which showed partial neuronal loss and astrocytosis.

Discussion

The significance of this case lies in the most unusual distribution of cerebral lesions in this hypotensive, hypothermic patient, i.e. bilateral columnar necrosis of brainstem. Review of clinical and experimental material dealing with global cerebral hypoxia due to cardiac arrest or hypotension indicates that the most vulnerable neural structures in adults are cerebral and cerebellar cortices. The pathology may be in the form of selective neuronal loss, in the form of boundary-zone infarcts or as a combination of the two processes. In children and young adults, and in experimental animals, deep cerebral structures and brainstem may be involved also. Occasionally, the impact of anoxic-ischemic necrosis has been virtually restricted to brainstem, thalamic nuclei and spinal cord. The brainstem structures most susceptible to anoxic-ischemic injury in humans include: inferior colliculi, inferior and superior olives, oculomotor nuclei, vestibular nuclei, nucleus solitarius, trigeminal nuclei, nucleus ambiguus, reticular zone of the substantia nigra, brainstem reticular formation, pontine nuclei, and nucleus cuneatus and gracilis. The vulnerability of these particular structures to anoxia has been attributed to various factors including peculiarities in the metabolism of the neurons which comprise those nuclei, regional variation of blood flow, and regional accumulation of lactic acid. The localizations of necrotic regions in the brainstem of the present case includes some of the above mentioned nuclei and tracts e.g., trigeminal, solitarius, and gracile tracts and nuclei. This pathologic observation cannot, however, be explained solely on the basis of the differential susceptibility of neurons because the necrotic regions extend well beyond the nuclei to contiguous regions of white matter.

Studies of vascular anatomy in the brainstem have shown that numerous branches leave the vertebrobasilar artery to penetrate the median, paramedian, and lateral zones. These arterial zones of supply are longitudinally oriented along the axis of the brainstem. Penetrating vessels supplying these areas do not anastomose with others in adjacent areas. When one compares this vascular pattern of brainstem to the localization of the lesions in the brainstem of our patient, the lesions correspond closely to the regions defined by the convergence of distal fields of distribution of the penetrating arteries. One may speculate that the prolonged, severe hypotension in this patient thus resulted in symmetric infarction in the most distally perfused regions, in a pattern analogous to the arterial end-zone pathology found in other subcortical structures. The hemorrhagic nature of these necrotic areas may be explained partly on the basis of coagulopathy documented by laboratory findings in this patient.

The absence of the conventional hypotensive lesions of cerebral hemispheres in this patient is quite intriguing and cannot be readily explained. It is conceivable that the influence of phenytoin and phenobarbital and...
of marked hypothermia protected the cerebral cortex selectively from the usual anoxic-ischemic changes. A lower cerebral metabolic rate might also have contributed to the relatively long survival of the patient, thus allowing brainstem injury to progress to massive tissue destruction.

Acknowledgement
We are grateful to Dr. John J. Moran for providing us with the autopsy material. We thank Mr. Alan Parker for technical help and Mrs. Peggy Coulter for her secretarial assistance.

References
Symmetric brainstem necrosis in an adult following hypotension: an arterial end-zone infarct?

J C Jurgensen, J Towfighi, R W Brennan and W H Jeffreys

*Stroke*. 1983;14:967-970
doi: 10.1161/01.STR.14.6.967

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/14/6/967

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/