Histopathology of transitory traumatic paraplegia in the monkey

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The microscopic appearance of the primate spinal cord within a 4-hour interval following the delivery of a direct force sufficient to produce a transitory paraplegia was investigated by light microscopy. The resulting hemorrhagic lesion involved primarily the central gray matter and was attributed to the direct effect of the trauma on the vessels in the gray matter with a consequent impairment of blood supply to the injured area. Chromatolysis, vacuolation, and alterations in cytoplasmic density and stainability were observed within the neurons. The edematous changes in the white matter, which were more marked in the internal layers relative to the external layers, appeared minimal and explain in part why the paraplegia was transient.

KEY WORDS: spinal cord injury • transitory paraplegia • spinal contusion

MOST of the information regarding the alterations in spinal cord morphology following trauma has been derived from postmortem material obtained at varying periods after injury from patients who were rendered permanently paraplegic. Consequently, little is known concerning the acute changes that occur in the spinal cord minutes and hours after injury. The importance of the early post-traumatic period has been shown experimentally by demonstrations of the efficacy of various forms of treatment in preventing what otherwise would have been a permanent paraplegia. Furthermore, although the work of Schneider and Scherm has done much to suggest possible mechanisms, still less is understood about the pathological processes occurring in the spinal cord of patients who initially incur a neurological deficit after an injury and later recover some or all of their functions.

To clarify this situation, we have sought in the present investigation to delineate the acute morphological changes that occur in the spinal cord of the primate during a period of 4 hours following the application of a force sufficient to produce a transient paraplegia.

Materials and Methods

We anesthetized 27 adult Rhesus monkeys (Macaca mulatta) with sodium pentobarbital (22 mg/kg) and performed a laminectomy that exposed the spinal cord at the T-10 level. Using the model initially devised by Allen and further refined by Albin, et al., we applied direct trauma in 18 animals by dropping a 20 gm weight a distance of 15 cm through a Teflon tube oriented perpendicularly to the cord. At the bottom of its descent the weight struck an impounder resting on the intact dura mater, thereby delivering a 300 gm-cm force to the spinal cord.
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The animals were divided into five groups, and the traumatized segments of cord were removed at 5 min, 15 min, 30 min, 1 hr, and 4 hrs post-contusion. Following removal, the segments were fixed by immersion in 10% formalin and then stained with hematoxylin and eosin, Nissl, and luxol fast blue and periodic acid-Schiff (PAS). The latter two stains were used to study the neurons and the myelin sheaths more closely. In nine animals the laminectomy was done but the spinal cords were not traumatized; these served as a control group.

An additional four animals were traumatized but allowed to survive for a period of 6 months. During this time frequent examinations of motor and sensory function were performed.

**Results: Chronic Group**

Immediately after the effects of the anesthesia had dissipated, all four traumatized animals in the chronic group were noted to have a complete motor and sensory paralysis involving the lower extremities. Within 12 hours, isolated movements of the toes were present. By 24 hours, weak placing responses and grimacing with painful stimuli were observed. Between 7 to 10 days, all of the animals were able to move about their cages readily, and at 6 months the animals were indistinguishable from unoperated animals.

**Results: Microscopic Observations**

**Blood Vessels**

Five minutes following trauma the appearance of the spinal cord was not strikingly altered from that of the normal cord. What changes occurred involved the less muscular vessels surrounding the central canal, which were noted to be distended but intact. Within the lumina, formed elements and serous fluid were observed but no erythrocyte degeneration or thrombus formation was apparent. Although the more thick-walled vessels in the area of the central canal contained abundant erythrocytes, they were not distended.

At 15 minutes, isolated ruptured thin-walled vessels with leakage of erythrocytes into the perivascular spaces were observed (Fig. 1) within the central gray matter.

Within 30 minutes, erythrocytes and serous fluid were noted in discrete collections in the perivascular spaces and extending into the surrounding parenchyma. The distribution of these alterations again was mainly in the area of the central canal but included the dorsal horns as well (Fig. 2).

By 1 and 4 hours, the initially discrete perivascular hemorrhages had begun to coalesce. These changes were now no longer...
confined to the area of the central canal and the dorsal horns but were evident throughout the gray matter. Accompanying the extravasation of blood into the parenchyma and the congestion within their lumina, many vessels displayed increased cellularity and homogenization of their walls. These degenerative changes were especially marked at 4 hours.

**Neurons**

At 5 minutes, the neurons within the gray matter retained their normal appearance with centrally placed nuclei and chromatin being evenly distributed throughout the cytoplasm. As time elapsed the cell membranes became more angular and were separated from the surrounding neuropil by pericellular clear spaces (Fig. 3).

In those sections stained by Nissl's method, the neurons exhibited two changes. By 1 and 4 hours the chromatin became powdery in appearance, and in the later sections the proportion of cells in which the chromatin stained poorly increased. In other neurons the chromatin, while retaining its stainability, was displaced by intracytoplasmic vacuoles. Less frequently vacuoles were noted within the nuclei. Similarly the neurons in the hematoxylin and eosin stained sections demonstrated alterations ranging from those cells in which the cytoplasm was eosinophilic with darkly basophilic nuclei to those in which the cell bodies were shrunken and in which there was loss of stainability forming "ghost cells." These changes were most widespread at 4 hours (Fig. 4).

**Axon Cylinders and Myelin Sheaths**

Accompanying the central changes, alterations in the white matter were also observed. Within 30 minutes, the white matter assumed a lacunar honeycombed appearance produced by a clear space that separated the myelin sheath from the axon cylinder. This change in which the thickness of the myelin sheaths and the diameter of the axons was not increased was present throughout the white matter (Fig. 5).

In later sections, the myelin sheaths within the internal layers of white matter bordering the central gray matter became pale-staining and their contours more irregular. Random axon cylinders within these distorted myelin sheaths were enlarged and occupied almost the entire space within the myelin sheath. At 4 hours the peripheral white matter retained its honeycombed appearance without exhibiting the degenerative changes seen more centrally.

**Discussion**

This study reaffirms the utility of the apparatus initially devised by Allen and further developed by Albin, et al., for producing and for quantitating experimental spinal cord trauma. The fact that we were unable
to produce a permanent paraplegia in our chronic animals with a blow of 300 gm-cm to the spinal cord, as others have, attests to the need for testing one's particular device with chronic preparations before drawing broad conclusions from acute experiments.

Although the experimental model employed in the study does not duplicate the injuries seen in clinical practice, there is a considerable similarity between the resulting lesion and those observed by Wolman and by Hughes in human material. This fact combined with the observation that what is seen microscopically in both instances is a function of the period of survival as well as the type and the degree of trauma would seem to have important implications for the treatment of these injuries.

The most striking observation in the present study is the evolution of the hemorrhagic lesion within the central gray matter. The progression from comparatively normal-appearing vessels initially to degenerated vessels within 4 hours, accompanied by congestion within the vascular lumina and extravasation into the surrounding parenchyma, would seem to indicate the direct effect of trauma on the vessels within the cord. The alteration in vascular permeability that results, as well as the demonstration of ruptured vessel walls as early as 15 minutes post-contusion, suggests that these are important mechanisms for the extravasation seen in contrast to diapedesis or rupture at a more distant point with migration of formed elements along perivascular spaces.

The alterations that occur in the neurons reflect as well the direct effect of trauma and the impairment of the blood supply to the injured area. The early chromatolytic changes seem to result from the traumatizing force itself rather than a disruption of axons, in which case one would expect to see these alterations at a later time. The intracytoplasmic vacuolation, the eosinophilic staining of cytoplasm, and the formation of "ghost cells" are similar to what Rand and Courville noted in cerebral contusion and are consistent with ischemia and necrosis of neurons. Although intracytoplasmic vacuolation appeared prominent, the relative frequency of each of the changes could not be determined. This was felt to be due to the fact that multiple processes were acting on individual neurons simultaneously.

The edematous changes occurring in the white matter and persisting in the periphery of the white matter were similar to those observed by Scheinker in cerebral trauma. The absence of degenerative changes in the periphery may be explained by the persistence of intact vasculature from which the external layers of white matter derive their blood supply. These findings in the white matter may also explain why the paralytic effects of an injury of this severity are transitory. With greater injury the changes in the peripheral white matter may be as severe as those in the more central white matter; however, this is yet to be determined.

The greater vulnerability of the vessels within the central gray matter in contrast to those in the white matter has been explained on the basis of their density within the gray matter and the absence of firm supporting tissue. In addition, other factors may be operative, such as the orientation of the vessels within the cord and/or whether they are elongated and narrowed or shortened and widened by the traumatizing force, as demonstrated by Brieg, et al. The occurrence of hemorrhages initially in the area of the central canal indicates that the veins that arise near the center of the cord, as shown by Krogh, are most susceptible to trauma al-
though the capillary bed within the gray matter is of uniform density. The segment of the microvasculature most susceptible to direct trauma and the probable mechanism by which injury of the microvasculature occurs have been reported.

It appears from the findings of this investigation that direct trauma to the spinal cord, sufficient to result in a transient paraplegia, affects the central gray matter more severely than the surrounding white matter. Consequently, there is only a temporary impairment in the conduction of ascending and descending impulses.

Summary

Twenty-seven adult Rhesus monkeys were subjected to direct trauma at the T-10 level. In the chronic group of animals, recovery from their initial complete sensory and motor paraplegia commenced within 12 hours and was complete within 6 months. A light microscopic study of the injured spinal cord in the acute group of animals showed pathological changes which were attributed to the direct effect of the traumatizing force and to the impairment of the blood supply to the injured area. The less marked alterations occurring in the white matter, in contrast to the hemorrhagic changes in the gray matter, seem to explain the transient nature of the paraplegia.

References


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