ISCHEMIA OF THE SPINAL CORD
AN EXPERIMENTAL STUDY*
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CAVITATION of the spinal cord has been reported in association with many different disease processes. There is increasing evidence that many of these secondary cavitations are produced by spinal cord ischemia. While the etiological sequences leading to spontaneous syringomyelia remain more obscure, some evidence has accumulated that they too involve vascular factors.

As early as 1887 Joffroy and Achard reported spinal cord cavitations in cases of hypertrophic pachymeningitis which they felt were caused by venous stasis and arterial thrombosis. Camus and Roussy made a similar report in 1914. More recently Lubin described spinal cord cavitation in cases of adhesive spinal arachnoiditis. Lichtenstein ascribed cavitations associated with Arnold-Chiari malformations to compression of the vertebral arteries and venous stasis.

Experimental work supports the vascular etiology of some cavities. Tauber and Langworthy produced spinal cord cavitation in cats by ligation of the anterior spinal artery. Several authors have produced spinal cord cavitations secondary to experimental arachnoiditis. Such cavitations were studied by McLaurin et al. who agreed with previous investigators that the lesions result from spinal cord ischemia. Their paper includes an excellent review of the literature on this subject.

The present investigation is intended to establish more clearly the nature of lesions produced by uncomplicated spinal cord ischemia. Special attention was given to avoid changes caused by surgery and other non-vascular factors.

MATERIALS AND METHODS

In all experiments, laminectomy was conducted under strict aseptic conditions in the mid-thoracic spine under pentobarbital sodium anesthesia. Healthy adult mongrel dogs weighing from 8.0 to 16.0 kg. were used.

Preliminary experiments showed that interruption of the superficial

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vessels of the spinal cord either by tearing, ligation, or coagulation produced so much ancillary surgical damage that clear-cut ischemic changes could not be delineated. Likewise, ligation of the anterior spinal artery alone or combined with multiple intradural root section—although resulting in demonstrable neurological deficits—resulted in a considerable amount of undesired scarring. Only when the dura mater was not opened were the histological changes secondary to careful surgery found to be minimal. Efforts were made to isolate the radicular blood vessels in the nerve root sleeves but such surgery again produced considerable scarring. It was therefore concluded that the radicular blood supply to the mid-thoracic spinal cord could best be interrupted by sectioning of the entire nerve root along with the blood vessels. Animals prepared by the section of from 1 to 4 sets of adjacent nerve roots showed either no neurological deficits or such deficits were extremely transient. However, this material served as good control for the changes induced by nerve section alone. Animals with 5 sets of adjacent nerve roots sectioned frequently showed transient neurological deficits. When the roots from 6 adjacent spinal cord segments were sectioned there was temporary paraplegia which on occasion proved to be replaced by paraparesis. This level was then taken as the basis for the present study.

A total of 42 dogs were prepared by the section of 6 adjacent pairs of spinal roots extradurally. These pairs usually included T6 through T11. Of these, 27 sur-

Fig. 1A. Cross section of spinal cord at T6 (hematoxylin and eosin X38) from animal subjected to extradural radiculectomy of T5, T6, T7, T8, T9, and T10. Note especially the loss of dorsal horn cells and the generalized gliosis of the gray matter.
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vived adequately for good postmortem studies including removal and examination of the spinal cord. These animals were sacrificed between 1 to 4 weeks after the initial surgery. From these the spinal cords of 16 were selected for careful histological studies. Each of these spinal cords was studied at many levels above and below the laminectomy as well as at the point of surgical attack. After proper fixation of the entire central nervous system, tissues were prepared in the routine manner and were sectioned and stained by various methods. Hematoxylin-eosin was used routinely, and in selected sections the gold chloride sublimate method for astrocytes and the Gros-Schultze method for axis cylinders were used. Occasional sections were stained with Sudan Black.

RESULTS

Clinically, the animals with ligation and section of 6 adjacent thoracic nerve root pairs with the accompanying blood vessels showed a band of loss of sensation corresponding to the nerve roots sectioned. In addition there was a caudad sensory loss of pain sensation which often reached up as far as the thoracic segments, especially in those animals showing paraplegia. In animals showing only paraparesis and inco-ordination there was a sensory

Fig. 1B. Area outlined in Fig. 1A magnified ×300 to demonstrate more clearly the loss of dorsal horn cells.
sparing in the caudal area which usually was present up to the lower lumbar dermatomes. Most of the animals showed these changes transiently, with the evidences of long-tract impairment being gone in 1 to 2 weeks.

Histologically, the most consistent and widespread change in all cases receiving microscopic examination was the loss of dorsal horn neurons, those of Clark's column being affected most severely. Between the area of neuron loss and the less disturbed anterior horns there often was found a zone of

![Cross section of spinal cord at T9 (hematoxylin and eosin X155). Section taken 10μ from point where central canal with otherwise intact ependymal lining communicates with cavity in the dorsal columns beyond the top of this microphotograph.](image)

incomplete neuron damage characterized by fragmentation, satellitosis, and neuronophagia. The coagulation and sclerotic type of nerve cell change was observed less frequently. This pattern of nerve cell damage seemed to be affected very little by differences in chronicity of the lesions. It is of particular interest that in the few experiments that failed to produce cavitation, the only clear-cut pathological change was the loss of dorsal horn neurons (Figs. 1 A and B). In most experiments the neuron loss extended several spinal cord segments above and below the region of experimentation.

Much less definite than the neuron damage, but coexistent with it, was
a mild generalized gliosis which involved the gray matter diffusely. This was seen best in the gold chloride preparations.

Cavitation was seen in 12 of the 16 spinal cords studied histologically. Most of these cavities were small, only one being noted grossly. The midline gray matter dorsal to the central canal was always involved at some level of each cavity. The larger cavities sometimes extended from this point along the dorsal horns, often involving the adjacent white matter of the posterior or lateral funiculi. Communication of the cavity with the central canal was a frequent finding (Fig. 2), but no attempt was made to demonstrate this in all cases.

Reactive changes in the interstitial neural elements were of mild degree and late development. Hematoxylin-eosin sections failed to show definite glial hyperplasia in the vicinity of the cavitation. Gold chloride preparations in some of the more chronic cavities demonstrated a characteristic change in the astrocytes bordering the cavity. These astrocytes had few processes but they were greatly hypertrophied and extended toward and into the cavity. In some places, the wall of the cavity appeared to be a palisade of these hypertrophied processes (Figs. 3 A and B). Gitter cell response occurred when the cavity involved the white matter with actual destruction
of the traversing nerve fibers (Figs. 4 A and B). In some cases the cavity extended medially and posteriorly for a short distance into the dorsal funiculus without evidence of nerve fiber destruction. In such instances, no significant phagocytosis was present (Fig. 1).

The central canal of some specimens was greatly enlarged and definitely abnormal in the region of ischemia. In most cases, however, the enlargement

![Fig. 3B. Area outlined in Fig. 3A magnified X300, demonstrating the tendency to palisading of the hypertrophied fibers of the astrocytes bordering the cavity.](image)

was only slight and could not be considered pathological without further study.

By comparison, the experiments involving intradural surgery showed that the leptomeninges were markedly fibrotic and often were incorporated in the dural scar. When the ischemia was produced by extradural means, the leptomeninges showed only minimal fibrosis, and adhesions were absent. In the latter experiments, considerable condensation of connective tissue
Fig. 4A. Cross section of spinal cord at T8 (hematoxylin and eosin ×50) showing cavitation in the white matter in which there is active phagocytosis with many gitter cells.

Fig. 4B. Area outlined in Fig. 4A magnified ×800.
was seen about the subarachnoid vessels, but the blood vessels themselves showed little histological change except for mild endothelial hyperplasia.

**DISCUSSION**

Of the methods that appeared to be available for obliteration of part of the blood supply to the spinal cord, none was capable of producing completely predictable lesions. Unpublished data from this laboratory indicated that occlusion of the aorta for approximately 35 minutes often produced paraplegia which was irreversible. Periods less than this seemed to produce changes which were extremely transient and most frequently could not be detected neurologically in the dog. Injection of particulate matter either produced no lesion whatever or resulted in profound and severe neurological damage which usually brought on the demise of the animal. From injection studies of the vasculature of the spinal canal of the dog, it appeared that the blood supply to the spinal cord was highly variable. If there were a single characteristic feature of the spinal cord in the midthoracic region, it centered about the fact that one or more of the radicular arteries could or did serve as the dominant source of blood. The most obvious course to follow in interruption of this supply was to attack these radicular vessels directly. The mere opening and closing of the dura mater with manipulations that tend to disrupt the arachnoid in itself produces considerable scarring. In the hands of the inexperienced operator, this scarring can be extensive indeed. In one of the preliminary animals when the operation was stopped because it was felt that trauma might have been produced inadvertently, cavitation similar to that previously reported was observed. Since these vessels are isolated with great difficulty, it was concluded that the best approach would be to interrupt them by section of the whole nerve root within the sleeve extradurally. The question then arose as to whether the neural impairment imposed by such generous sectioning of both anterior and posterior nerve roots over an extensive segment of the spinal cord might not in itself result in severe enough neurological impairment that the effect of interruption of the blood supply would be obscured. The variability in neurological deficit found in the various animals would speak rather definitely for differences in vascular supply rather than in the effect of loss of neurons, since the latter would tend to be rather constant. The extension of the effects beyond the limits of the gray matter would also speak strongly for the effects being vascular rather than direct neuronal.

In these experimental ischemic lesions of the spinal cord the most consistent and widespread histological change was loss of neurons in the dorsal horns. This effect usually extended several spinal cord segments above and below the region of experimentation. The neurons of Clark’s column were most susceptible to this change. Coexistent with this pattern of neuron loss was a mild gliosis which diffusely involved the gray matter in the ischemic portion of the spinal cord. Usually associated with the neuronal damage was cavity formation in the midline gray matter dorsal to the central canal. The
cavitation was much more restricted to the level of most severe ischemia than were the neuronal changes. The usual cavity appeared to be a passive separation of the tissue reaction. This type of cavity seemed to result from a spatial rearrangement of the tissue subsequent to shrinkage of the dorsal horn gray matter. This passive form of cavitation may be considered the same process as that leading to "hydrocephalus ex vacuo" in the brain. This type of cavitation was usually found in dogs whose functional impairment was mild.

In 3 of the cavitations studied histologically there was actual necrosis of the interstitial as well as the neural elements in the dorsal gray matter and adjacent white matter. These cases presented the usual picture of myelomalacia with active phagocytosis. This seems to represent a more severe ischemia of a sufficient degree to cause necrosis of the traversing long tracts. In conformity to this view, the 3 dogs with this type of lesion had severe and permanent functional impairment of the long tracts as demonstrated by paraplegia. These cases demonstrate that in more severe degrees of spinal cord ischemia myelomalacia as well as shrinkage of the gray matter contribute to the production of central cavitation.

The dominant role of neuron loss in spinal cord ischemia provides experimental support for the emphasis on this type of pathological change in some more generalized diseases of the central nervous system. Scholz reported that loss of "topistic units" of ganglion cells in the brain may be the dominant pathological change and of equal significance to encephalomalacia in some cases of cerebrovascular disease. In the present study the pattern of neuron loss is probably more dependent on circulatory factors than individual differences in susceptibility of neuron types to ischemia.

A consistent feature of the cavitation was its point of origin in the midline gray matter dorsal to the central canal. Whether the vascular interference was directed at the surface vessels, the anterior spinal vessels, or multiple radicular vessels had no effect on the point of origin. In 1 case, a typical small cavity was produced by merely opening and closing the dura mater. Cavitation in this region has also been seen in other experimental spinal cord injuries such as concussion.

While cavitation in the region just dorsal to the central canal is an early histological change in spinal cord ischemia, it does not appear to represent insufficiency of arterial blood supply from any particular vessel. It seems more likely that this lesion results from an impairment in the general circulatory state of the spinal cord. Interference with venous drainage may be the responsible factor. The central portion of the spinal cord is inherently devoid of venous collateral facility. Within the central region, the ventral gray matter is relatively well drained by large veins traversing the anterior median fissure. The posterior gray matter therefore appears most vulnerable to venous insufficiency. Venous blood from this area must drain through the entire substance of the spinal cord to reach the large surface veins. In a state of edema compressing all vessels within the spinal cord substance it
seems reasonable that venous drainage from the posterior central region would be most seriously impeded. Venous insufficiency is also suggested by involvement of the gray matter even in cases in which necrosis of the interstitial elements occurs. In arterial occlusions the interstitial elements of the gray matter are relatively resistant to necrosis.

There is striking similarity between these spinal cord cavitations and those produced by experimental arachnoiditis. The conclusion that vascular factors account for such cavitations is supported by the present investigation. Most of the spinal cord cavitations reported by these investigators, however, suggest a more severe degree of ischemia with necrosis of the long tracts and interstitial neural elements.

SUMMARY

The earliest histological change in mild spinal cord ischemia in dogs is loss of neurons in the dorsal horns. This is usually followed by shrinkage of the posterior gray matter with passive separation of the interstitial neural elements and cavity formation. In more severe degrees of spinal cord ischemia there is necrosis of the traversing long tracts and interstitial elements as well as the neuron loss. This produces a picture of myelomalacia with cavitation. Both types of cavitation involve primarily the central gray matter dorsal to the central canal, but may occasionally extend from this region into the adjacent white matter.

Venous insufficiency secondary to spinal cord edema may account for the pattern of neuron loss and the constant origin of cavitation in the dorsal gray matter. The reasons for this conclusion are discussed.

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REFERENCES